CLINICAL STUDY ON TREATMENT OF NON-ACUTE KNEE OSTEOARTHRITIS (KOA) USING ELECTRO-ACUPUNCTURE AT TOP TEN HIGHLY-RESEARCHED ACUPOINTS

By

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ABSTRACT

CLINICAL STUDY ON TREATMENT OF NON-ACUTE KNEE OSTEOARTHRITIS (KOA) USING ELECTRO-ACUPUNCTURE AT TOP TEN HIGHLY-RESEARCHED ACUPOINTS

YU, SHICHAO

Osteoarthritis (OA) is a common chronic, degenerative joint disease, involves multiple anatomical and physiological changes of joint tissues and bone regeneration characterised by cartilage degradation and subchondral bone sclerosis. This results in symptoms of OA such as pain, stiffness, swelling, deformation and limited joint movement, and is the main cause of disability. The most common OA is Knee Osteoarthritis (KOA) which is a degenerative joint condition that primarily affects the knee joints. It is the most common form of arthritis and occurs when the protective cartilage that cushions the ends of the bones in the knee joint gradually wears away, and prolongs fiction of the bear joint structure causing inflammation which leads to pain, stiffness, swelling, deformation and limited mobility. Knee joints are essential for weight-bearing, locomotion and various physical activities. The dysfunction of knee-joints due to KOA greatly impacts the normal life of patients and in serious and extreme cases, poses a danger to lives. This problem needs to be addressed as there is an

increased occurrence rate of KOA in both men and women, and the onset age is getting younger.

Modern medical treatment for KOA such as non-pharmacological treatment, pharmacological treatment and surgical treatment, have their advantages and shortcomings. Non-pharmacological treatments require high discipline by the patients and usually take longer time to remedy and recover; pharmacological treatments such as the use of non-steroidal anti-inflammatory drugs (NSAIDs), can temporarily relieve the symptoms but require long-term use and lack supporting evidence of long-term efficacy; and surgical treatment has certain therapeutic effects, but it is still an invasive therapy which often brings great physical, psychological and economic burdens to patients. In traditional Chinese medicine (TCM), there are various methods of treating KOA such as Chinese herbal, massage, cupping and acupuncture which are simple, easy to implement, and easy to be accepted by patients. Acupuncture is a commonly used treatment method for KOA and has the advantages of simplicity, no toxicity side effects, and is easily accepted by patients. One of the acupuncture methods is Electroacupuncture (EA) which combines traditional acupuncture and modern electronic medicine, has definite efficacy and high safety, and has been widely used in KOA clinical therapy.

In this research, the application of EA in KOA therapy has been studied and compared to other treatment methods to understand and determine its relevance and efficacy in improving the treatment, patient experience and worthiness of promotion in Malaysia and even, globally. The research study consisted of 3 parts - the questionnaire research, the literature research and the clinical research. In the questionnaire research, the application of TCM therapy methods in the treatment of KOA in Malaysian TCM clinics and hospitals was studied, analysed and compared with the situation in China. A questionnaire was designed surveying the age range of the patients and the TCM therapy methods for KOA, and was distributed to physicians in TCM clinics and hospitals in Malaysia and China. A total of 489 and 873 valid questionnaires were re-collected in Malaysia and China respectively. Based on the survey results, it was found that the onset age of KOA patients in Malaysia and China is concentrated between 50 to 59 years old which is in line with the characteristics of KOA where the high incidence rate is mainly in middle-aged and elderly people. The TCM methods commonly used in Malaysia vary such as Manual Acupuncture (MA) (81.60%), Massage (78.53%), Cupping (76.28%), Moxibustion (64.21%), Bloodletting (54.60%) and EA (48.26%). Contrarily in China, besides MA (93.13%), EA (84.19%) and Chinese Herbs (internal or external use) (80.53%) are frequently used for KOA treatment. The EA is widely used in China because of its precise curative effect and high safety, and has been incorporated into clinical pathways, second only to MA. The usage rate of EA in Malaysia is very low compared to in China and this trend could be due to the TCM physicians mainly focusing on non-invasive treatment methods such as Hot Compress Therapy, Scraping Therapy and Rehabilitation Treatment, which do not require deep knowledge and skills; and unified and standardised process when treating KOA and often rely on their familiarity with certain methods. Moreover, when evaluating clinical efficacy, it is mainly based on the patient's subjective self-perception and the physician's experience, lacking objective, standardized, and realistic evaluation criteria and systems.

In the literature research study, the TCM theory of acupuncture for KOA was reviewed and analysed. The criteria of acupoint selection and features of acupoint use for acupuncture in the KOA's clinical treatment were studied and examined in great detail based on literature search, data extraction and data analysis. The top ten high-frequency acupoints for acupuncture treatment of KOA were screened, identified and summarised; and provided a new and basic acupoint prescription for KOA, and to determine its suitability as a guide for clinical practice. The literature on randomized controlled trial (RCT) studies of acupuncture in the treatment of KOA over a defined period in the relevant databases of China National Knowledge Infrastructure (CNKI), Weipu Journal Full-text Database (VIP), Wanfang Data Knowledge Service Platform (Wanfang), China Biology Medicine disc (CBMdisc), PubMed and Embase were retrieved through computer and manual retrieval. After the data extraction was completed, the total number of occurrences of the acupoints used was counted and the number and rate of occurrences were used as indicators to analyse the frequency of use, channel tropism (the belongings to meridians), distance, locations of distribution, and the characteristics of acupoints (specific acupoint attributes). Statistical (descriptive) analysis of the relevant acupoints in the literature was conducted to explore the rules of acupoint selection and features of acupoint use in the treatment of KOA. The top ten highly-researched acupoints were specifically analysed.

Based on the 2,264 papers studied, 139 frequently used acupoints in the KOA treatment with acupuncture were screened out from the 12 main meridians such as Ren meridians, Du meridians, and extraordinary points (acupoints beyond meridians). The top 10 high-frequency acupoints by descending order are ST35 (Dubi), EX-LE4 (Neixieyan), GB34 (Yanglingquan), SP10 (Xuehai), ST36 (Zusanli), ST34 (Liangqiu), SP9 (Yinlingquan), EX-LE2 (Heding), SP6 (Sanyinjiao) and GB33 (Xiyangguan). The total frequency of use of 21 selected acupoints from the proximal part (at close range) of the lower limbs, especially at or around the knee joint, is 14,137 times with the rate of occurrence being 82.97%. The literature research study also revealed that the total usage frequency of the two meridians Stomach Meridian of Foot Yangming and the Spleen Meridian of Foot Taiyin.ST & SP is 9,053 times (about 53.13%) and ranked in the top two. The number of specific acupoints accounted for 55.40% of the commonly used acupoints in acupuncture treatment of KOA, and the Five-shu acupoints and the He acupoints were the most used. From this study, it was concluded that the acupoints selected for acupuncture treatment of KOA are mainly concentrated on the Spleen and Stomach Meridians, and lower limbs. Acupoints from the proximal part, along the meridian, and specific acupoints are mainly selected, and supplemented by the acupoints from the far part. Among the specific acupoints, Five-shu acupoints and He acupoints are used the most. The above-mentioned top 10 high-frequency acupoints can be used as a new basic acupoint prescription for acupuncture treatment of KOA as this new acupoint prescription can tonify the body's healthy energy while dispelling pathogenic factors, with the characteristics of combining differentiation of disease and syndrome. The combination of the selected 10 acupoints can have effects such as enhancing blood circulation, removing blood stasis, strengthening the spleen, eliminating dampness, dispelling wind and dispersing cold, promoting the circulation of Qi and stopping pain, nourishing Qi and Blood, strengthening tendons and bones and be prescribed with taking into account both the proximal and distal acupoints. The results of the subsequent clinical research based on this acupuncture prescription have also confirmed its effectiveness, and the new prescription can be used as a guide for clinical practice.

Upon identification of the top 10 highly-researched acupoints, the study proceeded with the clinical research study where RCT was used to validate the clinical effectiveness and to determine the scientific basis for the clinical efficacy of the acupoint prescriptions in the treatment of KOA. It is also important to explore the possible internal mechanism by which EA can treat KOA and improve its clinical symptoms. According to the result of sample size estimation and the ratio of 1:1:1, 207 eligible patients with KOA were randomly allocated into the Treatment Group (EA with the top ten highly-researched acupoints), Control Group 1 (Manual acupuncture (MA) with the top ten highly-researched acupoints), and Control Group 2 [Sham acupuncture (SA): MA with sham acupoints (the points does not belong to the main meridians and pain points)]. Each of the three groups will be treated with acupuncture once a day for 30 minutes each time. 6 times for a course of treatment, 2 courses in total, and take one day off between the two courses. Quantitative Score of Knee Osteoarthritis Symptom Classification (SKSC), Western Ontario and McMaster University Osteoarthritis Index (WOMAC), Lysholm Knee Score Scale (LKSS) and Visual Analogue Scale（VAS）were compared between the three groups before and after treatment. Venous blood was drawn from patients before and after treatment, and the changes in serum IL-1β and TNF-α were detected by Enzyme-Linked Immunosorbent Assay (ELISA). The data collected from the clinical research were analysed using SPSS 22.0 software.

From the results of the clinical research study, it was found that the three groups of patients were comparable in age, course of the disease, gender, and other baseline data, and the difference was not statistically significant ($P > 0.05$). The clinical effectiveness of the three groups of patients was as follows: the Treatment Group was 89.9%, the Control Group 1 was 75.4%, and the Control Group 2 was 5.8%; and there were statistically significant differences in the clinical effectiveness of the three groups ($\chi^2 = 113.690$, $P < 0.05$). There was no statistical difference ($P > 0.05$) among the three groups before treatment in SKSC, WOMAC, LKSS, VAS, IL-1β, and TNF-α content, and they were comparable; after treatment, the differences in the above indicators among the three groups were statistically significant ($P < 0.05$). The intra-group comparison of the above indicators of the three groups showed that the difference between the Treatment Group and the Control Group 1 before and after treatment was statistically significant, and all P values were < 0.05. It was also discovered that compared with before treatment, the scores of SKSC, WOMAC, VAS, IL-1β, and TNF-α in the Treatment Group and Control Group 1 after treatment were significantly decreased, and these scores in the Treatment Group were significantly lower than those in the Control Groups, and all P values were < 0.05; the LKSS score was higher than that before treatment, and the score in the Treatment Group was significantly higher than that in the Control Groups, and $P < 0.05$, indicating that the treatments of the Treatment Group and Control Group 1 were effective, and the Treatment Group was better than the Control Group 1. However, the above observation indicators of Control Group 2 did not change much, and with $P > 0.05$, there was no statistical difference, indicating that the effect of Control Group 2 before and after treatment was not obvious.

Based on the results of the clinical research study, it was concluded that both EA and MA combined with the top ten highly-researched acupoints have therapeutic effects on KOA. The two treatment methods both effectively improve clinical symptoms and signs of patients while reducing serum levels of inflammatory cytokines, including IL-1β and TNF-α. The EA yields better clinical efficacy compared to MA as it not only improves clinical symptoms but also enhances patients' quality of life. The acupuncture treatment at the points does not belong to the main meridians, acupoints and pain points, is not effective in treating KOA, and Sham Acupuncture does not exhibit a significant placebo effect, resulting in poorer clinical outcomes. Based on analysis, one of the proposed mechanisms of action for EA in treating KOA is its ability to regulate serum levels of IL-1β and TNF-α, ultimately reducing pro-inflammatory cytokines. The results of the clinical research study have validated the clinical efficacy and scientific basis of the acupuncture prescription used in the study, as well as the significant clinical efficacy of combining it with EA.

Based on the questionnaire, literature and clinical research studies, it is concluded that the combination of EA with the top ten highly-researched acupoints is a simple, convenient, and effective treatment method for KOA. It is also a safer, more efficient and easily implemented acupuncture treatment method for KOA, making it worthy of promotion in KOA treatment in Malaysia and can be extended to countries outside China.

Key words: Electro-acupuncture; Top ten highly-researched acupoints; Knee osteoarthritis; IL-1β, TNF-α; Clinical research; Mechanism research

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My previous years of clinical work have allowed me to accumulate some experience in clinical diagnosis and treatment and I have concluded that there are still some unsolved problems, especially those related to bone and joint diseases. I have also realised that my knowledge reserve and ability in the problems are limited, so, I have developed strong intent to further study and improve myself leading me completing my doctoral course study.

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APPROVAL SHEET

This thesis entitled **"CLINICAL STUDY ON TREATMENT OF NON-ACUTE KNEE OSTEOARTHRITIS (KOA) USING ELECTRO-ACUPUNCTURE AT TOP TEN HIGHLY-RESEARCHED ACUPOINTS"** was prepared by YU, SHICHAO and submitted as partial fulfillment of the requirements for the degree of Doctor of Philosophy (Chinese Medicine) at Universiti Tunku Abdul Rahman.

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SUBMISSION OF THESIS

It is hereby certified that **Yu, Shichao** (ID No: **19UMD05822**) has completed this thesis entitled "CLINICAL STUDY ON TREATMENT OF NON-ACUTE KNEE OSTEOARTHRITIS (KOA) USING ELECTRO-ACUPUNCTURE AT TOP TEN HIGHLY-RESEARCHED ACUPOINTS" under the supervision of Dr. Te Kian Keong (Supervisor) from the Department of Chinese Medicine, M. Kandiah Faculty of Medicine and Health Sciences, and Dr. Yap Yau Pin (Co-Supervisor) from the Department of Chinese Medicine, M. Kandiah Faculty of Medicine and Health Sciences.

I understand that the University will upload softcopy of my thesis in pdf format into UTAR Institutional Repository, which may be made accessible to UTAR community and public.

Yours truly,

Yu Shichao

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Yu, Shichao

DECLARATION

I, Yu, Shichao, hereby declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UTAR or other institutions.

Yu Shichao

Name: **YU, SHICHAO**

Date: **09 October 2023**

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LIST OF ABBREVIATIONS

ACL	Anterior Cruciate Ligament
AFM	Arthritis Foundation Malaysia
Ang-1	Angiopoietin-1
ANOVA	Analysis of Variance
BA	Balance Acupuncture
BGP	Bone Gla Protein
BLCP	Bloodletting Therapy via Channel Puncture
CBMdisc	China Biology Medicine disc
CGE	Catgut Embedding / Catgut Embedment in Acupoint
CMeSH	Chinese Medical Subject Heading
CNKI	China National Knowledge Infrastructure
COX	Cyclooxygenase
CRP	C-Reactive Protein
EA	Electro-acupuncture
EKAM	External Knee Adduction Moment
ELISA	Enzyme-Linked Immunosorbent Assay
ES	Emotional Scale
FGF	Fibroblast Growth Factor
FN	Fire Needle
HAQ	Health Assessment Questionnaire
HSS	Hospital for Special Surgery Scores
IL	Interleukin
ISOA	Index of Severity for Osteoarthritis
KN	Knife Needle
KOA	Knee Osteoarthritis
KOOS	Knee Injury and Osteoarthritis Outcome Score
LCL	Lateral Collateral Ligament
LKSS	Lysholm Knee Score Scale

LSD	Least Significant Difference
MA	Manual Acupuncture
MCL	Medial Collateral Ligament
MeSH	Medical Subject Heading
MMP	Matrix Metalloproteinase
NF-Kb	Nuclear Factor Kappa B
NHMS	National Health and Morbidity Survey
NRS	Numerical Rating Scale
NSAIDs	Non-steroidal Anti-inflammatory Drugs
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OMERACT	Outcome Measures in Rheumatology Clinical Trials
OMT	Osteopathic Manipulative Treatment
OPG	Osteoprotegerin
PCL	Posterior Cruciate Ligament
PG	Prostaglandins
PPI	Present Pain Intensity
PROM	Patient-Reported Outcome Measures
RCT	Randomized Controlled Trial
SA	Sham Acupuncture
SERC	Scientific and Ethical Review Committee
SF-12	the 12-item Short Form Health Survey
SF-36	the 36-Item Short Form Health Survey
SKSC	Quantitative Score of Knee Osteoarthritis Symptom Classification
SLE	Systemic Lupus Erythematosus
TA	Traditional Acupuncture
TCM	Traditional Chinese Medicine
TGF-β1	Transforming Growth Factor-β1
TIMP	Tissue Inhibitors of Metalloproteinase
TLR	Toll-like Receptor

TMJ	Temporomandibular Joint
TNF	Tumour Necrosis Factor
VAS	Visual Analogue Scale
VEGF	Vascular Endothelial Growth Factor
VIP	Weipu Journal Full-text Database
Wanfang	Wanfang Data Knowledge Service Platform
WNA	Warm Needle Acupuncture
WOMAC	Western Ontario and McMaster University Osteoarthritis Index

CHAPTER 1

INTRODUCTION

1.0 Background

Osteoarthritis (OA) is a common chronic, degenerative joint disease, also known as degenerative arthritis or hypertrophic arthritis (March et al., 2016). It involves multiple anatomical and physiological changes of joint tissues and bone regeneration characterized by cartilage degradation and subchondral bone sclerosis. Under the combined mechanical and biological influences, the chondrocytes, extracellular matrix and subchondral bone undergo an imbalance "degradation-synthesis" (Li and Liu, 2014; Li et al., 2015), which leads to the degeneration and damage of articular cartilage, bone restructuring, osteophyte formation, synovitis et al. (Nie, 2022; Allen et al., 2022). This results in symptoms of OA such as pain, stiffness, swelling, deformation, and limited joint movement and is the main cause of disability. It not only affects a patient's physical function, but also impacts mental health, sleeping quality, work participation, and mortality in serious cases (Allen et al., 2022). It also affects various joints such as the knee, hip, lumbar facet joints, and temporomandibular joint (TMJ), where knee osteoarthritis (KOA) is the most common clinical incident (Katz et al., 2021; Lu et al., 2022; Tong et al., 2022). It is a leading cause of knee pain and dysfunction among older adults (Loeser, 2010).

Knee osteoarthritis (KOA), also known as knee joint hypertrophic arthritis, is a bone and joint disease based on degenerative pathological changes. Its pathological characteristics are mainly the primary or secondary degeneration and structural disorder of knee joint cartilage, accompanied by subchondral bone hyperplasia, cartilage exhaustion, synovitis, and other conditions. Based on this foundation, the joints, surrounding tissues, and joint structures gradually become damaged, causing knee stiffness, pain, swelling, and resulting deformation, and ultimately leading to dysfunction of the knee joint (He et al., 2021; Deng et al., 2020; Tian et al., 2019). This disease has the characteristics of resulting high disability rate, prolonged recovery, high recurrence, and progressive disease aggravation (Wu, 2020), therefore it is called "non-fatal cancer".

Age and obesity are the two main risk factors for the occurrence and development of osteoarthritis (Iijima et al., 2022; Sharma, 2021). With the aging of the global population and the increase in obesity, the incidence of various degenerative diseases has sharply increased, and the onset age is getting younger, the incidence and prevalence of arthritis and KOA will further increase (Litwic et al., 2013). While it is causing physical and mental suffering and economic losses to patients, this disease also has an increasingly important impact on public health and the medical care systems. Therefore, it has become the focus of orthopedic physicians and even, society as it impacts greatly on the development of society (de Andrade et al., 2022; Long et al., 2020).

The modern medical treatment for knee osteoarthritis is mainly divided into three categories: non-pharmacological treatment, pharmacological treatment, and surgical treatment. Each of these treatments has its advantages and shortcomings. Non-pharmacological treatments mainly include health education, lifestyle changes, consultation and encouragement for obese patients to lose weight, wearing orthotics, muscle strengthening, aerobic exercise programs, etc. Pharmacological treatments mainly focus on non-steroidal anti-inflammatory drugs (NSAIDs), Corticosteroids, Hyaluronic acid, and Glucosamine drugs. Although drug use can temporarily relieve the symptoms, most of them require long-term use and lack supporting evidence of long-term efficacy. There are also side effects such as gastrointestinal damage, nephrotoxicity, and cardiovascular toxicity (Lin, 2018; Li et al., 2022; Li et al., 2020), and some drugs are expensive. Although surgical treatment has certain therapeutic effects, it is still an invasive therapy with large surgical trauma in some cases with many contraindications, which also bring great physical, psychological, and economic burdens to patients (Xing and Lin, 2019; Su et al., 2022).

There are various methods of treating KOA in traditional Chinese medicine (TCM), which are simple, easy to implement, and easy to be accepted by patients. Acupuncture is a commonly used treatment method for KOA. *Ling Shu · Guan Zhen* edited and compiled by Tian and Liu (2005) states: "The fifth is called Shu Ci (the Shu needling). This acupuncture method is to directly insert and pull out vertically. The depth of the needle insertion is relatively deep, reaching the bone, to treat Bone Bi (Bone Impediment, Bone Paralysis)." Acupuncture has the advantages of simplicity, no toxicity side effects, etc., and is easily accepted by patients. Although the mechanism of acupuncture for KOA is still under study, its analgesic effect has long been recognized by experts (Liu, 2023).

Electroacupuncture, as a treatment method combining traditional acupuncture and modern electronic medicine, has definite efficacy and high safety, which has been widely used in the clinical treatment of KOA (Lin et al., 2020; Zhu et al., 2018).

Due to its geographical location and historical factors, Malaysia has conserved and maintained an excellent tradition of TCM. A questionnaire survey has been conducted to understand the current TCM treatment measures for treating KOA in Malaysian TCM clinics, as well as the proportion of various TCM treatment methods used, especially the application of EA therapy for KOA. The survey prepares the further design of research topics and studies on the existence and development of TCM in Malaysia.

There are many records and publications on the studies of using acupuncture to treat KOA, and there is also a large number of research literature on the EA treatment for KOA. However, many physicians have different understandings of the disease and have different opinions on the selection of acupoints for acupuncture treatment of KOA. Therefore, it is necessary to collect, sort out, and analyse these acupoint prescriptions in the literature to discover the acupoints and respective characteristics, and regularities of the acupoints selection. This study focuses on clinical literature related to acupuncture treatment for KOA. Through studying relevant literature, sorting out and summarizing the acupoints used and basic fundamental principles, exploring the meridian theory and acupoint selection rules for acupuncture treatment of KOA to develop significant guiding principles for clinical practice.

Study has demonstrated that KOA has a close and positive relationship with biological factors such as Interleukin-1 beta (IL-1β) and Tumor Necrosis Factor-alpha (TNF-α) (Wang et al., 2020). Higher levels of IL-1β and TNF-α expression are found in the serum and synovial fluid of arthritis patients compared with heathy people (Dinarello C A. 2019). So, by measuring level of IL-1β and TNF-α, we can indirectly determine the severity of KOA (Wang, 2020).

Based on the above research work, this study takes the potential advantages of TCM in the treatment of KOA, and combines it with scientific research methods to study, investigate and evaluate the clinical efficacy of EA, combined with the top ten highly-researched acupoints to treat KOA, and its effect on serum IL- 1β and TNF-α of KOA patients' serum, which provides non-toxic side effect, more convenient, efficient and economical acupoint selection, and acupuncture treatment program to KOA patients. The study also explores and analyses some possible internal mechanisms of EA to improve and treat the clinical symptoms of KOA, enrich the clinical and theoretical research of EA analgesia, and provide an experimental basis for this therapy.

In summary, this project consists of three parts: 1. Research on the application of TCM therapy in the treatment of patients with KOA in Malaysia; 2. Explore the rules and characteristics of acupoints selection for acupuncture treatment of KOA based on literature search, data extraction and data analysis; 3. Evaluate and validate the clinical efficacy as well as determine the scientific basis of the top ten highly-researched acupoints in the treatment of KOA and the impact on related inflammatory factors combined with EA through clinical research.

This research project was supported by Universiti Tunku Abdul Rahman (UTAR) through the UTAR Research Fund (UTARRF) under project number: IPSR/RMC/UTARRF/2019-C1/T03. In addition, this research with the title "Clinical Study on Treatment of Non-acute Knee Osteoarthritis (KOA) Using Electro-acupuncture at Top Ten High-selected Acupoints" has been registered in Chinese Clinical Trial Registry with the registration number: ChiCTR2000034783. An ethics application had been submitted to the UTAR Scientific and Ethical Review Committee (SERC) and the Ethical Approval letter for the Research Project was obtained before the implementation of this research project with the number: U/SERC/89/2020.

The Chinese medicine terms used in this thesis are referenced to *World Health Organization (WHO) International Standard Terminologies on Traditional Chinese Medicines* [ISBN 978-92-4-004232-2 (electronic version)] or [ISBN 978-92-4-004233-9 (print version)] with copyright World Health Organization (2022 Edition).

2.0 Problem Statements

(a) Current Status in TCM Treatments of KOA in Malaysia

The first problem statement is the incidence rate of KOA in Malaysia is also very high. However, according to my personal experience in Malaysia and my communication with Malaysian TCM practitioners, it was found that there were various methods used in the treatment of KOA. There is no standard clinical method, selection of treatment options and the evaluation of clinical efficacy. Therefore, it is necessary to further understand the treatment methods used by TCM practitioners and the proportion of various treatment methods.

(b) Shortcomings of Existing Treatments

The second problem statement is that in the treatment of KOA, modern medicine has used glucocorticoids and non-steroidal anti-inflammatory drugs (NSAIDs) in the early stage and has achieved certain curative effects, however, most patients can only be treated symptomatically, as it only controls the acute symptoms such as relief the pain, but cannot completely cure the disease (Fei and Zhang, 2019). The toxicity side effects on gastrointestinal, kidney, and cardiovascular are also prominent in long-term use of those drugs (Wang, 2020). Hyaluronic Acid (HA) can relieve the pain of KOA by lubricating joints and reducing friction. However, there is no significant evidence that HA can delay the progression of the disease and promote the regeneration of articular cartilage (Conduah et al., 2009; Li, 2022). In the later stage of treatment, if necessary, the technique of arthroscopic minimally invasive cleaning or knee replacement is often used. However, there are problems arisen, such as high cost, high technical requirements, and short service life of artificial joints. Therefore, it is necessary to explore one or more therapeutic options that are safer, more effective and more convenient with fewer side effects.

(c) Lack of Unified Rules for Acupoints Selection

The third problem statement is that acupuncture plays an important role in the TCM treatment of KOA. In the previous studies on acupuncture for KOA, the selections of acupoints were varied, there was no fixed and unified acupoints selection standard. It is necessary to explore and study the rules of acupoint selection and establish a new basic acupoint prescription for treating KOA with acupuncture.

(d) Wide Variation in Clinical Efficacy

The fourth problem statement is that the treatment of KOA with internal or external use of Chinese herbs or acupuncture, physiotherapy, massage, and small needle-knife therapy have their benefits and shortcomings, however, the respective clinical efficacy was reported differently. Even for the treatment of KOA with acupuncture, there are large clinical efficacy variations reported in the previous studies. Therefore, it is necessary to conduct clinical research to verify the indicators such as the clinical efficacy of MA and EA.

(e) Unclear Mechanism of Acupuncture Treatment of KOA

The fifth problem statement is that most of the previous studies on the acupuncture treatment of KOA were observational studies based on clinical efficacy, and there are relatively few in-depth research reports on the intrinsic mechanism of acupuncture treatment of KOA. Therefore, it is necessary to study the internal mechanism of action from the cellular and molecular levels.

(f) Need to Validate Clinical Efficacy of New Acupoints Prescription and EA

The last problem statement is that in response to the above problems, it is necessary to carry out clinical research to verify the effectiveness and scientificity of the new acupoints prescription and EA combined with the prescription therapy from multiple aspects such as clinical observation and internal mechanisms.

It is believed that there is still a long way to find a treatment method that has definite clinical curative effects, safe, simple to operate, and with minimal toxic-side effects, however, this research study provides an opportunity to uncover more unexplored sciences in the field.

3.0 Research Objectives

This research study is divided into 3 studies – Questionnaire Research, Literature Research and Clinical Research, each with its objectives.

The objectives of Questionnaire research are:

(a) To study and analyse the application of TCM therapy methods in the treatment of KOA in Malaysian TCM clinics and hospitals, and compare with the situation in China; and

(b) To prepare for the further design of research topics and research on the existence and development of Malaysian TCM.

The objectives of Literature Research are:

(a) To study the TCM theory of acupuncture for KOA;

(b) To explore and analyse the rules for acupoint selection and features of acupoint use of acupuncture in the clinical treatment of KOA based on literature search, data extraction and data analysis;

(c) To screen and summarize the top ten high-frequency acupoints for acupuncture treatment of KOA; and

(d) To explore and provide a new and basic acupoint prescription for KOA, and to determine its suitability as a guide for clinical practice.

The objectives of Clinical Research are:

(a) A randomized controlled trial (RCT) was used to validate the clinical effectiveness and to determine the scientific basis for the clinical efficacy of the acupoint prescriptions in the treatment of KOA; and

(b) To explore the possible internal mechanism that EA can treat KOA and improve its clinical symptoms.

CHAPTER 2

LITERATURE REVIEW

ADVANCES IN CLINICAL RESEARCH ON THE TREATMENT OF KOA WITH ACUPUNCTURE IN THE LAST 15 YEARS

OA is a chronic degenerative disease characterised by the degeneration and wear of articular cartilage, osteophytes, synovitis, and structural changes in the joint capsule, ligaments, and associated muscles (Zhao et al., 2017). With the inflammatory response and degenerative changes in the bones, joints and soft tissues, swelling, pain, dysfunction of functional activities and even joint deformities, gradually appear in the relevant parts, and at the terminal stage, it can cause loss of joint function. Therefore, the disease is also known as the degenerative disease. Therefore, the OA is also known as degenerative arthritis, proliferative arthritis, proliferative osteoarthritis, etc.

OA commonly occurs and progresses with age. It predominantly affects the middle-aged and elderly population with a higher incidence rate among women compared to men (Wang, 2021). In China, the overall prevalence of OA is approximately 15%, with the prevalence increasing from 10% to 17% among individuals over the age of 40, up to 50% among those over 60, and reaching as high as 80% among individuals over 75 (Everard et al., 2013; Tie et al., 2018).

The primary clinical manifestations of OA include pain, swelling, joint deformity and functional impairment in the affected joints. In severe cases, these symptoms can lead to disability. OA is a significant cause of disability and pain, affecting over 300 million people worldwide (Derrien et al., 2004). While the disease can affect various joints in the body, and is commonly found in joints such as hands, hips, knees and spine, the knee joint is the most commonly involved joint (Routy et al., 2018).

The knee joint is a weight-bearing joint that is responsible for supporting much of the body's weight during activities such as walking, running, and jumping. Its own anatomical structures and physiological characteristics determine that it belongs to the hyperactive joint. Due to its crucial role in weight-bearing and mobility, the knee joint is vulnerable to various factors that can lead to strain and degenerative changes. Factors such as excessive or repetitive stress on the joint, poor biomechanics, injuries, and certain environmental conditions can contribute to the development of knee problems. Pathogenic factors such as wind, cold, and dampness also can lead to the occurrence of degenerative diseases in the knee joint. These problems on the knee joint are easier to affect the functional activities of the human body.

KOA is characterised by degenerative changes in the articular cartilage, and chronic inflammation involving the bone, synovium, joint capsule, and other structures of the joint. It involves limited destruction of the articular cartilage and the formation of bone fragments at the edges of the joint (Zhang et al., 2023; Chen et al., 2022). The progression of KOA is typically slow, leading to joint dysfunction. The main clinical manifestations of KOA include knee pain, swelling, stiffness, and functional impairment (Li and Zhao, 2022; Zhang et al., 2023).

For the prevalence of KOA in the elderly, in the USA, it ranges from 13% to 20% (Deshpande et al., 2016), in Europe from 9% to 17% (Postler et al., 2018), in the Middle East from 22% to 25% (AlKuwaity et al., 2018) and in Asian countries from 10% to 38% (Cho et al., 2015; Nishimura et al., 2012). According to the guidelines for Osteoarthritis developed by the Chinese Association of Traditional Chinese Medicine, it is stated that the incidence rate of KOA among individuals aged 55-64 reaches 40% (Chinese Association of Traditional Chinese Medicine, 2013). Studies (Qiu, 2005; Wang, 2021; Huang, 2012; Mao et al., 2022) have shown that the overall prevalence of KOA in middle-aged and older adults over the age of 40 gradually increases with age, ranging from 6.5% to 36.4%. Among men, the prevalence ranges from 4.3% to 27.3%, and among women, it ranges from 8.8% to 42.7%. The prevalence reaches 50% in patients over 60 years of age and 65% in those older than 75 years of age. The prevalence and incidence of KOA increase with age, and it is more common in women than in men. Various factors contribute to the development of KOA, mainly including age, obesity, previous joint trauma, inflammation and genetic factors, and these factors can interact and increase the risk of developing the disease (Lv and Zhang, 2016). The impact of KOA on individuals' quality of life underscores the importance of early diagnosis, appropriate management and interventions to alleviate symptoms and improve joint function.

In Western medicine, KOA is viewed as a degenerative condition that affects the bones, joints and associated structures of the body. This leads to a series of pathological changes, including degeneration and erosion of the articular cartilage; formation of osteophytes (bone spurs); damage to the meniscus; and inflammation of the synovium (He and Wang, 2023; Lu et al., 2023). In terms of treatment, Western medicine mainly employs both surgical and non-surgical approaches.

Non-surgical treatments mainly focus on symptomatic relief and supportive care. These include (1) the use of glucocorticoids and nonsteroidal anti-inflammatory drugs (NSAIDs) to manage pain and inflammation. Protective or nutritive cartilage drugs may also be prescribed. While these medications can provide certain efficacy in controlling acute symptoms like pain, long-term use can have toxic side effects on the gastrointestinal tract, kidneys, and cardiovascular system (Hu and Li, 2015; Zhang et al., 2016; Hu et al., 2020; Madani et al., 2020). (2) Intra-articular injection therapies, such as sodium hyaluronate injections, may also be utilised to provide temporary relief. However, most non-surgical treatments only offer short-term benefits, temporarily relieve symptoms, and do not halt the progression of the disease. In some cases, inappropriate treatment may even accelerate the progression of the disease and lead to further severe functional impairment.

Surgical treatments for KOA include minimally invasive arthroscopic surgery and knee joint replacement surgery. Arthroscopic procedures involve using small incisions and specialised instruments to assess and treat joint pathology.

The knee joint replacement surgery, on the other hand, replaces the damaged joint with an artificial joint. However, these surgical options come with challenges such as high costs, technical requirements, the limited life span of artificial joints, and the potential need for revision surgeries in the future (Lv et al., 2021).

In TCM, there is no specific or clear term to name KOA. While according to the symptoms and signs exhibited by this disease, TCM classifies it into the category of, such as "arthralgia syndrome", "flaccidity syndrome", "bone impediment", "muscle impediment", "bone flaccidity", "muscle flaccidity" and "arthralgia syndrome", etc. (in Chinese, the names are Bi Zheng (痹证), Gu Bi (骨痹), Jin Bi (筋痹), Gu Wei (骨痿), Jin Wei (筋痿), Wei Zheng (痿证) etc.) TCM has its own unique advantages in the diagnosis and treatment of bone and joint diseases, especially KOA, and has abundant of theoretical knowledge. It has a long history of medication and acupuncture, and has a variety of diagnoses and treatment methods. Under the guidance of the holistic concept and the theory of syndrome differentiation and treatment in TCM, TCM places great emphasis on the relationship between the entire body (wholeness) and the affected area (part), and emphasises treating the root cause of the disease. Acupuncture, as one of the traditional methods for treating KOA in TCM, has been used for centuries and is a simple, safe, non-toxic, and no side-effect treatment method. It is a commonly used clinical treatment method that is easily accepted by patients. Acupuncture has the functions of dredging the meridians and collaterals, promoting the smooth flow of Qi and Blood, harmonizing Yin and Yang to balance the Yin and Yang of the body, and helping the body's positive Qi (healthy Qi) to expel pathogenic factors. Studies (Zou, 2004; Sha, 2021; Sun, 2021; Li et al., 2021) have shown that acupuncture can promote injuries repair and the regeneration of soft tissues such as skin, muscles, tendons, ligaments, fascia, as well as nerves, bone and cartilage tissues. It has been found to effectively improve knee joint function in patients with KOA.

The literature on the treatment of KOA with acupuncture is indeed extensive, and acupuncture has a long-standing history as a treatment modality for the disease. However, with the advancements in modern technology, acupuncture techniques have evolved over time to adapt to current clinical practices. In recent years, the incidence of KOA has been on the rise due to factors such as an aging population and lifestyle changes. Consequently, there has been a growing number of research and clinical applications focusing on acupuncture as a treatment for KOA. This increased interest aims at the efficacy and safety of acupuncture in managing KOA conditions. It is essential to review the relevant clinical studies on acupuncture treatment for KOA conducted within the last 15 years. This is to provide a more comprehensive and systematic summary of the most recent research findings and advancements in clinical studies related to acupuncture treatment for KOA; to reflect the latest developments and trends in this field; and to ensure that the review includes the most up-to-date and accurate information available while avoiding the influence of outdated or unreliable literature on the results of the review. This approach can enhance the scientific validity and credibility of the review, as well as lay the foundation for future studies and research in this area.

1.0 Acupuncture Treatment

Acupuncture treatment, commonly seen in clinical practice and literature reports, primarily includes Traditional Acupuncture (filiform needle acupuncture) Therapy, Warm Needle Acupuncture Therapy, Fire Needle Therapy, Electro-acupuncture Therapy, Knife-needle Therapy, Blood-letting Therapy via Channel Puncture, Balance Acupuncture Therapy, Catgut Embedment in Acupoint Therapy (Catgut Embedding) and Comprehensive Therapy.

1.1 Traditional Acupuncture Therapy

Traditional Acupuncture (TA) Therapy, also called manual acupuncture (MA), primarily involves the use of filiform needles for acupuncture at the acupoints, which is a crucial aspect of TCM, and a common and indispensable treatment method for KOA using acupuncture (Guo et al., 2021). By inserting needles into specific meridians and acupoints, this therapy can regulate the circulation of Qi and Blood in the body; promote the metabolism of local tissues; and improve the restorative capacity of the locally affected tissues. Studies (Yao et al., 2021; Yang and Liu, 2021) have demonstrated that acupuncture can reduce the local inflammatory response in the knee joint of KOA patients; promote the proliferation of chondrocytes; inhibit the apoptosis of chondrocytes; and reduce the expression and release of inflammatory factors such as TNF-α and IL-1β. These effects contribute to the amelioration of clinical symptoms, enhancement of the quality of life in KOA patients, and achievement of therapeutic objectives.

To assess the clinical efficacy of acupuncture in treating KOA, Tu et al. (2021 conducted a study where 42 KOA patients were randomly assigned into two groups: the acupuncture group receiving conventional acupuncture treatment (21 cases) and the sham acupuncture group receiving superficial non-acupoint needling (21 cases). In the acupuncture group, 5-6 local acupoints (such as ST35 (Dubi), EX-LE4 (Neixieyan), EX-LE2 (Heding), SP9 (Yinlingquan), SP10 (Xuehai), ST36 (Zusanli), etc.) and 3-4 distal acupoints (such as GB31 (Fengshi), GB36 (Waiqiu), GB39 (Xuanzhong), GB41 (Zulinqi), etc.) were selected for conventional needle insertion. Both groups received a total of 8 weeks of treatment three times per week. Results showed that the acupuncture group had significantly higher scores of pain and daily activity when compared to the sham acupuncture group after treatment and during follow-up ($P < 0.05$). Acupuncture treatment had demonstrated more significant improvements in pain and daily activity function of the affected joints in comparison to sham acupuncture. These findings had indicated that acupuncture can alleviate pain symptoms and enhance daily activity capacity in KOA patients.

Zhou et al. (2021) conducted a study involving 52 KOA patients who received either acupuncture or medication treatment for 3 weeks. In the acupuncture group, acupoints of SP10 (Xuehai), ST34 (Liangqiu), SP9 (Yinlingquan), GB34 (Yanglingquan), and SP6 (Sanyinjiao) were selected for the acupuncture treatment, while the control group received oral Celecoxib capsules. The results showed that both groups exhibited significant reductions in Visual Analog Scale (VAS) scores, Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores, and significant improvements in Lysholm Knee Scoring

Scale (LKSS) scores. Furthermore, the acupuncture group demonstrated significantly greater improvements in scores compared to the medication group. These findings had indicated that acupuncture is more effective than medication (Celecoxib capsules) in reducing pain, improving joint mobility, enhancing daily activity function and increasing the overall quality of life in KOA patients. Therefore, the efficacy of acupuncture in this regard is evident.

Chen (2019) conducted a study involving 54 KOA patients who were treated with either TA or oral Celecoxib capsules. Acupoints such as GB34 (Yanglingquan), SP9 (Yinlingquan), and two additional acupoints (A'shi points) near the knee joint, or EX-LE4 (Neixieyan), ST35 (Dubi), were selected for acupuncture treatment. After two weeks of treatment, both groups showed reductions in VAS and WOMAC scores. From a mean ± standard deviation perspective, the acupuncture group exhibited significant decreases in serum C-Reactive Protein (CRP) and IL-6 levels ($P < 0.05$). In contrast, the changes in serum IL-6 levels and CRP levels were less pronounced in the Celecoxib group compared to the acupuncture group. The changes in serum CRP levels in the acupuncture group were positively correlated with the changes in VAS scores ($r = 0.576$, $P < 0.05$). These results had indicated that both methods can alleviate knee joint pain and improve knee joint function, but acupuncture demonstrates much more superior efficacy. Moreover, acupuncture had significantly influenced the levels of serum inflammatory factors in KOA patients.

A meta-analysis study conducted by Andrew et al. (2018) demonstrated the effectiveness of acupuncture in treating osteoarthritis pain. When compared to sham acupuncture, acupuncture was found to significantly alleviate pain levels and improve knee joint function in KOA patients. Furthermore, the therapeutic effects of acupuncture persisted over time, suggesting that the observed benefits cannot be solely attributed to placebo effects. For patients suffering from chronic pain, referral for acupuncture treatment is a reasonable choice. This recommendation aligns with the guidelines established by the American College of Rheumatology (2012 edition) (Hochberg et al., 2012), which suggests acupuncture as a recommended approach when pharmacological treatments are ineffective.

1.2 Warm Needle Acupuncture Therapy

Warm Needle Acupuncture (WNA) Therapy is a treatment method that combines acupuncture and moxibustion. It involves attaching a moxa cone or moxa wool to the end of an acupuncture needle and igniting it. Therefore, warm needle acupuncture combines the needling effects of acupuncture, which can regulate Qi and Blood, dredge the Meridians and collaterals, promote blood circulation and remove stasis, while also incorporating the therapeutic effects of moxibustion, which can warm the meridians and dispel cold, alleviate pain, and promote blood circulation and remove stasis. Utilising the dual treatment effects of needling and moxibustion, it aims to relieve or eliminate swelling and pain in the knee joint, thereby achieving the goal of treating the disease (Liu et al., 2021). This treatment method can be traced back to the classical book named *Shang*

Han Lun (Treatise on Cold Injury) and has a long history of application (Chen et al., 2019).

In a study conducted by Li et al. (2018), WNA treatment was added to the conventional therapy (control group) for KOA. The main acupoints selected for the treatment group included ST35 (Dubi), ST34 (Liangqiu), SP10 (Xuehai), ST36 (Zusanli), GB34 (Yanglingquan), and A'shi points. The results showed that the addition of WNA led to a better reduction in the levels of IL-1β, matrix metalloproteinase-1 (MMP-1), matrix metalloproteinase-3 (MMP-3), and transforming growth factor-β1 (TGF-β1) in the synovial fluid of the knee joint. It also resulted in greater improvements in VAS, WOMAC, and LKSS scores. Additionally, the total effective rate in the treatment group was 90.91%, higher than the 75.00% in the control group. These findings had indicated that: (1) WNA can effectively improve functional activities and alleviate pain in KOA patients, demonstrating good clinical efficacy; and (2) WNA can regulate the expression of various cytokines in the synovial fluid of KOA patients' knee joints, downregulating their levels, thereby reducing damage to tissues such as cartilage and exerting a therapeutic effect on KOA.

In a study conducted by Sun et al. (2021), WNA treatment was added to the control group (treated with topical application of flurbiprofen gel patch) for KOA. The results showed that the total effective rate in the observation group was 87.0%, higher than the 60.0% in the control group. Furthermore, the application of WNA effectively reduced the levels of IL-1β, interleukin-6 (IL-6), and TNF-α in the synovial fluid; and significantly downregulated the relative expression levels of Toll-like receptor 4 (TLR4), MyD88 and nuclear factor kappa B (NF-κB) mRNA in the synovial fluid. It also effectively reduced scores of VAS, WOMAC, Health Assessment Questionnaire (HAQ), and the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36). These findings had indicated that WNA can alleviate clinical symptoms, help restore joint function, improve the quality of life in KOA patients, and demonstrate good clinical efficacy. It also suggested that WNA can inhibit the release of inflammatory factors and reduce damage to articular cartilage, thereby achieving relatively good therapeutic effects.

The research conducted by Lin et al. (2019) demonstrated that WNA can increase the levels of serum osteoprotegerin (OPG), bone gla protein (BGP) and fibroblast growth factor-2 (FGF-2), while reducing the levels of MMP-3, vascular endothelial growth factor (VEGF) and angiopoietin-1 (Ang-1). These findings suggested that WNA can improve free radical metabolism in patients with KOA, lower the levels of inflammatory factors, inhibit the proliferation of osteoclasts, improve bone metabolism, and promote the repair of damaged cartilage cells. As a result, it reduces the inflammatory response, alleviates joint effusion and synovial thickening, and improves the clinical symptoms of KOA patients. This study also provided some insights into the potential underlying mechanisms of the WNA Therapy method in the treatment of KOA.

1.3 Fire Needle Therapy

Fire Needle (FN) Therapy is a specialised acupuncture technique in which the needle is heated by a flame and quickly inserted into specific affected areas or acupoints of the body for treatment. The main principle behind this therapy is the interaction between the stimulation produced by acupuncture at the acupoints and the heat generated by the flame. By stimulating the body's meridian system, nerves and immune system, fire needle therapy aims to warm the channels, dispel cold and dampness, eliminate stasis and nodules, and relieve Bi syndrome (He and Liang, 2017; Feng, 2021).

Through the clinical research, Zhang (2016) found that FN Therapy, through thermal stimulation, can dilate capillaries and accelerate blood flow, which helps to dilute and absorb metabolic by-products and inflammatory factors in the local area of the knee joint. This improves the state of blood stasis, reduces tissue swelling, relieves muscle spasms, lowers soft tissue tension, alleviates stimulation of nerve endings, and provides pain relief.

Gao (2021) treated KOA patients using FN Therapy (33 cases) and ordinary acupuncture (33 cases). The selected acupoints were ST34 (Liangqiu), SP10 (Xuehai), ST35 (Dubi), EX-LE4 (Neixieyan), GB34 (Yanglingquan), ST36 (Zusanli), and A'shi points. The results showed that the total effective rate in the FN group was 72.4%, higher than the ordinary acupuncture group's 58.1%. FN Therapy was superior to ordinary acupuncture in improving patients' knee joint function, pain, overall symptoms and overall health. It may also be more effective than ordinary acupuncture in improving the psychological health and social function of patients with KOA. The study suggested that the mechanism of action of FN Therapy in treating KOA is through the high temperature of the fire needle, which can dispel cold pathogens, stimulate the flow of Qi in the meridians, and promote its circulation. Therefore, FN Therapy is commonly used to treat pain and stiffness caused by cold pathogens.

Ding and Ma (2021) randomly allocated 120 patients with KOA into two groups: the FN group and the sodium diclofenac group. The acupoints selected for the treatment were EX-LE4 (Neixieyan), Waixiyan (ST35 (Dubi)), GB34 (Yanglingquan) and EX-LE2 (Heding). The results showed that after treatment, the expression of IL-1 and IL-6 in the serum of the FN group was significantly lower than that of the sodium diclofenac group. The scores of each part of WOMAC and total scores showed a significantly greater decrease in the FN group compared to the sodium diclofenac group. This had indicated that FN Therapy has significant clinical efficacy in treating KOA, with a notable reduction in the expression levels of IL-1 and IL-6 in the patients' serum. It can be widely used in clinical practice.

1.4 Electro-acupuncture Therapy

EA Therapy is a treatment method that combines modern technological development with traditional acupuncture techniques. It involves the application of pulsed electric currents on specific acupuncture points, building upon the traditional needle insertion. It offers advantages such as fast onset of action, good therapeutic efficacy, and minimal adverse reactions. EA has demonstrated significant advantages in the treatment of knee joint disorders (Xie et al., 2023; Cao, 2021).

Liu and Wu (2022) randomly allocated 90 patients with KOA into three groups: medication group (oral Celecoxib), acupuncture group and EA group (acupoints: ST34 (Liangqiu), SP10 (Xuehai), ST35 (Dubi), EX-LE4 (Neixieyan), GB34 (Yanglingquan), EX-LE2 (Heding), SP6 (Sanyinjiao)). The results showed that after treatment, the EA group had significantly lower VAS scores, WOMAC scores, and serum levels of IL-1β and TNF-α when compared to the acupuncture group and medication group. Moreover, the total effective rate was higher in the EA group (86.67%) than in the acupuncture group (73.33%) and the medication group (70.00%). These findings had indicated that EA, MA and Celecoxib can alleviate the clinical symptoms of KOA and reduce the levels of relevant inflammatory factors in the serum. However, EA shows greater advantages over MA and conventional medication, suggesting its potential for clinical application.

Han and Sun (2018) used EA and MA to treat KOA. The results showed that EA had significant advantages in improving patients' walking speed and stability, effectively enhancing the walking ability of KOA patients. It can effectively improve the functional limitations of KOA patients and their activity levels.

Xu (2020) conducted a multicenter randomized single-blind trial with 300 KOA patients, comparing EA with sham acupuncture. The acupoints selected for EA and sham acupuncture were SP10 (Xuehai), ST34 (Liangqiu), ST35 (Dubi), EX-LE4 (Neixieyan), ST36 (Zusanli), SP9 (Yinlingquan), SP6 (Sanyinjiao) and KI3 (Taixi). The results showed that EA effectively reduced VAS scores, WOMAC scores, and Lequesne index in KOA patients. It alleviated knee pain and stiffness, improved knee joint mobility, enhanced functional capacity, and led to significant improvements in SF-36 questionnaire scores across all eight dimensions compared to before treatment. Additionally, the outcomes of the EA group were significantly better than those of the sham acupuncture group. This study confirmed the effectiveness and safety of EA in treating KOA, demonstrating its significant therapeutic effects in relieving joint-pain and improving patients' quality of life. It also affirmed that EA is easy to administer with minimal side effects, provides substantial clinical evidence and warrants further promotion of EA as a treatment for KOA.

In the study conducted by Shi et al. (2020) on the treatment of KOA with EA, it was found that both EA and MA could effectively reduce the levels of inflammatory cytokines such as TNF-α, IL-1β, and IL-13, thereby, treating mild to moderate KOA, but EA had demonstrated a more significant reduction in these inflammatory factors compared to MA.

Jiao et al. (2018) conducted a study, through the observation of various indicators before and after treatment in 39 KOA patients, it was found that EA could increase the levels of IL-10 in the serum and reduce the levels of TNF-α ($P < 0.05$). It could significantly improve the Emotional Scale (ES), Present Pain Intensity (PPI) scores and knee joint mobility in KOA patients. This suggested that EA may improve the clinical symptoms of KOA patients by upregulating the anti-inflammatory cytokine IL-10 and downregulating the pro-inflammatory cytokine TNF-α levels.

1.5 Knife-needle Therapy

Knife-needle (KN) Therapy is a special medical technique that combines the characteristics of Western surgical knives and traditional Chinese acupuncture needles. It is a closed-release procedure developed based on acupuncture theory, occupying a middle ground between acupuncture and surgical incisions. During the treatment, a specialized knife-needle instrument is used to perform cutting, peeling and releasing of the affected area. Additionally, it can also stimulate the local meridians and acupoints. Using the therapy can achieve the purpose of adjusting the mechanical balance of joints, promoting blood circulation and removing blood stasis, releasing adhesions, dredging collaterals, and alleviating pain, thereby, improving the symptoms of KOA (Li et al., 2022; Liu, 2017; Fan et al., 2022).

Zhou et al. (2022) conducted a systematic review and meta-analysis to evaluate the clinical efficacy of KN Therapy in the treatment of KOA. The findings indicated that KN Therapy had significant effects in improving the overall effective rate, LKSS, and reducing VAS, WOMAC and TNF-α levels. It also demonstrated certain advantages in improving clinical symptoms of KOA, protecting knee joint cartilage, and restoring knee joint function.

Wang et al. (2022) treated 65 patients with KOA using KN Therapy (treatment group) and MA (control group). The results showed that after treatment, both groups had a significant reduction in VAS scores, but the KN Therapy group had a more significant reduction ($P < 0.05$). The Hospital for Special Surgery (HSS) knee joint scores, including pain, function, activity and total scores, were significantly improved, with the KN Therapy group showing a more significant improvement ($P < 0.05$). The KN Therapy group also demonstrated a significant improvement in the number of steps per minute ($P < 0.05$). In terms of overall efficacy, the KN Therapy group outperformed the MA group. These findings indicated that KN Therapy is more effective than MA in alleviating pain in KOA patients. By adjusting the balance of soft tissues, it can better restore the mechanical structure of the knee joint, thereby, improving joint function, activity level, and steps per minute in KOA patients. This treatment method, with its unique characteristics in TCM, is worthy of clinical promotion.

Shi and Liu (2019) used small KN Therapy (observation group) and intra-articular sodium hyaluronate injection (control group) to treat KOA. The results showed that the clinical total effective rate was 90.91% in the observation group and 77.78% in the control group, with a statistically significant difference ($P < 0.05$). Both groups showed improvements in WOMAC scores and VAS scores ($P < 0.05$), but the improvement was more significant in the observation group ($P < 0.05$). Regarding superoxide dismutase (SOD), nitric oxide (NO) and malondialdehyde (MDA), the KN Therapy group exhibited better regulatory effects than the control group ($P < 0.05$). These findings indicated that knife-needle therapy can enhance antioxidant capacity, improve symptoms such as pain, joint stiffness and joint dysfunction more effectively, and demonstrate significant therapeutic efficacy.

The study conducted by Lin et al. (2021) on the use of ultrafine KN Therapy for elderly KOA showed that after treatment, the VAS and WOMAC scores of patients significantly decreased, and the levels of IL-1, TNF-α, and PGE2 significantly decreased, lower than those in the control group. Moreover, the LKSS score, and SF-36 score significantly improved and were higher than those in the control group. These findings indicated that KN Therapy can alleviate pain in KOA patients, decrease the levels of inflammatory factors, reduce inflammatory responses, improve knee joint function and activity, promote bone recovery, and enhance the patients' quality of life.

1.6 Bloodletting Therapy via Channel Puncture

Bloodletting Therapy via Channel Puncture (BLCP) is a method in which tools like triangular needles are used to directly puncture the superficial veins at the affected area to release stagnant blood and treat diseases. Its theoretical foundation is based on the theories of TCM, including the meridian theory and Qi-blood theory. It functions by dredging meridians and collaterals, facilitating the smooth flow of Qi and Blood, and resolving stasis to alleviate pain. It has shown good therapeutic effects for Bi syndrome (Peng and Zeng, 2022; Cong et al., 2007; Chen et al., 2023). When used to treat KOA, BLCP directly targets the superficial veins around the knee joint and releases stagnant blood. This action promotes local blood circulation, disperses and clears metabolic by-products and inflammatory factors accumulated in the affected area; and improves the microenvironment of the lesion and its surroundings, thus achieving the therapeutic goals.

Wang et al. (2014) treated 60 patients with KOA using BLCP (treatment group) and oral enteric-coated diclofenac sodium sustained-release capsules (control group). The results showed that the total effective rate in the treatment group was 86.7%, which was higher than the control group's of 73.3% ($P < 0.05$). Both VAS and WOMAC scores decreased in comparison to before treatment, with better outcomes in the treatment group than in the control group. This indicated that BLCP can effectively improve pain, stiffness, and functional impairment in patients with KOA; and its efficacy is superior to that of Western medicine. It has the advantages of simplicity, convenience and low cost, making it a valuable treatment option for primary care, especially in community settings.

Peng (2018) treated 60 patients with KOA using MA (control group) and MA combined with BLCP (treatment group). The selected acupoints for needling were mainly EX-LE4 (Neixieyan), ST35 (Dubi), GB34 (Yanglingquan), SP9 (Yinlingquan), SP10 (Xuehai), ST34 (Liangqiu), ST36 (Zusanli) and A'shi points. The BLCP was primarily performed at SP10 (Xuehai), ST34 (Liangqiu), A'shi points and abnormal reaction points around the knee joint. The results showed that the total effective rate in the treatment group was 93.3%, while it was 80.0% in the control group ($P < 0.05$). Both groups demonstrated a decrease in WOMAC scores and traditional Chinese medicine syndrome scores after treatment, but the treatment group exhibited a more significant reduction compared to the control group ($P < 0.05$). This suggested that BLCP can enhance the therapeutic effects of acupuncture alone and effectively improve the clinical symptoms of patients. It is worth promoting this approach.

Hu and Guo (2018) treated KOA by combining WNA, BLCP and cupping on top of the oral administration of Western medicine (control group). After treatment, in both groups, Lequesne, WOMAC and McGill scores decreased compared to before treatment; with the scores in the observation group being lower than those in the control group ($P < 0.05$). Three months after the treatment, the observation group exhibited significantly lower blood flow signal grades and lower levels of IL-1, TNF-α and MMP-2 in the joint fluid compared to the control group ($P < 0.05$). This indicated that acupuncture combined with BLCP can significantly improve the symptoms of patients and alleviate inflammatory reactions.

1.7 Balance Acupuncture Therapy

Balance Acupuncture (BA) Therapy is a relatively new acupuncture treatment method proposed in recent years. In 2009, it was officially included as a recommended technique for the promotion of common diseases by the National Administration of Traditional Chinese Medicine. Based on the core theory of " Balance between Yin and Yang, Essence Governs Spirit" ("Yin Ping Yang Mi, Jing Shen Nai Zhi") from the *Huang Di Nei Jing (the Yellow Emperor's Inner*

Canon) translated and annotated by Yao, C.P., 2022, it emphasises that maintaining a balanced state is the foundation of good health, and the cause of diseases is the disruption of the body's inherent balance. The key to the treatment of disease is to restore balance. Therefore, BA Therapy is employed to gradually restore and achieve a new state of balance through the stimulation of peripheral nerve targets, and subsequently regulated by the central nervous system. This approach aims to achieve the goal of treating diseases and has the advantages of rapid effectiveness and immediate pain relief (Zhang et al., 2012; Zhou and Guo, 2018; Yang, 2022).

Zhang et al. (2018) treated 70 patients with KOA using BA Therapy (treatment group) and conventional acupuncture (control group) and observed the results of gait tests and VAS scores. The results showed that the VAS scores in both groups showed a decreasing trend, and the treatment group had a more significant decrease ($P < 0.05$). The step length and walking speed in both groups had significantly increased, and the peak value of the External Knee Adduction Moment (EKAM) had significantly decreased. Additionally, the changes in the treatment group were greater than those in the control group ($P < 0.05$). These findings indicated that BA Therapy can improve the pain symptoms of KOA patients. The possible mechanism is that after applying specific acupoints using BA Therapy, the stimulation relieves the central inhibition caused by pain, and facilitates the activation of muscles around the knee joint. This reduces the internal joint moment and increases the stability of the knee joint, thereby providing a therapeutic effect.

Li (2014) treated 31 patients with KOA using BA Therapy in the treatment group, while the control group of 30 patients received MA. The overall effective rate in the treatment group was 93.54%, which was significantly higher than the control group's rate of 83.3% ($P < 0.05$). After treatment, the treatment group showed significantly better results than the control group in terms of VAS scores, the Symptom Severity Grading and Quantification Scale for Knee Osteoarthritis. The treatment group exhibited superior improvement in walking pain, joint swelling, and joint mobility compared to the control group. However, the efficacy of the two groups was similar in terms of morning stiffness or pain after waking up and pain during rest. These findings indicated that BA Therapy has certain advantages in the treatment of KOA.

1.8 Catgut Embedment in Acupoint Therapy

The embedding thread technique, also named Catgut Embedment in Acupoint Therapy or catgut embedding (CGE), based on acupuncture theory, is an emerging long-lasting acupuncture treatment method that involves inserting and leaving protein or medication threads into acupoints of the human body to provide continuous stimulation. It is an extension and development of acupuncture and an important component of acupuncture (Ren, 2004; Lu and Wang, 2022). By gradually degrading within the body, the thread exerts long-term stimulation on the acupoints and meridians, allowing the stimulation pattern to transition from repetitive and multiple stimulations to long-lasting stimulation (Sun et al., 2014). Therefore, it can effectively regulate the meridians, adjust the organs, harmonize Qi and Blood, and restore the balance of Yin and Yang (Yang et al., 2015; Deng and Halikjiang, 2018). Due to its long-lasting stimulation mechanism, frequent acupuncture treatments are unnecessary, providing convenience, and improving patient compliance in clinical acupuncture therapy for various diseases (Sun, 2011).

Pan et al. (2020) treated 70 patients with KOA using different methods: acupuncture with CGE Therapy and MA. The acupoints used in both groups were SP10 (Xuehai), ST34 (Liangqiu), SP9 (Yinlingquan), GB34 (Yanglingquan), EX-LE4 (Neixieyan), ST35 (Dubi) and A'shi points. The results showed that both groups experienced a significant decrease in VAS scores ($P < 0.05$) and a significant increase in Knee Injury and Osteoarthritis Outcome Score (KOOS) total scores ($P < 0.05$) after treatment. However, there was no significant difference in VAS scores and KOOS total scores between the two groups ($P > 0.05$). This indicated that both CGE Therapy and MA can effectively alleviate pain and improve joint function in patients with KOA, with no significant difference in efficacy between the two methods.

Huang (2022) treated 40 patients with KOA using two different methods: acupuncture with CGE Therapy (treatment group) and intra-articular injection of sodium hyaluronate (control group). The results showed that the total effective rate was 88.00% in the treatment group and 80.77% in the control group ($P < 0.05$). The levels of WOMAC score and IL-1, TNF-α in the synovial fluid were significantly reduced after treatment, with better outcomes in the treatment group compared to the control group ($P < 0.05$). This indicated that acupuncture with

CGE Therapy can lower the levels of IL-1 and TNF-α in the synovial fluid, effectively improve clinical symptoms in patients, and achieve precise therapeutic effects.

Dong et al. (2019) treated KOA patients by combining acupuncture with CGE Therapy (treatment group) and sham acupuncture using a needle guide tube (control group) based on basic treatment. The results showed that the total effective rate was 100% in the treatment group, while it was only 26.67% in the control group. After the treatment, both groups showed a decrease in scores according to the Traditional Chinese Medicine Syndrome -Therapeutic Efficacy Assessment Criteria and WOMAC score, with a more significant decrease in the treatment group ($P < 0.05$). There was a significant difference between the two groups ($P < 0.05$). This indicates that both methods can improve the clinical symptoms of KOA patients, but acupuncture with CGE Therapy has a better therapeutic effect compared to sham acupuncture.

1.9 Comprehensive Therapy

Comprehensive Therapy, also called combination therapy, refers to the use of two or more different treatment methods to treat KOA, as opposed to a single treatment method. TCM offers various treatment methods for KOA, such as acupuncture, massage, topical and oral herbal medicine, which have shown certain advantages in treating the disease. Through literature review and clinical experience, it has been observed that Comprehensive Therapy is widely used in clinical practice, with various combinations of treatments. Common combinations include acupuncture + medication, acupuncture + massage, acupuncture + cupping, acupuncture + massage + medication, and so on. The majority of research findings indicated that Comprehensive Therapy generally achieves better therapeutic efficacy than a single treatment method (Zhang et al., 2022).

Hu (2020) conducted a treatment study on 100 patients with KOA using EA (control group) and EA combined with Zhu's Yi Zhi Chan Pushing Method (experimental group). The results showed significant differences ($P < 0.05$) in various scores between the two groups after treatment and during the 90-day follow-up compared to before treatment. The total effective rate in the experimental group was 75%, while in the control group, it was 50%; and the difference was statistically significant ($P < 0.05$). This suggested that EA combined with Zhu's Yi Zhi Chan Pushing Method is more effective in improving knee joint stiffness and pain symptoms, as well as restoring knee joint mobility, compared to using EA alone. Combination Therapy maximizes the advantages and characteristics of both methods and demonstrates superior clinical efficacy compared to a single-treatment approach.

Zheng (2013) treated 60 patients with KOA using two different methods: acupuncture combined with topical herbal medicine application (treatment group) and acupuncture alone (control group). After 4 treatment courses, significant differences were observed in the WOMAC scores and subscale scores of both groups compared to before treatment. The treatment group had a significantly lower pain index and daily activity difficulty index than the control group, and the total effective rate in the treatment group was 96.67% compared to 93.33% in the control group. The results indicated that both methods are effective in treating KOA, but the treatment group showed better results in relieving pain and improving functional impairment in KOA patients. This suggested that the combination of acupuncture and topical herbal medicine application therapy has a superior therapeutic effect for KOA compared to acupuncture alone.

Kang et al. (2021) treated 70 patients with KOA using two different methods: WNA Therapy combined with Cupping Therapy (treatment group) and acupuncture alone (control group). The control group received acupuncture at the acupoints of ST36 (Zusanli), GB34 (Yanglingquan), SP9 (Yinlingquan), ST35 (Dubi) and EX-LE4 (Neixieyan). In the treatment group, WNA Therapy was performed using moxibustion after acupuncture, combined with Cupping Therapy at the acupoints of SP10 (Xuehai), ST34 (Liangqiu) and A'shi points. After four weeks of treatment, the total effective rate was 91.4% in the treatment group and 71.4% in the control group, with a significant difference ($P < 0.05$). Both groups showed decreased in WOMAC and VAS scores, and the treatment group had lower scores than the control group. This indicates that WNA Therapy combined with Cupping Therapy is more effective than acupuncture alone in reducing knee joint swelling and pain, improving joint mobility, and enhancing the quality of life for patients.

Wang et al. (2022) treated 80 patients with KOA using different methods: glucosamine hydrochloride capsules + tonifying kidney and activating blood formula (Bu Shen Huo Xue Fang) (control group) and glucosamine hydrochloride capsules + tonifying kidney and activating blood formula (Bu Shen Huo Xue Fang) + WNA Therapy (study group). WNA was performed at the acupoints of EX-LE5 (Xiyan), ST34 (Liangqiu), SP10 (Xuehai), GB34 (Yanglingquan) and ST36 (Zusanli). After one month of treatment, the total effective rate in the study group was 95.00%, which was higher than the control group's rate of 80.00%. After treatment, both groups showed significant decreases ($P < 0.05$) in WOMAC scores, as well as serum levels of IL-1, TNF-α, serum N-telopeptide of type-I collagen (NTXI) and cartilage oligomeric matrix protein (COMP) compared to before treatment; with the study group showed significantly lower levels than the control group during the same period ($P < 0.05$). This indicated that the combination of tonifying kidney and activating blood formula (Bu Shen Huo Xue Fang) with WNA has a significant effect on KOA. It can effectively improve the symptoms and knee joint function of KOA and protect the articular cartilage from damage by effectively reducing the levels of inflammatory factors and bone-cartilage markers.

2.0 Comparative Analysis of the Acupuncture Methods

By reviewing the previous reports and literature on the treatment of KOA, as well as conducting research and analysis on the several acupuncture treatment methods mentioned above, it can be found that different acupuncture therapy methods are all able to alleviate patients' symptoms and achieve certain therapeutic effects in the treatment of KOA. Due to the differences in the mechanisms of action among various acupuncture methods, each treatment approach has its own unique characteristics, advantages and disadvantages. Therefore, it is necessary to compare and analyse them.

WNA Therapy, FN Therapy, and EA Therapy are all treatment methods that combine different additional stimulation techniques with traditional acupuncture for the treatment of diseases. These three methods have a common underlying principle of action, as they all involve stimulating acupoints to regulate the body's Qi, blood, meridians and other physiological functions to achieve the goal of treating diseases. However, there are still some differences among them:

(a) Different stimulation methods: WNA Therapy involves applying heat stimulation through moxibustion, FN Therapy utilises stimulation through the use of fire, and EA Therapy employs electrical current for stimulation;

(b) The varied intensity of stimulation: WNA Therapy provides relatively mild stimulation, FN Therapy involves relatively more intense stimulation, and EA Therapy delivers a relatively strong stimulation, with the ability to adjust the intensity of the stimulation; and

(c) Slightly different indications: WNA Therapy is suitable for conditions characterised by poor blood circulation and deficiency of Qi and Blood; FN Therapy is beneficial for ailments such as rheumatism, cold-induced paralysis, and muscle strain; and EA Therapy applies to disorders of the nervous system, muscle spasms, paralysis and pain-related conditions.

On top of the above, WNA Therapy requires someone to stay by to conduct close supervision during the procedure, as improper operation can easily lead to skin burns or scalds, and even cause fire accidents. It is challenging to precisely control the distance between the moxibustion cone and the skin, which can make the patient prone to skin-burning sensation, even cause skin burns or scalds and result in discomfort for the patient.

FN Therapy involves a thicker needle body, even the thinnest fire needle has a diameter of 0.5 mm. Combined with the high temperature, mild burns can occur at the needling site. Improper operation can lead to infections or scar formation. The local pain sensation during needling is intense, making it unfavourable for deep needling and less easily accepted by patients (Liu and Li, 2018). The fundamental principles of FN Therapy emphasises fast speed of needling, accuracy of needle placement, and precision of needle depth. Therefore, FN Therapy requires good control over the force applied during needling, the depth of insertion, and the accuracy of needle insertion points, which imposes stricter requirements on the practitioner (Wang, 2022).

KN Therapy, compared to traditional acupuncture, has disadvantages such as greater trauma, intense pain sensation during needling, and limitations in scar repair. These factors can easily generate fear in patients and result in poor compliance. KN Therapy requires a higher level of anatomical knowledge during operation compared to traditional acupuncture, as improper manipulation can easily lead to damage to blood vessels, nerves, tendons and other structures of the body. Furthermore, KN Therapy has a relatively higher demand for a sterile operating environment to prevent the risk of infection.

Although BLCP can rapidly eliminate blood stasis and pathogenic factors, it can also easily cause damage to blood vessels or lead to infections if performed improperly, resulting in unexpected conditions such as subcutaneous hematoma, bleeding and petechiae or bruising. The process of BLCP can cause pain and trauma, and make patients feel uncomfortable. Additionally, BLCP is not suitable for everyone and has certain limitations in terms of specific population groups, such as elderly individuals, those with weakened physical conditions, and pregnant women who are not recommended to undergo BLCP.

BA Therapy, which has emerged relatively recent, is commonly used in the treatment of conditions of neck, shoulder, back and leg pains, such as shoulder periarthritis, low back pain, and cervical spondylosis. However, there have been significant differences in the reported clinical efficacy of this therapy for treating the aforementioned diseases in previous literature, and there is a lack of in-depth mechanistic research. Therefore, further research is needed to better understand its mechanisms of action and efficacy.

The technique of CGE Therapy emerged in modern times, but it has gradually flourished with the continuous development and improvement of materials science. However, its dissemination and application overseas are still relatively limited, and in some countries, the use of CGE Therapy is not permitted. This is mainly due to the high requirements for aseptic and sterile operations for the practitioners. Improper handling can easily lead to infections and damage to nerves and blood vessels, and in serious cases, internal organs can be affected. After the completion of the embedded thread treatment, most patients experience strong sensations of soreness, numbness, distention and heaviness in the treated area, which can last for several days and cause discomfort to the patients. Moreover, there is also a risk of allergic reactions to the thread material and some unexpected occurrences such as liquefaction of adipose tissue at the needle insertion site and extrusion of the thread material at the insertion site, which causes panic and fear in patients, thus creating apprehension towards this treatment method. Furthermore, there have been reports (Huang, 2022) indicating that in practical clinical applications, CGE Therapy is less commonly used in the treatment of KOA.

EA Therapy has the advantage of replacing the manual lifting, thrusting and twisting techniques of acupuncture. With the combined application of electrical current stimulation, it has also expanded the scope of acupuncture treatment. EA Therapy is widely used in clinical practice, continuously propelling traditional acupuncture toward new directions and developments (Xie et al., 2023). EA devices, in clinical practice, have features such as safety, simplicity in operation and good controllability, making them generally well-received by patients. However, this therapy method is not suitable for patients with implanted cardiac pacemakers.

3.0 Summary

3.1 Acupuncture Treatment for KOA Shows Good Clinical Efficacy

In recent years, with the increasing aging population, the incidence of KOA has been rising. With the emphasis on TCM by the government, especially after the outbreak of the COVID-19 pandemic, people have increasingly recognised and accepted the important role of TCM, including acupuncture. Acupuncture therapy has been widely applied and recognized in clinical practice. With the development of modern technology, TCM is also advancing its research in modernisation and more comprehensively. Therefore, the contents and methods of acupuncture therapy are becoming more diverse, and its application scope is expanding. Acupuncture therapy has unique therapeutic effects in the treatment of bone and joint diseases, as well as functional disorders, and it is commonly used in the treatment of KOA.

Regardless of the acupuncture treatment methods, they all possess the fundamental therapeutic effects of acupuncture. During the treatment process, whether targeting the overall body or specific treatment areas, it can dredge meridians and collaterals, harmonize Yin and Yang, regulate the circulation of Qi and Blood, and achieve therapeutic effects such as promoting blood circulation, removing blood stasis, dredging meridian and activating collaterals, reducing swelling and relieving pain, smoothing joints, improving joint mobility, and alleviating inflammatory responses (Wu and Du, 2021). In recent years, in the relevant literature reports on acupuncture treatment for KOA, whether used as a single modality or in combination with other treatments, acupuncture has shown positive clinical outcomes for KOA.

3.2 Gradual Improvement in Research Quality

Based on the recent clinical research publications on KOA, most of clinical studies on acupuncture treatment for KOA have adopted randomised controlled methods, which indicates that a gradual improvement in research quality. With the implementation of large-scale studies and epidemiological investigations at the national level, along with the development, updates, and release of guidelines related to KOA, the diagnostic criteria and inclusion standards for research participants have gradually become more comprehensive, stable, standardised, and unified.

3.3 Existing Challenges

The current clinical research on acupuncture treatment for KOA still faces the following challenges:

3.3.1 Most Studies Focus on Clinical Efficacy Observation

Apart from some research reported in doctoral and master's theses, majority of published journal articles primarily concentrate on studying the clinical efficacy of acupuncture treatment for KOA, particularly in terms of short-term efficacy, lacking long-term observation and follow-up. Moreover, when evaluating clinical efficacy, most researchers mainly rely on rating scales such as WOMAC, VAS and so on. These scales involve subjective judgments and can be influenced by factors such as patients' cognitive and comprehension abilities, as well as the clarity of explanation by medical personnel. This can lead to research biases and reduce the credibility of the study results. Although the treatment methods have their own characteristics and demonstrate efficacy, there are significant differences in the reported clinical efficacy (Feng, 2015), with some studies even claiming an efficacy rate of 100%.

3.3.2 Lack of Exploration into the Underlying Mechanisms of Acupuncture Treatment for KOA

While factors related to the onset and progression of KOA have been extensively studied, the mechanisms of acupuncture treatment for KOA are not yet fully understood. Most journal articles have relatively limited research on the underlying mechanisms of acupuncture treatment for KOA, especially in terms of systematic and in-depth investigations. This undoubtedly diminishes the scientific rigor of the relevant research.

3.3.3 Inadequate Consideration of Sample Size Calculation and Lack of Multi-centre, Large Sample Randomized Controlled Trials (RCTs)

Evidence-based medicine suggests that sufficient sample size is necessary to ensure adequate statistical power in experiments (Deng et al., 2020). In the previously published literature, most studies reported the exact efficacy of acupuncture treatment for KOA, whether through a single treatment method or combined applications. However, some articles did not explicitly state whether the selection of sample size was based on rigorous sample size estimation. Additionally, there is a lack of multi-centre, large-sample RCTs. For instance, some studies included only around 20 cases, which to some extent reduces the credibility of the reported results and efficacy.

3.3.4 Most Clinical Studies Primarily Utilise Comprehensive Therapy and Emphasize Longitudinal Comparisons

The longitudinal comparison refers to comparing the efficacy and safety of a treatment method on the same group of subjects or the same patient at different time points. In the clinical studies of acupuncture treatment of KOA, most of them are carried out with Comprehensive Therapy. However, the reference objects selected for comparison in studies with multiple methods of combined application often have different qualitative characteristics. For example, in some studies, the treatment group received acupuncture with FN Therapy + WNA Therapy, while the control group received Western medication treatment. Therefore, when analysing the curative effect, it is unclear to the reader whether the main therapeutic effect is produced by WNA Therapy, FN Therapy, or Comprehensive Therapy.

4.0 Prospects in the Future

The prospects of acupuncture therapy in KOA treatment are as below:

(a) The observation indicators related to clinical efficacy evaluation should be gradually standardised. The standardised objective quantitative indicators which can reflect changes in the condition of the research should be included as much as possible in the research. When conducting therapeutic efficacy evaluations, a combination of subjective and objective indicators should be used to make the assessment more comprehensive, thereby reducing errors caused by subjective factors and improving the scientific and accurate nature of the research results. When conditions permit, patient follow-up visits should be carried out as much as possible, or the research plan should be improved to track and observe long-term therapeutic efficacy in patients;

(b) With the rapid development of modern scientific technology, techniques in cellular biology and molecular biology are increasingly mature. The detection techniques for signalling pathway transductions and differences in the expression of genes are becoming more standardised and improved. Therefore, in future research, the systematic study of the underlying mechanisms of acupuncture treatment for KOA can be potentially conducted at a deeper and more comprehensive level. This can provide scientific evidence to expand the clinical application of acupuncture and enrich the theory of acupuncture (Guan et al., 2018);

(c) When designing research protocols, it is important to carefully consider the sample size and dropout rate to calculate the minimum sample size required for conducting clinical studies. Additionally, when conditions permit, collaborative efforts with other hospitals or institutions can be employed to conduct multi-centre and large-sample size clinical studies. This approach ensures that the data and results obtained by the research are statistically significant, scientific, reliable, and credible; and

(d) Prior to conducting clinical research, it is essential to develop comprehensive, rigorous, and logically sound research protocols; then discuss the contents of their innovativeness, scientific validity, and feasibility. And it is important to carefully take the selection of appropriate reference objects or groups into consideration. It is also important to conduct horizontal comparisons of different treatment methods within the comprehensive therapy to evaluate and compare their therapeutic effects and safety. Such comparisons can assist researchers in determining which treatment method yields more prominent effects, ultimately leading to the identification of the optimal treatment approach.

5.0 Conclusion

In conclusion, there is still much work needs to be done in the field of acupuncture for treating KOA. The objective is to find a treatment method that is clinically effective, safe, convenient and well-received by patients. It is necessary to provide scientific, reliable and convincing research evidence, as well as explore the underlying mechanisms of acupuncture in treating KOA. These efforts will contribute to the advancement and innovation of acupuncture therapy and further enhance our understanding of acupuncture theory. These areas will be the main directions and primary focus of future clinical research.

CHAPTER 3

QUESTIONNAIRE RESEARCH

RESEARCH ON THE APPLICATION OF TCM THERAPY IN THE TREATMENT OF PATIENTS WITH KOA IN MALAYSIA

1.0 Background

Due to geographical location and historical factors, Malaysia has conserved and maintained an excellent tradition of TCM. Similar to other countries, KOA also has a significant incidence in Malaysia. According to my personal experience in Malaysia and my communication with Malaysian TCM practitioners, it was found that there are various methods used in the treatment of KOA, however, there is a lack of research and reports on the existing TCM therapy methods for KOA in Malaysia. Therefore, we conducted this study and hoped to understand the existing TCM therapies for KOA in Malaysia, and the proportion of various TCM therapies via a questionnaire survey. With the outcomes, we prepare for further research on the existence and development of TCM in Malaysia and obtain valuable information about the current situation and development of TCM in Malaysia, and prompted us to further explore and solve the problems found in this research.

2.0 Materials and Methods

2.1 Questionnaire Design

2.1.1 The Contents of Questionnaire

The questionnaire was designed based on the background and purpose of the study. The main content of the questionnaire covers two aspects of the survey: the therapy methods used in the treatment of KOA, and the age range of the patients who attended the TCM clinics and hospitals. For both survey questions, the TCM practitioners or physicians can select multi-choices (i.e. select more than one answer). Therefore, when tabulating the results, the total percentage of all age range and all therapy methods can be more than 100%. There was no content related to the privacy of the patient's name, contact information, address, etc. involved. Please refer to APPENDIX G for the questionnaire.

2.1.2 Survey Targets

The TCM practitioners or physicians work in TCM clinics or hospitals in Malaysia and China respectively.

2.2 Conduct Survey

TCM practitioners and physicians in TCM clinics or hospitals in Malaysia and China were surveyed to understand the information about the two aspects via e-mail, WhatsApp, WeChat, and telephone calls. The survey was extended to China because the information collected can be used as a benchmark to analyse the trends in Malaysia.

2.3 Questionnaire Return and Data Processing

The results were uniformly entered into the electronic version of the questionnaire. After reviewing, the valid data were imported into Excel 2019 for data analysis and preparation of charts or figures.

3.0 Results

3.1 Questionnaire Return

A total of 489 and 873 valid questionnaires were recollected from Malaysia and China respectively. Based on these questionnaires, data sorting and analysis were carried out.

3.2 Age Range of the Patients

According to the characteristics of the age of KOA, the age range (unit: years) of the patients was divided into 18-29, 30-39, 40-49, 50-59, 60-69, 70-79, and 80-. From the analysed data of the valid questionnaires recollected, it was found that the main age groups of KOA patients visited TCM clinics or hospitals in Malaysia were 50-59 years old (97.14%, 475/489), 60-69 years old (92.43%, 452/489), 70-79 years old (82.21%, 402/489). In China, the main age groups of KOA patients were 50-59 years old (96.79%, 845/873), 60-69 years old (90.84%, 793/873), 70-79 years old (72.16%, 630/873). The results are presented in Figure 3.1 and Figure 3.2.

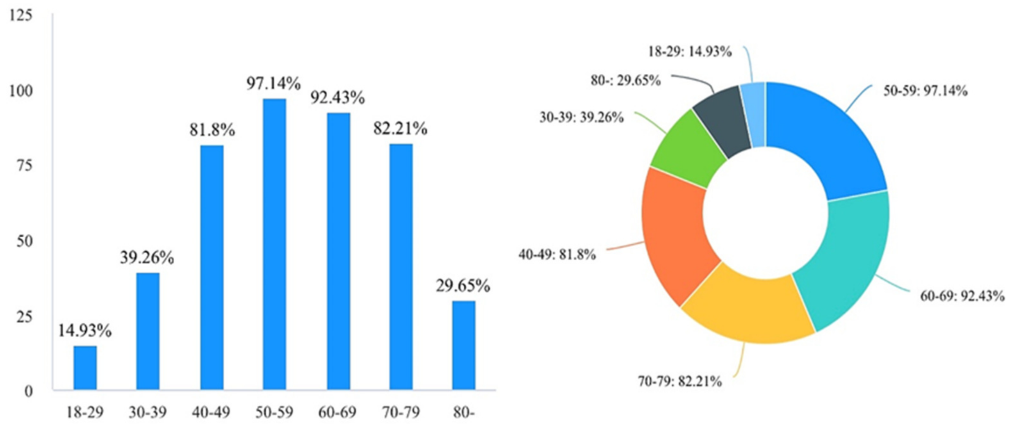

Figure 3.1: Age Range of the KOA Patients in Malaysia

(Note: Vertical axis: The proportion of patients of each age group in Malaysia. Horizontal axis: Age ranges of the KOA patients in TCM clinics or hospitals in Malaysia.)

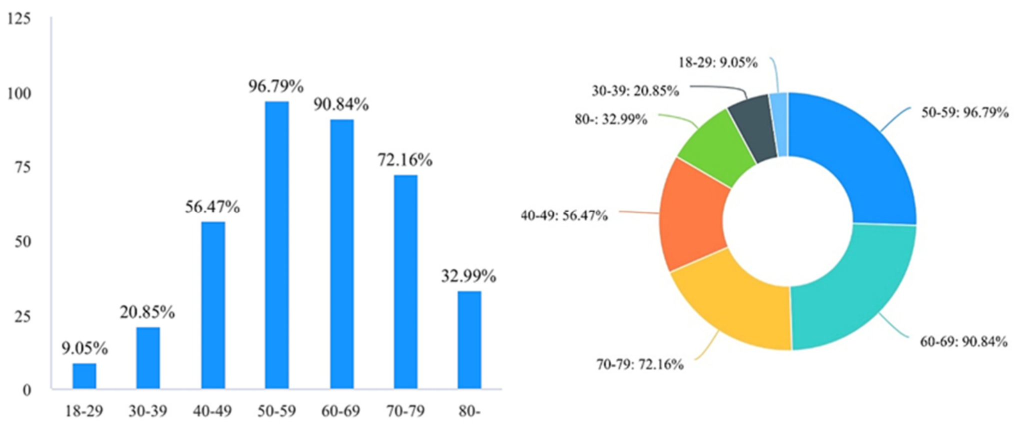

Figure 3.2: Age Range of the KOA Patients in China

(Note: Vertical axis: The proportion of patients of each age group in China. Horizontal axis: Age ranges of the KOA patients in TCM clinics or hospitals in China.)

In the analysis of the data, we converted the number of occurrences into a ratio, and used percentages for statistical description. The main age group of patients with KOA in Malaysia and China is 50-59 years old, followed by 60-69 years old, with over 90% of patients falling within these age ranges. The specific comparison of the age range of the KOA patients in Malaysia & China can be seen in the butterfly chart (Figure 3.3).

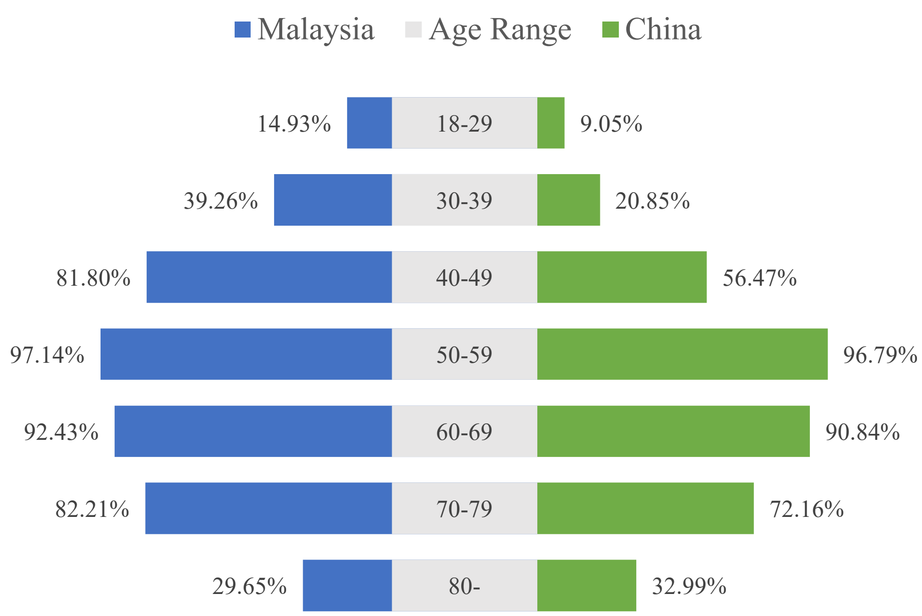

Figure 3.3: Age Range of KOA Patients in Malaysia & China

3.3 TCM Therapy Methods Used in the Treatment of KOA

There are various methods used by TCM practitioners or physicians in the two countries to treat KOA, MA is used as the mainstream TCM therapy in Malaysia

(81.60%, 399/489) and China (93.13%, 813/873); Besides MA, Malaysia uses Massage (78.53%, 384/489), Cupping (76.28%, 373/489), Moxibustion (64.21%, 314/489), Bloodletting (54.60%, 267/489), Electroacupuncture (48.26%, 236/489), and Chinese herbs (41.31%, 202/489), etc. as the treatment methods; while China uses treatment methods such as Electroacupuncture (84.19%, 735/873), Chinese Herbs (80.53%, 703/873), Massage (72.51%, 633/873), Moxibustion (68.84%, 601/873), Cupping (58.53%, 511/873), etc. The usage rate of electroacupuncture in Malaysia (48.26%) is not as high as in China (84.19%). The results are presented in Figure 3.4 and Figure 3.5.

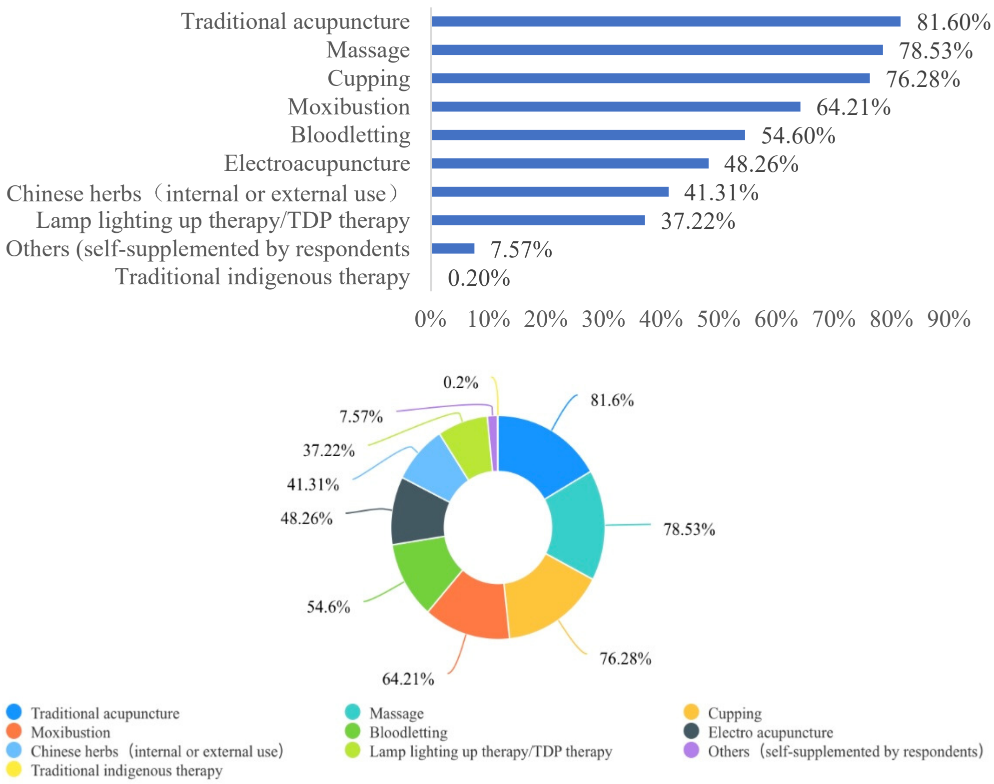

Figure 3.4: Therapy Methods Used in the Treatment of KOA in Malaysia

(Note: Vertical axis: Therapy methods used in the treatment of KOA in Malaysia. Horizontal axis: The proportion of each therapy method used in the KOA treatment in Malaysia.)

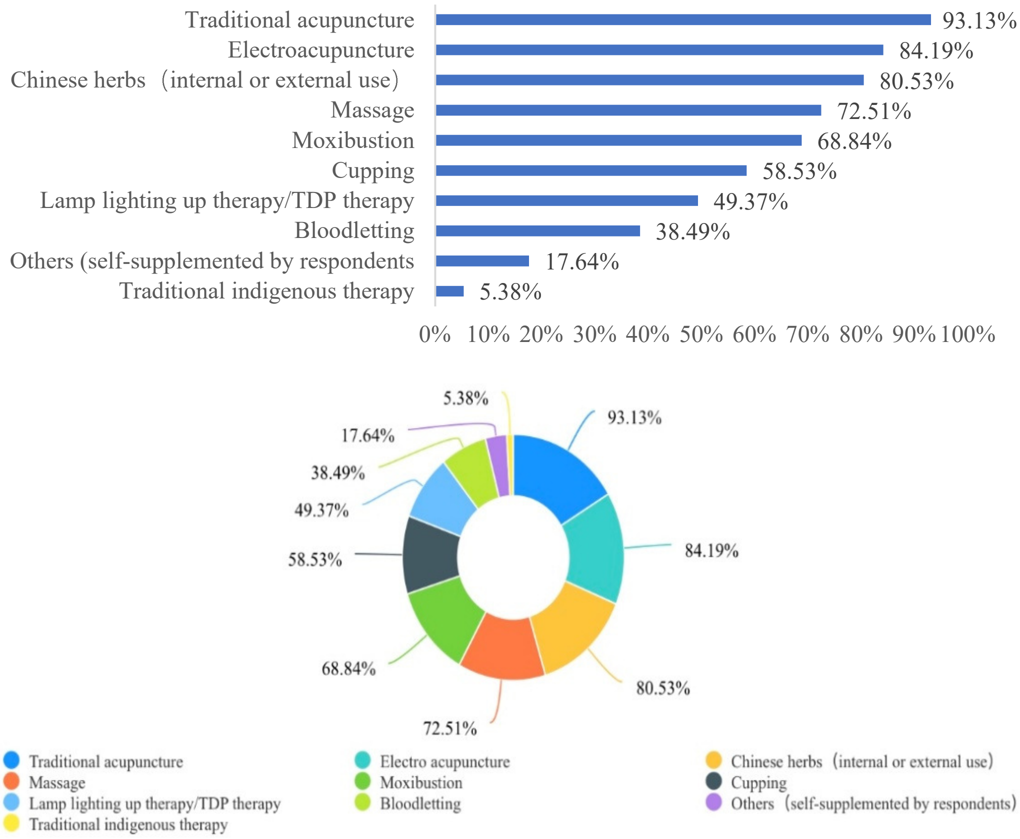

Figure 3.5: Therapy Methods Used in the Treatment of KOA in China

(Note: Vertical axis: Therapy methods used in the treatment of KOA in China. Horizontal axis: The proportion of each therapy method used in the KOA treatment in China.)

In addition to the above-mentioned treatment methods, other treatment methods supplemented by TCM practitioners or physicians in the two countries include:

(a) In Malaysia: Hot Compress, High-frequency Hyperthermia, Scraping (Gua Sha), Beryllium Needle, Lance Needle, the Unarmed Bone-setting, Manual Osteopathy, Osteopathic Manipulative Treatment (OMT), Knife Needle Therapy, Traditional Bone-setting Therapy, Application of TCM Orthopedic medical devices, Salt Pack (Hot Compress), Hit at Certain Acupoints, and Rehabilitation Treatment (Rehabilitation Exercise).

The application of Salt Packs is also a kind of Hot Compress, so it is classified as Hot Compress therapy in the statistics; the Unarmed Bone-setting, Manual Osteopathy, OMT, and Application of TCM Orthopedic medical devices are collectively classified as "Osteopathic Manipulative Treatment (OMT)" in the statistics; Beryllium Needle and Lance Needle belonged to Special Acupuncture methods; according to the frequency of occurrence, the frequency from high to low is as follows: Knife Needle Therapy (37.84%, 14/37), Hot Compress therapy (16.22%), Scraping (13.51%), Rehabilitation Treatment (10.81%), OMT (10.81%), Special Acupuncture (5.41%), High-frequency Hyperthermia (2.70%), Hit at Certain Acupoints (2.70%); and

(b) In China: Knife Needle Therapy, Small Curved Needle, Arthrocentesis Drug Delivery (Intra-articular Injection), Rehabilitation Treatment (Rehabilitation Exercise), Catgut Embedding, Hot Compress, Osteopathy (Bone-setting), Intra-articular Injection of Platelet-rich Plasma.

Small Curved Needle belongs to Knife Needle Therapy; Intra-articular Injection of Platelet-rich Plasma is also a type of Intra-articular Injection Therapy, and it is classified as Intra-articular Injection Therapy in the statistics; according to the number of occurrences, the frequency from high to low is as follows: Knife Needle Therapy (50.00%, 77/154), Intra-articular Injection Therapy (35.06%), Catgut Embedding (9.74%), Rehabilitation Treatment (1.95%), Hot Compress (0.65%), Osteopathy (Bone-setting) (0.65%).

As per Section 3.2. the specific comparison of the therapy methods used in the treatment of KOA in Malaysia and China can be seen in the butterfly chart (Figure 3.6).

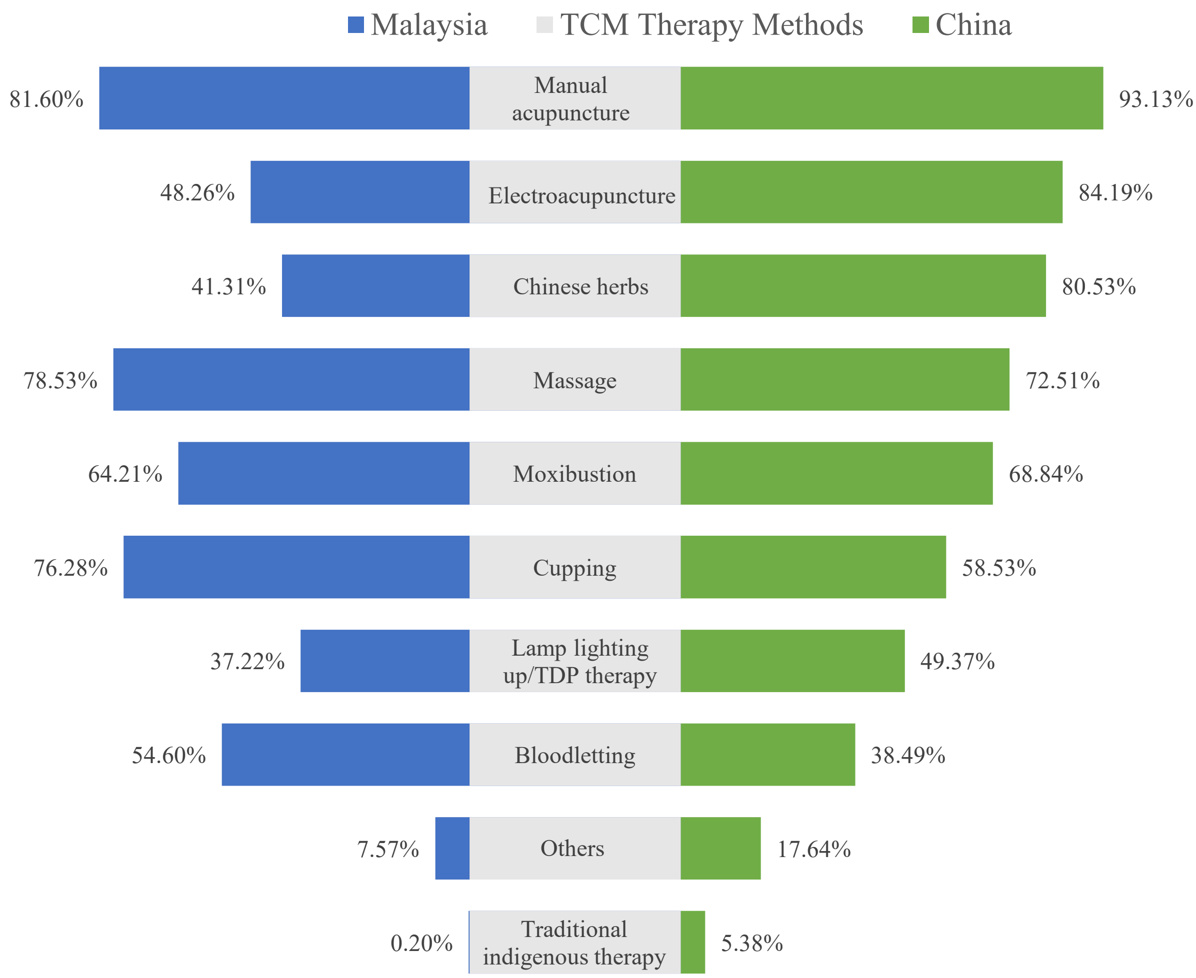

Figure 3.6. TCM Therapy Methods for KOA in Malaysia & China

4.0 Discussion

Due to its unique physiological structure, the knee joint is characterised as being susceptible to strain and degenerative changes. KOA is a common bone and joint disease in middle-aged and elderly people, and is the main cause of knee pain and functional impairment in the elderly (Jaiswal et al., 2021). Malaysia, located near the equator, has a tropical rainforest climate with a hot and humid climate throughout the year. Most local people prefer fans or air conditioning, and the unique geographical environment and lifestyle have led to KOA becoming one of the common bone and joint diseases with a relatively high incidence rate in the region, especially among the middle-aged and elderly. The statistical data from the Clinical Practice Guidelines on the Management of Osteoarthritis released by the Ministry of Health Malaysia reveals that 9.3% of adult Malaysians are experiencing knee joint pain, with over half of these patients having clinical evidence (Malaysia Health Technology Assessment Section, 2010). According to a report from Oriental Daily News Malaysia, data from the Arthritis Foundation Malaysia (AFM) indicates that approximately 10% to 20% of Malaysian adults suffer from osteoarthritis, with KOA being the most common form (Oriental Daily News, 2014). Among KOA patients in Malaysia, approximately 23% are aged 55 and above, while those aged 65 and above constitute around 39% (Chen, 2017; Zakaria et al., 2009).

4.1 Age Range of Patients with KOA in Malaysia and China

The findings of the Questionnaire Research on the trends of the age of the patients are as below:

(a) Based on the analysis of the valid questionnaires recollected, it can be seen that for the age range of patients with KOA who seek medical treatment in TCM clinics or hospitals, whether it is in Malaysia or China, the majority of patients are aged between 50 and 69 years old, with over 90% of patients' age falling within this age range. In Malaysia, the age distribution is mainly concentrated in the age groups of 50-59 years (97.14%, 475/489), 60-69 years (92.43%, 452/489), and 70-79 years (82.21%, 402/489). Similarly, in China, the age distribution also shows the same trend: 50-59 years old (96.79%, 845/873), 60-69 years old (90.84%, 793/873), and 70-79 years old (72.16%, 630/873). These results are consistent with the rules reported in the previous literature, and are consistent with the characteristics that the incidence of KOA is mainly in middle-aged and elderly people;

(b) In these two countries, the percentage of KOA patients seeking medical treatment increases with age, and forms a peak in the age group of 50-60 years old, indicating that the overall prevalence and trend of the disease increase with age. The age group with the lowest percentage of patients is the 18-30 age group, which is consistent with the law of bone development in the process of human growth and development. Young people generally have a strong physique, with complete and well-structured bone, joint cartilage, and subchondral bone, with normal bone metabolism. Unless it is because of trauma, tumor, infection or continuous high-intensity use of the knee joint, there will be relatively little OA of the knee, especially degenerative KOA;

(c) The data obtained from the survey show that whether in Malaysia or China, once patients reach the age of 80 or older, the percentage of patients with KOA begins to decline significantly, which may be related to the following conditions:

(i) Some patients suffering from the prolonged pain and sadness caused by KOA choose to undergo surgical treatments such as total knee arthroplasty (TKA) when appropriate age and physical conditions allow. Generally, TKA surgery is not the first choice of treatment and is usually only considered when non-surgical treatments are ineffective and exhausted. According to the recommendations of the American Association of Hip and Knee Surgeons, the average age of TKA patients is 68 years old, but the age range for surgical applicability is relatively broad. Typically, the optimal age range for TKA is between 50 and 80 years old because patients in this age range usually have more severe knee joint disease, are relatively younger and healthier than patients over 80 years old, and have a shorter recovery period after surgery, leading to better surgical outcomes and improvement in quality of life. According to a study published in The Journal of Arthroplasty, TKA surgery can be performed on patients younger than 50 years old, but a more careful evaluation and planning are necessary. For patients under 60 years old, expected lifespan and activity level after surgery should be important considerations in determining the appropriateness of surgery. For patients over 80 years old, surgical risks may increase, and therefore, more cautious evaluation is necessary. Thus, most TKA surgeries are completed before the age of 80, and after surgery, the number of patients choosing TCM treatment decreases significantly;

(ii) Due to the high teratogenicity and disability of KOA, most patients aged 80 or older who have suffered from long-term KOA may have knee joint deformities or functional activity disorders. Without the help of family members, it is difficult for them to go to TCM clinics or hospitals for treatment;

(iii) The limitation of the characteristics of the treatment method: TCM treatment usually requires a longer treatment process, such as acupuncture, Chinese herbal steaming, and moxibustion, etc., which may require multiple treatments to achieve good results and effect. For patients aged 80 or older, it may be difficult to undergo TCM treatment due to their physical conditions that do not allow for a long process of treatment, or because of challenges in mobility and logistic arrangement;

(iv) Trust in treatment: TCM treatment has a high level of trust in certain cultural backgrounds, but in other cultural backgrounds, there may be some suspicion and distrust. For patients aged 80 or older, they may be more inclined to accept Western medical treatment, or rely more on traditional family remedies (homeopathy) rather than undergo TCM treatment; and

(v) Allocation of medical resources: In some areas, the medical resources for TCM treatment are relatively limited, which may also make it difficult for patients aged 80 or older with KOA to access TCM treatment.

In summary, the aforementioned factors may lead to a relatively low proportion of TCM treatment in patients in this age group; and

(d) The proportion of patients with KOA in Malaysia is significantly higher than that in China across most age groups, especially among those aged 40-49 years old (81.8% in Malaysia compared to 56.47% in China). Moreover, the age distribution of patients with KOA in Malaysia tends to be younger than that in China. For instance, 39.26% of patients in Malaysia are aged between 30-39 years old, whereas the proportion is only 20.85% in China. Conversely, 97.14% of patients in China are aged between 50-59 years old, while the proportion is only 81.8% in Malaysia. These differences may be attributed to the following factors:

(i) Excessive use of knee joints: In Malaysia, many individuals engage in physically demanding work or stand for prolonged periods, which may lead to excessive use of their knee joints, increasing the risk of developing KOA;

(ii) Nutritional intake: Malaysian diets may contain an excess of high-sugar, high-fat, and high-salt foods, while balanced nutritional food intake may be inadequate, which may increase the risk of KOA;

(iii) Weight: According to the results of the National Health and Morbidity Survey (NHMS) in Malaysia, the obesity rate in Malaysia increased from 4.4% to 15.1% in the 15 years from 1996 to 2011, an increase of nearly 3.5 times; and the overweight rate also increased from 16.6% in 1996 to 29.4% in 2011(Oriental Daily News, 2014). Higher rates of obesity in Malaysia may increase the risk of KOA, as excess weight puts extra stress on the knee joints, making them more prone to wear and tear;

(iv) Living environment and habits: The climate in Malaysia is hot and humid all year round. Most locals like to blow fans or air conditioners, and like to wear shorts, which makes the knee joints more vulnerable to factors such as wind, cold, dampness (humidity), and so on, thus accelerating the degeneration of the knee joints and causing KOA, and have a preference for cold beverages. Excessive consumption of cold beverages can impair the spleen and stomach, disrupting their normal physiological functions. This can lead to the accumulation of dampness, which then transforms into phlegm-dampness. When the phlegm-dampness stagnates in the meridians, if it persists at or around the knee joint, it can cause knee arthralgia or knee osteoarthritis; and

(v) Poor awareness of the importance of protecting knee joints: There is a lack of awareness among the youngsters on the importance of protecting their knee joints from moistures or cold stream such often kneeing on the cold and moist floor with bare skin, which may weaken the knee joint leading to KOA.

Because of the above, there is more and further research needed to determine the role of these factors in the high incidence and prevalence of KOA in Malaysia. Overall, the data suggests that KOA is more prevalent among older populations in both Malaysia and China. Despite that the data has shown that there are some differences between the age ranges of KOA patients in the two countries, with Malaysia having a higher percentage of KOA patients in most age ranges compared to China. These findings may have implications for healthcare providers and policymakers in both countries to address the needs of patients with KOA.

4.2 TCM Therapy Methods Used in the Treatment of KOA in Malaysia and China

In Malaysia and China, the current status of diagnosis, treatment, and management of KOA is relatively well-established, and patients can get a variety of treatment options, including drug therapy, physical interventions, and surgical interventions. In general, pharmacological treatment usually includes medications such as analgesics, anti-inflammatory drugs, and corticosteroids or steroids, which are administered to relieve pain and reduce inflammation. Physical interventions include physical therapy, exercise therapy, and rehabilitation, aimed at restoring joint function and relieving pain. Surgical interventions are usually reserved for those patients who are with more serious conditions and whose symptoms have not been relieved or improved by other treatments. In addition to traditional Western medicine treatment, Malaysia and China have recognised the importance of TCM in treating KOA which includes acupuncture, Chinese herb therapy, and other treatment methods.

Through the analysis of the survey results, it was found that:

(a) In Malaysia, there are significantly more acupuncture clinics and TCM clinics providing acupuncture treatment for patients with KOA than expected. TCM practitioners or acupuncturists in Malaysia usually use a combination of treatments such as Massage (Tuina), Cupping, and other TCM therapies to treat patients with joint osteoarthritis. In addition, many hospitals in Malaysia, including both government and private hospitals, also provide acupuncture treatment. Some hospitals even have dedicated acupuncture therapists in their physical therapy departments;

(b) There are a variety of TCM treatment methods used by TCM practitioners or physicians in the two countries for the treatment of KOA, but MA is the mainstream and predominant TCM treatment method in both countries (Malaysia (81.60%, 399/489) and China (93.13%, 813/873)). Other treatment methods such as Massage (78.53%), Cupping (76.28%), Moxibustion (64.21%), Bloodletting (54.60%), Electroacupuncture (48.26%), and Chinese Herbs (41.31%) are also used as the main treatment methods in Malaysia. In China, Electroacupuncture (84.19%), Chinese Herbs (80.53%), Massage (72.51%), Moxibustion (68.84%), and Cupping (58.53%) were the main treatment methods.

Acupuncture treatment is considered to be an effective adjuvant and complementary therapy, which can relieve pain and reduce inflammation. For KOA, acupuncture can dredge and promote circulation in the meridians of the whole body and regulate local Qi and Blood, it has the functions of expelling wind and dispersing cold, promoting blood circulation, and removing blood stasis, dredging collaterals, and relieving pain (Wang et al., 2023). Electroacupuncture is a technique and treatment method combined with electrical stimulation based on traditional acupuncture to strengthen the therapeutic effect of traditional acupuncture. At the same time, it also has the effect of bioelectricity. The mechanism of electroacupuncture may be that after the integration of electrical signals in the central nervous system, the electrical signal regulates the neurotransmitters released by the autonomic nervous system, hormones released by the endocrine system, and other substances and transmitters. By influencing the signal transduction pathway to regulate the body's immune response and cytokine secretion, it relieves and alleviates the clinical symptoms of KOA (Bai et al., 2015; Ding, 2019). Bloodletting therapy for KOA involves puncturing the superficial blood vessels at the site of the knee joint lesion using tools such as three-edged needles to release a small amount of blood (stagnant blood), thereby adjusting Qi and Blood, regulating the circulation of Qi, promoting local blood circulation and tissue metabolism. By improving the microcirculatory status around the knee joint, it can relieve symptoms and treat the disease (Wang et al., 2021; Xu et al., 2021). The Knife Needle Therapy is an operative technique developed based on acupuncture theory that lies between acupuncture and knife cutting. It involves cutting, peeling, and relaxing the affected area using special needle tools, while also stimulating local meridians and acupoints, to achieve the purpose of promoting blood circulation, dissolving stasis, and relieving pain, and improving the symptoms of KOA (Li et al., 2021; Liu et al., 2012; Wang et al., 2018). Additionally, Chinese herbal medicine treatment can help promote joint repair and alleviate symptoms such as pain;

(c) Regarding the application of electroacupuncture, China has included this therapy in the clinical pathway for the treatment of KOA. However, Malaysia does not practice this approach. The usage rate of electroacupuncture in Malaysia for treating KOA is lower than that in China (Malaysia: 48.26%; China: 84.19%); and

(d) In addition to the aforementioned treatment methods, other complementary treatment methods for KOA are employed by TCM practitioners in both Malaysia and China. In Malaysia, these include Hot Compress, High-frequency Hyperthermia, Scraping (Gua Sha), Beryllium Needle, Lance Needle, the Unarmed Bone-setting, Manual Osteopathy, OMT, Knife Needle Therapy, Traditional Bone-setting Therapy, Application of TCM Orthopedic medical devices, Salt Pack (Hot Compress), Hit at Certain Acupoints, and Rehabilitation treatment. In China, include Knife Needle Therapy, Small Curved Needle, Intra-articular Injection, Rehabilitation Treatment, Catgut Embedding, Hot Compress, Osteopathy (Bone-setting), and Intra-articular Injection of Platelet-rich Plasma.

It can be seen that the treatment methods used by TCM practitioners or physicians in these two countries for treating KOA are more diverse. Although some treatment methods, such as Knife Needle Therapy, Rehabilitation Treatment, Hot Compress therapy, and Osteopathy (Bone-setting) are commonly used in both countries, there are also some significant differences. Although the Knife Needle Therapy is the most commonly used supplementary treatment method in both countries, but the frequency of usage in China is higher than that in Malaysia, it is more widely used in China (50.00%) than in Malaysia (37.84%). Moreover, non-invasive treatments such as Hot Compress therapy, Scraping Therapy, and Rehabilitation Treatment are the main supplementary treatments used by Malaysian TCM practitioners, while invasive operations such as Intra-articular Injection Therapy and Catgut Embedding therapy constitute a significant proportion of China's supplementary treatments. Through the medical education and work experience I received in China, as well as my insights after communicating with local TCM practitioners in Malaysia, and my understanding of the laws and regulations supporting TCM in Malaysia, the reasons for the above situation and the factors contribute to the differences can be summarized as follows:

(a) The special nature of TCM itself: TCM is a traditional medical system that originated in China, and different countries and regions may have different cultural and traditional medical backgrounds, which may result in differences in the methods of TCM treatment methods. Additionally, different countries and regions may also have different levels of research and recognition of TCM treatment methods, leading to differences in their clinical practices;

(b) The different historical cultural traditions and customs of the two countries: Malaysia is comprised of three major ethnic groups, Malay, Chinese, and Indian, each race has its medical traditions, sense of identity and self-belonging. Although there is cultural exchange and integration, each group still develops and maintains its unique characteristics;

(c) The views and attitudes of the two countries on the use of TCM methods in routine diagnosis and treatment: Both China and Malaysia use Western medicine as the main method of diagnosis and treatment in their countries, but TCM originated and developed in China, with a long history, rich culture, and well inheritance. Therefore, in China, TCM is widely applied and researched as traditional medicine, and its treatment methods have also been more recognised and developed. TCM has its own importance and status in China, especially after experiencing the COVID-19 epidemic, which further enhanced China's emphasis on TCM. Therefore, in Chinese hospitals and clinics, TCM treatment methods may be more diverse and mature, including traditional methods such as Acupuncture, Chinese Herbal Medicine, and Massage, as well as some modern TCM treatment technologies. In Malaysia, TCM, Malay medicine, Indian medicine are classified as traditional and complementary medicine, so TCM in Malaysia is mainly for Chinese, but in our other research projects, we also found that Malays and Indians are gradually accepting and recognising TCM. These differences in attitude towards TCM can be attributed to the different cultural traditions, customs, and medical backgrounds of the two countries;

(d) The laws and regulations formulated by the respective countries for TCM:

Factors such as the professional classification and curriculum system of China's TCM colleges and universities allow students in China's TCM colleges and universities to learn, master, and acquire a good understanding of modern medicine while learning traditional Chinese medicine knowledge. The department setting of the hospital of TCM also demonstrates the important connection between TCM and modern medicine. Therefore, China's laws and regulations on TCM provide TCM physicians with more flexible treatment options and allow TCM physicians to take a wider range of diagnostic and treatment measures, including invasive operations such as Acupoint Injection and Catgut Embedding. However, the legislations and regulations of traditional and complementary medicine in Malaysia have strict, specific, and clear restrictions on the diagnostic and therapeutic activities of TCM practitioners, acupuncturists, tuina therapists, etc., resulting in them not being able to use non-TCM treatment methods, and operations with obvious aseptic requirements, such as catgut embedding, intra-articular injection, and other therapies; and

(e) There are various methods used by TCM clinics or hospitals in Malaysia to treat KOA, which not only demonstrates the inheritance and development of TCM by local TCM practitioners, but also from the other side, reflects some problems discovered when communicating with local TCM practitioners. For example, local TCM practitioners do not have a unified and standardized process when treating KOA, it is often based on which certain method is familiar to the TCM practitioner. Moreover, the evaluation of clinical efficacy, is mainly based on the patient's self-perception and the TCM practitioner’s experience, there is a lack of objective, standard, and realistic evaluation criteria and systems. China, in contrast, has formulated standardised clinical pathways and various evaluation criteria for TCM and Western medicine diagnosis and treatment of KOA. This is also one of the places where Malaysian TCM can draw on and learn from in the future development and innovation.

In general, the treatment methods adopted by TCM practitioners or physicians in both countries for KOA are diverse, with some commonalities but also noticeable differences. However, this provides patients with many opportunities to choose appropriate treatment methods based on their individual conditions and receive treatment under the guidance of TCM practitioners or physicians.
In conclusion, this research allowed us to understand the treatment of KOA with TCM in Malaysia, which laid a foundation for us to further understand the current situation and development of TCM in Malaysia and prompted us to further explore how to solve the identified problems.

5.0 Conclusion

Based on the above, it can be concluded that:

(a) The main age range of patients with KOA in Malaysia and China is 50-59 years old (Malaysia: 97.14%, 475/489; China: 96.79%, 845/873), which is in line with the feature that the incidence of KOA is mainly in middle-aged and elderly people;

(b) There are various treatment methods used by TCM practitioners or physicians in the two countries to treat KOA, however, MA is used as the mainstream TCM therapy in Malaysia and China. In addition to MA, Malaysia uses Massage, Cupping, and Moxibustion as the main treatment methods, while China has additional main treatment methods such as EA and Chinese Herbs Therapy on this basis;

(c) EA has been widely used in China because of its precise curative effect and high safety and has been incorporated into the clinical pathways, ranking second only to MA. However, the usage rate of electroacupuncture in the treatment of KOA in Malaysia is not as high as in China;

(d) The supplementary therapies in Malaysia mainly focus on non-invasive operations, such as Hot Compress therapy, Scraping therapy, Rehabilitation Treatment, etc., while in China, invasive operations such as Intra-articular Injection Therapy and Catgut Embedding Therapy account for a large proportion of the supplementary therapies; and

(e) TCM practitioners in Malaysia do not have a unified and standardised process when treating KOA and often rely on their familiarity with certain methods. Moreover, when evaluating clinical efficacy, it is mainly based on the patient's subjective self-perception and the physician's experience, lacking objective, standardized, and realistic evaluation criteria and systems.

6.0 Existing Problems and Prospects

During this research study, some problems were encountered:

(a) The content of the questionnaire survey is not comprehensive enough. In the future, additional questionnaire items can be added to collect more extensive and diverse information; and

(b) Due to the time-bound nature of the research project, the limited time for the questionnaire survey, and the impact of the COVID-19 Pandemic, only online research was carried out instead of offline research. In addition, everyone has a high degree of vigilance and awareness of unfamiliar network links or fraudulent calls, therefore, the response rate of the questionnaire was only slightly more than 50%. In the future, methods such as expanding publicity, increasing the number of questionnaires distributed, expanding the survey channels of questionnaires, and enlarging the sample size can be implemented to improve the reliability and credibility of the research results.

CHAPTER 4

LITERATURE RESEARCH

EXPLORE THE RULES AND CHARACTERISTICS OF ACUPOINTS SELECTION FOR ACUPUNCTURE TREATMENT OF KOA BASED ON LITERATURE RESEARCH AND ANALYSIS

1.0 Research Object

The literature review of randomized controlled trial (RCT) on clinical research of acupuncture in the treatment of KOA was published in domestic and foreign journals from January 2005 to December 2019.

2.0 Research Methods

2.1 Literature Search

2.1.1 Search Terms

Relevant subject terms used for search will be determined by consulting the Medical Subject Headings (MeSH) and the Chinese Medical Subject Headings(CMeSH) are as below:

(a) The Chinese Keywords Search:

(i) Type of Disease

Subject Headings: 骨关节炎, 膝; Free Words: 膝关节骨性关节炎, 膝骨关节炎, 膝骨关节病, 膝骨性关节炎, 膝关节退行性骨关节病, 膝关节退行性骨关节炎, 增生性膝骨关节炎, 膝关节炎;

(ii) Intervention Measures

Subject Headings: 针灸疗法, 针刺疗法, 针刺, 电针, 温针疗法; Free Words: 针灸,针灸治疗, 温针, 电针疗法, 电针灸, 温针灸;

(iii) Type of Study

Subject Headings: 随机对照试验; Free Words: 随机对照, 随机对照研究, 随机对照实验, 随机 and

(iv) Literature Time Range

1st January 2005 to 31st December 2019;

(b) The English Keywords Search:

(i) Type of Disease

Subject Headings: Osteoarthritis, Knee; Free Words: Knee Osteoarthritides; Knee Osteoarthritis; Osteoarthritis of Knee; Osteoarthritis of the Knee;

(ii) Intervention Measures

Subject Headings: Acupuncture, Electroacupuncture; Free Words: Acupuncture Treatment; Acupuncture Treatments; Treatment, Acupuncture; Therapy, Acupuncture; Pharmacoacupuncture Treatment; Treatment, Pharmacoacupuncture; Pharmacoacupuncture Therapy; Therapy, Pharmacoacupuncture; Electroacupuncture therapy; Needle warming therapy;

(iii) Type of Study

Subject Heading: randomized controlled trial; Free Words: randomised control; randomised controlled study; randomised controlled experiment; randomized; and

(iv) Literature Time Range

1st January 2005 to 31st December 2019.

2.1.2 Source of Search Database

The relevant sources of databases are such as China National Knowledge Infrastructure (CNKI), Weipu Journal Full-text Database (VIP), Wanfang Data Knowledge Service Platform (Wanfang), China Biology Medicine disc (CBMdisc), PubMed and Embase.

2.1.3 Search Strategy

The combination of "subject headings + free words" is used to search the relevant databases by combining computer search and manual search, and all the search results are downloaded and imported into EndNoteX9 for file management.

The search expression is "① (subject heading or free words) AND ② (subject heading or free words) AND ③ (subject heading or free words) AND ④".

(Note: ① is "Type of Disease"; ② is "Intervention Measures"; ③ is "Type of

Study"; ④ is "Literature Time Range"). For example, take PubMed search as an example:

Search: ((("Osteoarthritis, Knee"[Mesh]) OR ((((Knee Osteoarthritides[Title/Abstract]) OR (Knee Osteoarthritis[Title/Abstract])) OR (Osteoarthritis of Knee[Title/Abstract])) OR (Osteoarthritis of the Knee[Title/Abstract]))) AND (((("Acupuncture"[Mesh]) OR (((((Acupuncture Therapy[Title/Abstract]) OR (Acupuncture Treatment[Title/Abstract])) OR (Acupuncture Treatments[Title/Abstract])) OR (Treatment, Acupuncture[Title/Abstract])) OR (Therapy, Acupuncture[Title/Abstract]))) OR ((((Pharmacoacupuncture Treatment[Title/Abstract]) OR (Treatment, Pharmacoacupuncture[Title/Abstract])) OR (Pharmacoacupuncture Therapy[Title/Abstract])) OR (Therapy, Pharmacoacupuncture[Title/Abstract]))) OR ("Electroacupuncture"[Mesh]))) AND (randomized controlled trial[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract]) Filters: from 2005 – 2019.

2.2 Formulate the Inclusion and Exclusion Criteria of Literature and Acupoints

2.2.1 Literature Inclusion Criteria

The literature inclusion criteria considered are:

(a) Type of Literature

The clinical research literature on acupuncture treatment of KOA, source includes journals, masters and doctoral theses, and conferences. The original research must be a randomized controlled trial, and the literature must indicate that the research types are "randomized controlled trial", "randomized control", "random allocation", "randomized controlled study", "randomized controlled experiment", and "randomized". The language is limited to Chinese and English;

(b) Research Object

The research object in the literature must have a clear diagnosis of traditional Chinese medicine or Western medicine, and the diagnostic results are "knee arthralgia", "knee arthralgia disease", or "knee osteoarthritis", which can include alternative names with the same meaning, such as "degenerative knee joint arthritis", "knee hyperplastic arthritis". There are no restrictions on factors such as age, gender, race, and course of disease for the research object;

(c) Diagnostic Basis

There must be clear international or domestic diagnosis and treatment guidelines and industry-recognized diagnostic and therapeutic evaluation standards for "knee osteoarthritis", such as "Clinical Guidelines for Diagnosis and Treatment of Knee Osteoarthritis (Xi Bi Bing) in Orthopedics and Traumatology of Traditional Chinese Medicine", "Guideline on Diagnosis and Treatment of Osteoarthritis developed by the Orthopaedics Branch of Chinese Medical Association", "Guiding Principles of Clinical Study on New Drug of Traditional Chinese Medicine", Clinical Criteria for KOA Formulated by the American College of Rheumatology (ACR), etc.; or other recognized diagnostic criteria; or have been clearly diagnosed as "Xi Bi Bing", "knee arthralgia", "knee osteoarthritis", "osteoarthritis of the knee", or aliases with the same meaning by Traditional Chinese Medicine or Western Medicine;

(d) Intervention Measures

There are at least two intervention measures. The treatment group (experimental group) or the control group needs to use acupuncture as the main treatment method, including MA, EA, warm needling, acupoint injection, fire needling, acupoint embedding, and so on; there are specific acupuncture prescriptions with clear therapeutic effects; it can be used alone or in combination with other non-surgical treatment methods but must use acupuncture as the main treatment method;

(e) The name of acupoints used in the research must be clear, standardised, and specific: and

(f) Evaluation of research results: The observation indicators and efficacy evaluation criteria are not limited, and can include the Visual Analogue Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Hospital for Special Surgery Scores (HSS), Index of Severity for Osteoarthritis (ISOA), Numerical Rating Scale (NRS), the 12-item Short Form Health Survey (SF-12), the Expectation and Credibility of the Treatment Rating Scale, effective rate, total effective rate, etc., but the obtained results must be valid and effective.

2.2.2 Literature Exclusion Criteria

The literature exclusion criteria considered are:

(a) Type of Literature

A Meta-analysis, systematic review, review, retrospective study, descriptive studies, case report, expert commentary, expert recommendations, physician experience self-report; literature published in abstract form with incomplete descriptions or without full text; literature similar to this article on acupoint selection; non-randomized, non-controlled, non-clinical trial studies;

(b) Research Object

Basic experimental research with animals as research objects, including animal models, animal cytology and animal histology, etc.; the research objects cannot be defined according to the contents of the literature; clinical study that groups patients according to characteristics such as gender, age, and so on; a clinical study that drug interference cannot be excluded; clinical study of unclear diagnosis of KOA; KOA with synovitis as the main symptom; the KOA involved is not a primary disease, but is caused by diseases such as stroke, trauma, infection, gout, autoimmune diseases (Systemic Lupus Erythematosus, SLE), rheumatism, rheumatoid arthritis, malignant tumors, and other diseases;

(c) Diagnostic Basis

The KOA diagnostic and efficacy evaluation criteria used in the literature are not recognized or general standards; the diagnosis is not made according to the existing guidelines or diagnostic criteria; the diagnostic criteria and efficacy evaluation criteria of KOA are self-made;

(d) Intervention Measures

Clinical studies on the treatment of KOA with the following methods as the main intervention measures, but without combined use or control use of acupuncture methods mentioned in the inclusion criteria:

(i) Non-acupuncture therapies: drugs (oral, external application, external cleansing, fumigation), moxibustion, auricular-acupoint sticking, Tuina, massage, acupressure, electromagnetic wave therapy, laser acupuncture, Qigong, shock wave therapy, functional exercise, iontophoresis, etc.;

(ii) Unconventional acupuncture therapies: needle knife treatment, balance acupuncture, scalp acupuncture therapy, cutaneous acupuncture, carpus-ankle acupuncture, plum acupuncture therapy, umbilical acupuncture therapy, abdominal acupuncture, silver needle therapy, holographic acupuncture therapy, ear points acupuncture therapy, internal heat needle therapy, bozhen therapy, bloodletting therapy, intra;

(iii) Arthroscopy, needle knife arthroscopy, knee joint replacement, and other surgical therapies; and release surgery aimed at separating tissue inflammatory adhesions; or

(iv) the methods of surgery combined with acupuncture used to treat KOA in the study.

(e) Literature without specific acupoint description; acupoints are selected outside the scope of the fourteen regular meridian points and extraordinary points;

(f) The sample size in the literature is less than 10 (Ding and Tang, 2019);

(g) The data of the research results are unreliable, and the results obtained are not statistically significant; and

(h) Repeatedly published literature:

For the literature published in different periods based on the same clinical study, only the latest publication will be retained; For the phased reports in different periods of the same long-term clinical study, keep the final published literature (the research has been completed) or the most recent published literature (studies not yet completed); the rest are excluded.

2.2.3 Acupoints Inclusion Criteria

Standardised acupoints are located in the twelve regular meridians, Ren meridian, Du meridian, and extraordinary acupoints, including main points and coordination of acupoints.

2.2.4 Acupoints Exclusion Criteria

The acupoints exclusion criteria are as below:

(a) Acupoints that do not belong to the scope of the fourteen main meridian points or extraordinary acupoints; A'shi acupoint (Tianying point), Shenque point (forbidden to be acupunctured), ear acupoints, trigger points, tender points, and muscle or tendon attachment points;

(b) Acupoints are selected for carpus-ankle acupuncture, holographic acupuncture therapy, abdominal acupuncture, scalp acupuncture therapy, ear points acupuncture therapy, balance acupuncture, and other therapies; and

(c) Dong's extraordinary acupoints (Dong Shi Qi Xue), Jin's three needles (Jin San Zhen), and other self-invented acupoints.

2.3 Literature Collection, Organising and Screening

The literature retrieved from each database was imported into EndNoteX9 software.

According to the established literature inclusion and exclusion criteria, two researchers respectively checked the duplication of the imported literature and removed duplicate literature, and then screened and organised the remaining literature:

(a) Step 1: Used EndNoteX9 software to conduct preliminary check~~s~~ for duplications and remove the duplicate literature which had been imported;

(b) Step 2: Read the titles and abstracts of the literature, and manually screened and removed the duplicate literature according to the title, author, abstract and other information of the literature. For the literature published in different periods based on the same clinical study, only the latest publication could be retained; For the phased reports in different periods of the same long-term clinical study, kept the final published literature (the research has been completed) or the most recent published literature (studies not yet completed); the rest needed to be excluded;

(c) Step 3: Read and screened the literature after the second deduplication, removed the literature that did not meet the inclusion criteria or met the exclusion criteria, and then downloaded the full text of the remaining literature to conduct a more comprehensive review and assessment;

(d) Step 4: Read the full texts, conducted further screening, then retained and organized the valid literature that had been selected from this screening step; and

(e) Step 5: Researchers cross-checked the results of the valid literature kept by each other to determine whether they meet the inclusion and exclusion criteria. For any disputed literature, discussions were held, or a third party to consulted for arbitration. The final selection of literature to be included was determined.

2.4 Data Extraction, Organisation, and Statistical Analysis

2.4.1 Data Extraction and Input

The full text of the final included literature was read again, Microsoft Office 2019 Excel was used to design the data extraction table, data and information extraction was carried out according to the inclusion and exclusion criteria of acupoints, and the database of acupuncture treatment of KOA was established. The extracted data and information mainly include the title of the literature, first author's name, the name of acupoints, intervention method, cooperation method, meridian distribution (channel tropism) of acupoints, acupoint location, etc. If multiple acupoints are used simultaneously in the same meridian in one study, this meridian will only be counted once (for example: in a study, ST36 (Zusanli) and ST35 (Dubi) appear at the same time, both of which belong to the Stomach Meridian of Foot Yangming, then the using frequency of the Stomach Meridian is counted as 1 time).

2.4.2 Standardisation of Acupoints

With reference to "*Acupuncture and Moxibustion*" (New Century 3rd Edition) (Wang and Du, 2012), the names and aliases of acupoints are uniformly standardized. For example, "ST35 (Dubi)" and "Waixiyan" are unified and standardized as "ST35 (Dubi)"; the unified specification of " EX-LE5 (Xiyan)" is "EX-LE4 (Neixieyan) + ST35 (Dubi)"; the unified specification of "Juegu" and "GB39 (Xuanzhong)" is "GB39 (Xuanzhong)"; "Zuyangguan", "GB33 (Xiyangguan)" are standardized as "GB33 (Xiyangguan)"; "Dantianxue" is standardized as "CV4 (Guanyuan)"; "Er Ling" is standardized as "GB34 (Yanglingquan) + SP9 (Yinlingquan)"; "Baliaoxue" is standardized as "BL31 (Shangliao) + BL32 (Ciliao) + BL33 (Zhongliao) + BL34 (Xialiao)".

2.4.3 Statistical Analysis

Upon completion of data and information extraction, the acupoints commonly used in the literature for the acupuncture treatment of KOA were counted. Microsoft Office 2019 Excel and SPSS 22.0 statistical software were used to count the total number of occurrences of the acupoints used. Taking the number of occurrences and rate of occurrence (percentage) as indicators, the relevant acupoints in the kinds of literature were statistically and descriptively analyzed from the aspects of the frequency of use, channel tropism (the belongings to meridians), distance, locations of distribution, and the characteristics of acupoints (specific acupoint attributes), etc. to explore the rules of acupoint selection and features of acupoints used in the treatment of KOA by acupuncture. The top ten highly--researched acupoints were specifically analysed.

3.0 Literature Research Results

3.1 Literature Search Results

According to the strategy and rules of literature research in Section 2.0, the literatures on acupuncture treatment of KOA that had been published in the past 15 years were searched, a total of 7,898 articles were identified. Based on the inclusion and exclusion criteria, and the merged repetitive literatures in the database, 2,264 valid literatures that met the requirements were finally screened out, including 2,220 Chinese literatures and 44 English literatures.

The specific steps and results are shown in Figure 4.1.

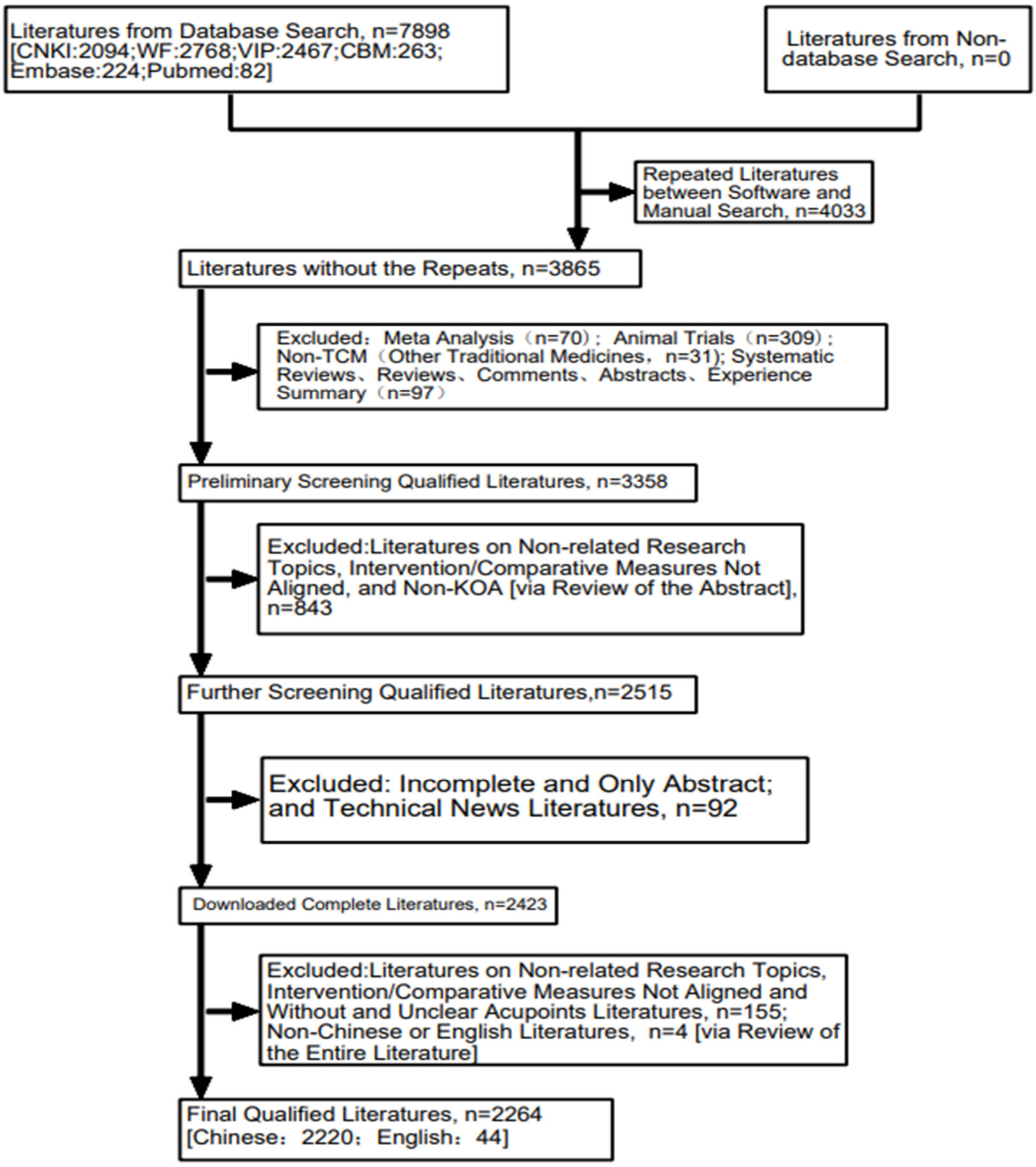

Figure 4.1: Flow Chart of Literature Search and Screening

3.2 Acupoint Extraction Results and Analysis

3.2.1 Results of Final Selected Acupoints and the Analysis of the Number of Occurrences and Rate of Occurrence (Percentage)

According to the inclusion and exclusion criteria of acupoints, after the standardized processing, 139 acupoints commonly used in acupuncture treatment of KOA were finally identified and the frequency of use (unit: times) ranked in descending order as follows:

ST35 (Dubi) (2123), EX-LE4 (Neixieyan) (1977), GB34 (Yanglingquan) (1869), SP10 (Xuehai) (1755), ST36 (Zusanli) (1609), ST34 (Liangqiu) (1558), SP9 (Yinlingquan) (1374), EX-LE2 (Heding) (861), SP6 (Sanyinjiao) (363), GB33 (Xiyangguan) (337), BL40 (Weizhong) (302), BL23 (Shenshu) (269), KI3 (Taixi) (250), GB39 (Xuanzhong) (244), CV4 (Guanyuan) (229), LR8 (Ququan) (160), BL17 (Geshu) (131), CV6 (Qihai) (109), LR3 (Taichong) (104), LI11 (Quchi) (94), LR7 (Xiguan) (83), ST40 (Fenglong) (76), GV14 (Dazhui) (71), GB31 (Fengshi) (63), ST32 (Futu) (61), BL18 (Ganshu) (57), BL57 (Chengshan) (55), BL39 (Weiyang) (52), BL60 (Kunlun) (50), LI4 (Hegu) (46), BL11 (Dazhu) (45), KI10 (Yingu) (43), GB20 (Fengchi) (41), GV3 (Yaoyangguan) (40), BL20 (Pishu) (39), GV4 (Mingmen) (35), GB30 (Huantiao) (23), CV12 (Zhongwan) (23), ST31 (Biguan) (17), BL25 (Dachangshu) (17), SP8 (Diji) (15), PC6 (Neiguan) (15), SP3 (Taibai) (14), BL12 (Fengmen) (13), KI7 (Fuliu) (13), ST44 (Neiting) (13), SP5 (Shangqiu) (13), BL36 (Chengfu) (12), BL55 (Heyang) (12), SP11 (Jimen) (12), Xixia (12), LI10 (Shousanli) (11), SP4 (Gongsun) (9), ST33 (Yinshi) (9), LU5 (Chize) (8), CV17 (Danzhong) (8), LR2 (Xingjian) (7), GV16 (Fengfu) (6), ST41 (Jiexi) (6), GV20 (Baihui) (5), KI4 (Dazhong) (5), PC3 (Quze) (5), BL21 (Weishu) (5), ST43 (Xiangu) (5), BL37 (Yinmen) (5), GB41 (Zulinqi) (5), SI3 (Houxi) (4), GB40 (Qiuxu) (4), HT3 (Shaohai) (4), ST25 (Tianshu) (4), GB36 (Waiqiu) (4), LR9 (Yinbao) (4), KI6 (Zhaohai) (4), BL32 (Ciliao) (4), BL31 (Shangliao) (4), BL56 (Chengjin) (3), SP15 (Daheng) (3), Siqiang (3), ST38 (Tiaokou) (3), TE5 (Waiguan) (3), CV10 (Xiawan) (3), EX-B2 (Yaojiaji) (3), KI1 (Yongquan) (3), LI12 (Zhouliao) (3), GB32 (Zhongdu) (3), BL34 Xialiao (3), BL33 (Zhongliao) (3), ST4 (Dicang) (2), BL58 (Feiyang) (2), BL38 (Fuxi) (2), GB29 (Juliao) (2), KI2 (Rangu) (2), ST37 (Shangjuxu) (2), BL65 (Shugu) (2), TE10 (Tianjing) (2), ST39 (Xiajuxu) (2), SI8 (Xiaohai) (2), Xiliao (2), SI6 (Yanglao) (2), TE4 (Yangchi) (2), SI5 (Yanggu) (2), LI5 (Yangxi) (2), BL54 (Zhibian) (2), EX-UE9 (Baxie) (1), ST42 (Chongyang) (1), BL2 (Cuanzhu) (1), SP2 (Dadu) (1), PC7 (Daling) (1), BL13 (Feishu) (1), BL26 (Guanyuanshu) (1), GB37 (Guangming) (1), ST24 (Huaroumen) (1), LI15 (Jianyu) (1), BL64 (Jinggu) (1), KI8 (Jiaoxin) (1), EX-LE1 (Kuangu) (1), BL28 (Pangguangshu) (1), GV26 (Renzhong) (1), LI3 (Sanjian) (1), BL22 (Sanjiaoshu) (1), ST2 (Sibai) (1), TE9 (Sidu) (1), LI13 (Shouwuli) (1), HT7 (Shenmen) (1), BL62 (Shenmai) (1), CV9 (Shuifen) (1), CV13 (Shangwan) (1), ST26 (Wailing) (1), Xipangxue (1), BL15 (Xinshu) (1), GB43 (Xiaxi) (1), EX-B7 (Yaoyan) (1), GB38 (Yangfu) (1), GB35 (Yangjiao) (1), LR10 (Zuwuli) (1), LR6 (Zhongdu) (1), LR4 (Zhongfeng) (1), BL52 (Zhishi) (1), KI9 (Zhubin) (1).

Note:

(a) Xixia, is an extraordinary acupoint stated in the *Qian Jin Yi Fang (Thousand Ducat Prescriptions)* (Sun, Tang Dynasty). The acupoints are located beneath the knee, below the tip of the patella, at the patellar ligament and on the tibial side of ST35 (Dubi).

(b) Siqiang, is an extraordinary acupoint that is mentioned in the *Chang Yong Xin Yi Liao Fa Shou Ce (Handbook of Common New Medical Methods)* (Guangzhou Military Region Logistics Department Health Division, 1970). The acupoints are located on the midline of the tight extension, 5.5 cun above the midpoint of the patella or 4.5 cun directly above the midpoint of the upper edge of the patella, which is the medial of 1.5 cun below the ST29 (Futu).

(c) Xiliao, is an extraordinary acupoint. The acupoint is documented in the *Jing Wai Qi Xue Hui Bian (Compilation of Extraordinary Acupoints)* (Chinese Acupuncture Research Society, 1951). The acupoint is located at the knee joint, level position with the transverse crease of the popliteal fossa, 3.0 cun directly above the SP9 (Yinlingquan).

(d) Xipang, are extraordinary acupoints that are mentioned in the *Tai Ping Sheng Hui Fang (Peaceful Holy Benevolence Formulae)* (Wang, Northern Song Dynasty). The acupoints are located at the knee, at the inner and outer ends of the popliteal fossa transverse creases.

The top 20 acupoints according to the frequency of use are shown in Figure 4.2 and Table 4.1.

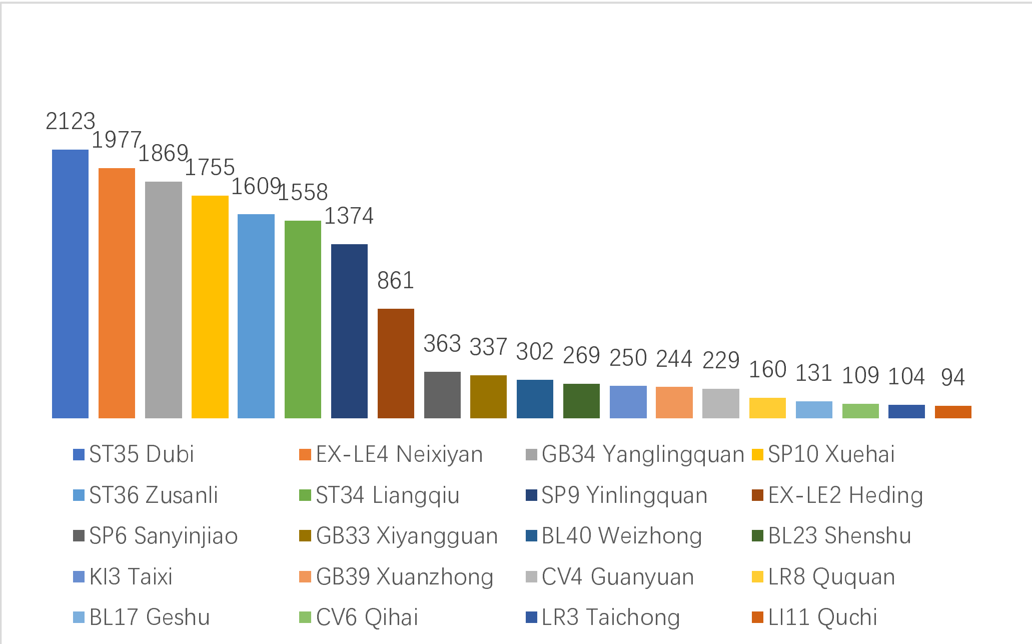

Figure 4.2: Top 20 High-frequency Acupoints for Treatment of KOA (unit: times)

Table 4.1: Top 20 High- frequency Acupoints for Treatment of KOA

No.	Acupoint	No. of occurrence (times)	Rate of occurrence (%)	No.	Acupoint	No. of occurrence (times)	Rate of occurrence (%)
1	ST35	2123	12.46	11	BL40	302	1.77
2	EX-LE4	1977	11.60	12	BL23	269	1.58
3	GB34	1869	10.97	13	KI3	250	1.47
4	SP10	1755	10.30	14	GB39	244	1.43
5	ST36	1609	9.44	15	CV4	229	1.34
6	ST34	1558	9.14	16	LR8	160	0.94
7	SP9	1374	8.06	17	BL17	131	0.77
8	EX-LE2	861	5.05	18	CV6	109	0.64
9	SP6	363	2.13	19	LR3	104	0.61
10	GB33	337	1.98	20	LI11	94	0.55

3.2.2 Meridian Distribution (Channel Tropism) of Acupoints Commonly Used in the Treatment of KOA with Acupuncture

The 139 acupoints commonly used in the literature about the treatment of KOA were classified according to the meridians they locate. And the distribution of the meridians to which acupoints belong was counted according to the total frequency of use of acupoints on each meridian. The meridians to which the 139 acupoints belong were found to cover 12 main meridians, Ren meridian, Du meridian, and the extraordinary points (acupoints beyond the 14 regular meridians).

According to the total usage frequency of acupoints in the order from high to low, the 10 meridians were (unit: times):
Stomach Meridian of Foot Yangming (ST, 5494), Spleen Meridian of Foot Taiyin (SP, 3559), Extraordinary points (EX, 2862), Gallbladder Meridian of Foot

Shaoyang (GB, 2599), Bladder Meridian of Foot Taiyang (BL, 1099), Ren Meridian (CV, 374), Liver Meridian of Foot Jueyin (LR, 361), Kidney Meridian of Foot Shaoyin (KI, 321), Large Intestine Meridian of Hand Yangming (LI, 159), Du Meridian (GV, 158), Pericardium Meridian of Hand Jueyin (PC, 21), Small Intestine Meridian of Hand Taiyang (SI, 10), Lung Meridian of Hand Taiyin (LU, 8), Triple Burner Meridian of Hand Shaoyang (TE, 8), Heart Meridian of Hand Shaoyin (HT, 5).

The Meridians Distribution of Acupoints Commonly Used in the Treatment of KOA with Acupuncture are shown in Table 4.2 and 4.3.

Table 4.2: The No. of Occurrence of the Cited Acupoints and Their Respective Meridians

No.	Meridian	Acupoints (unit: times)
1	ST	ST35 (Dubi)(2123), ST36 (Zusanli)(1609), ST34 (Liangqiu)(1558), ST40 (Fenglong)(76), ST32 (Futu)(61), ST31 (Biguan)(17), ST44 (Neiting)(13), ST33 (Yinshi)(9), ST41 (Jiexi)(6), ST43 (Xiangu)(5), ST25 (Tianshu)(4), ST38 (Tiaokou)(3), ST4 (Dicang)(2), ST37 (Shangjuxu)(2), ST39 (Xiajuxu)(2), ST42 (Chongyang)(1), ST24 (Huaroumen)(1), ST2 (Sibai)(1), ST26 (Wailing)(1)
2	SP	SP10 (Xuehai)(1755), SP9 (Yinlingquan)(1374), SP6 (Sanyinjiao)(363), SP8 (Diji)(15), SP3 (Taibai)(14), SP5 (Shangqiu)(13), SP11 (Jimen)(12), SP4 (Gongsun)(9), SP15 (Daheng)(3), SP2 (Dadu)(1)
3	EX	EX-LE4 (Neixieyan)(1977), EX-LE2 (Heding)(861), Xixia(12), Siqiang(3), EX-B2 (Yaojiaji)(3), Xiliao(2), EX-UE9 (Baxie)(1), EX-LE1 (Kuangu)(1), Xipangxue(1), EX-B7 (Yaoyan)(1)
4	GB	GB34 (Yanglingquan) (1869), GB33 (Xiyangguan)(337), GB39 (Xuanzhong)(244), GB31 (Fengshi)(63), GB20 (Fengchi)(41), GB30 (Huantiao)(23), GB41 (Zulinqi)(5), GB40 (Qiuxu)(4), GB36 (Waiqiu)(4), GB32 (Zhongdu)(3), GB29 (Juliao)(2), GB37 (Guangming)(1), GB43 (Xiaxi)(1), GB38 (Yangfu)(1), GB35 (Yangjiao)(1)
5	BL	BL40 (Weizhong)(302), BL23 (Shenshu)(269), BL17 (Geshu)(131), BL18 (Ganshu)(57), BL57 (Chengshan)(55), BL39 (Weiyang)(52), BL60 (Kunlun)(50), BL11 (Dazhu)(45), BL20 (Pishu)(39), BL25 (Dachangshu)(17), BL12 (Fengmen)(13), BL36 (Chengfu)(12), BL55 (Heyang)(12), BL21 (Weishu)(5), BL37 (Yinmen)(5), BL32 (Ciliao)(4), BL31 (Shangliao)(4), BL56 (Chengjin)(3), BL34 Xialiao(3), BL33 (Zhongliao)(3), BL58 (Feiyang)(2), BL38 (Fuxi)(2),

No.	Meridian	Acupoints (unit: times)
5	BL	BL65 (Shugu)(2), BL54 (Zhibian)(2), BL2 (Cuanzhu)(1), BL13 (Feishu)(1), BL26 (Guanyuanshu)(1), BL64 (Jinggu)(1), BL28 (Pangguangshu)(1), BL22 (Sanjiaoshu)(1), BL62 (Shenmai)(1), BL15 (Xinshu)(1), BL52 (Zhishi)(1), KI9 (Zhubin)(1)
6	CV	CV4 (Guanyuan)(229), CV6 (Qihai)(109), CV12 (Zhongwan)(23), CV17 (Danzhong)(8), CV10 (Xiawan)(3), CV9 (Shuifen)(1), CV13 (Shangwan)(1)
7	LR	LR8 (Ququan)(160), LR3 (Taichong)(104), LR7 (Xiguan)(83), LR2 (Xingjian)(7), LR9 (Yinbao)(4), LR10 (Zuwuli)(1), LR6 (Zhongdu)(1), LR4 (Zhongfeng)(1)
8	KI	KI3 (Taixi)(250), KI10 (Yingu)(43), KI7 (Fuliu)(13), KI4 (Dazhong)(5), KI6 (Zhaohai)(4), KI1 (Yongquan)(3), KI2 (Rangu)(2), KI8 (Jiaoxin)(1)
9	LI	LI11 (Quchi)(94), LI4 (Hegu)(46), LI10 (Shousanli)(11), LI12 (Zhouliao)(3), LI5 (Yangxi)(2), LI15 (Jianyu)(1), LI3 (Sanjian)(1), LI13 (Shouwuli)(1)
10	GV	GV14 (Dazhui)(71), GV3 (Yaoyangguan)(40), GV4 (Mingmen)(35), GV16 (Fengfu)(6), GV20 (Baihui)(5), GV26 (Renzhong)(1)
11	PC	PC6 (Neiguan)(15), PC3 (Quze)(5), PC7 (Daling)(1)
12	SI	SI3 (Houxi)(4), SI8 (Xiaohai)(2), SI6 (Yanglao)(2), SI5 (Yanggu)(2)
13	LU	LU5 (Chize)(8)
14	TE	TE5 (Waiguan)(3), TE10 (Tianjing)(2), TE4 (Yangchi)(2), TE9 (Sidu)(1)
15	HT	HT3 (Shaohai)(4), HT7 (Shenmen)(1)

Table 4.3: Meridian Distribution of Acupoints Commonly Used in the Treatment of KOA with Acupuncture

No.	Meridian	No. of Occurrence (times)	No. of Acupoints	No.	Meridian	No. of Occurrence (times)	No. of Acupoints
1	ST	5494	19	9	LI	159	8
2	SP	3559	10	10	GV	158	6
3	EX	2862	10	11	PC	21	3
4	GB	2599	15	12	SI	10	4
5	BL	1099	34	13	LU	8	1
6	CV	374	7	14	TE	8	4
7	LR	361	8	15	HT	5	2
8	KI	321	8				

3.2.3 Analysis of the Distance from the Selected Acupoints in the Treatment of KOA with Acupuncture

Based on the distance between acupoints and the lesion (knee joint), the 139 acupoints were divided into two categories - Proximal part (located near the knee joint) and Distal Part (located far away). 21 acupoints were selected from the proximal part, and the total frequency of use was 14,137 times (the rate of occurrence was 82.97%); 118 acupoints were selected from the distal part with a total usage frequency of 2901 times (the rate of occurrence was 17.03%). The results showed that, in acupuncture treatment of KOA, although the number of acupoints selected at the proximal part was less than those in the distal part, the frequency of use of acupoints near the knee joint was much higher than that of acupoints located far away. This indicates that the acupoints used for acupuncture to treat KOA are mainly selected from the proximal parts (at, nearby or around the knee joint), and supplemented by selected acupoints from the distal part.

Specific results are shown in Table 4.4 and Table 4.5.

Table 4.4: The Selected Acupoints at the Proximal or Distal Part

Proximal or Distal Part	Acupoints (unit: times)
Proximal Part	ST35 (Dubi)(2123), EX-LE4 (Neixieyan)(1977), GB34 (Yanglingquan)(1869), SP10 (Xuehai)(1755), ST36 (Zusanli)(1609), ST34 (Liangqiu)(1558), SP9 (Yinlingquan)(1374), EX-LE2 (Heding)(861), GB33 (Xiyangguan)(337), BL40 (Weizhong)(302), LR8 (Ququan)(160), LR7 (Xiguan)(83), BL39 (Weiyang)(52), KI10 (Yingu)(43), BL55 (Heyang)(12), Xixia(12), LR9 (Yinbao)(4), BL38 (Fuxi)(2), Xiliao(2), EX-LE1 (Kuangu)(1), Xipangxue(1)

Proximal or Distal Part	Acupoints (unit: times)
Distal Part	SP6 (Sanyinjiao)(363), BL23 (Shenshu)(269), KI3 (Taixi)(250), GB39 (Xuanzhong)(244), CV4 (Guanyuan)(229), BL17 (Geshu)(131), CV6 (Qihai)(109), LR3 (Taichong)(104), LI11 (Quchi)(94), ST40 (Fenglong)(76), GV14 (Dazhui)(71), GB31 (Fengshi)(63), ST32 (Futu)(61), BL18 (Ganshu)(57), BL57 (Chengshan)(55), BL60 (Kunlun)(50), LI4 (Hegu)(46), BL11 (Dazhu)(45), GB20 (Fengchi)(41), GV3 (Yaoyangguan)(40), BL20 (Pishu)(39), GV4 (Mingmen)(35), GB30 (Huantiao)(23), CV12 (Zhongwan)(23), ST31 (Biguan)(17), BL25 (Dachangshu)(17), SP8 (Diji)(15), PC6 (Neiguan)(15), SP3 (Taibai)(14), BL12 (Fengmen)(13), KI7 (Fuliu)(13), ST44 (Neiting)(13), SP5 (Shangqiu)(13), BL36 (Chengfu)(12), SP11 (Jimen)(12), LI10 (Shousanli)(11), SP4 (Gongsun)(9), ST33 (Yinshi)(9), LU5 (Chize)(8), CV17 (Danzhong)(8), LR2 (Xingjian)(7), GV16 (Fengfu)(6), ST41 (Jiexi)(6), GV20 (Baihui)(5), KI4 (Dazhong)(5), PC3 (Quze)(5), BL21 (Weishu)(5), ST43 (Xiangu)(5), BL37 (Yinmen)(5), GB41 (Zulinqi)(5), SI3 (Houxi)(4), GB40 (Qiuxu)(4), HT3 (Shaohai)(4), ST25 (Tianshu)(4), GB36 (Waiqiu)(4), KI6 (Zhaohai)(4), BL32 (Ciliao)(4), BL31 (Shangliao)(4), BL56 (Chengjin)(3), SP15 (Daheng)(3), Siqiang(3), ST38 (Tiaokou)(3), TE5 (Waiguan)(3), CV10 (Xiawan)(3), EX-B2 (Yaojiaji)(3), KI1 (Yongquan)(3), LI12 (Zhouliao)(3), GB32 (Zhongdu)(3), BL34 Xialiao(3), BL33 (Zhongliao)(3), ST4 (Dicang)(2), BL58 (Feiyang)(2), GB29 (Juliao)(2), KI2 (Rangu)(2), ST37 (Shangjuxu)(2), BL65 (Shugu)(2), TE10 (Tianjing)(2), ST39 (Xiajuxu)(2), SI8 (Xiaohai)(2), SI6 (Yanglao)(2), TE4 (Yangchi)(2), SI5 (Yanggu)(2), LI5 (Yangxi)(2), BL54 (Zhibian)(2), EX-UE9 (Baxie)(1), ST42 (Chongyang)(1), BL2 (Cuanzhu)(1), SP2 (Dadu)(1), PC7 (Daling)(1), BL13 (Feishu)(1), BL26 (Guanyuanshu)(1), GB37 (Guangming)(1), ST24 (Huaroumen)(1), LI15 (Jianyu)(1), BL64 (Jinggu)(1), KI8 (Jiaoxin)(1), BL28 (Pangguangshu)(1), GV26 (Renzhong)(1), LI3 (Sanjian)(1), BL22 (Sanjiaoshu)(1), ST2 (Sibai)(1), TE9 (Sidu)(1), LI13 (Shouwuli)(1), HT7 (Shenmen)(1), BL62 (Shenmai)(1), CV9 (Shuifen)(1), CV13 (Shangwan)(1), ST26 (Wailing)(1), BL15 (Xinshu)(1), GB43 (Xiaxi)(1), EX-B7 (Yaoyan)(1), GB38 (Yangfu)(1), GB35 (Yangjiao)(1), LR10 (Zuwuli)(1), LR6 (Zhongdu)(1), LR4 (Zhongfeng)(1), BL52 (Zhishi)(1), KI9 (Zhubin)(1)

Table 4.5: The Distance of the Selected Acupoints in the Treatment of KOA with Acupuncture

No.	Proximal or Distal part	No. of occurrence (times)	Rate of occurrence (%)	No. of acupoints	Rate of acupoints (%)
1	Proximal Part	14137	82.97	21	15.11
2	Distal Part	2901	17.03	118	84.89

3.2.4 The Analysis of the Distribution of Commonly Used Acupoints in

the Treatment of KOA by Acupuncture

In this analysis, the human body was divided into five major parts: head and neck, chest and abdomen, waist and back, upper limbs, and lower limbs. Then classification and statistical analysis were conducted on the distribution of the final 139 acupoints included. The distribution of the 139 acupoints in the five major parts of the human body was further counted and categorised based on the total frequency of their usage in each part.

The total frequency of the acupoints used in each part of the body (unit: times) were ranked in descending order as follows: Lower limbs: 74 acupoints, used a total of 15,638 times (the rate of occurrence is 91.78%); Waist and back: 23 acupoints, used a total of 677 times (the rate of occurrence is 3.97%)); Chest and Abdomen: 11 points, used 383 times (the rate of occurrence is 2.25%); Upper limbs: 23 points, used 212 times (the rate is 1.24%); Head and Neck: 8 points, used 128 times (the rate is 0.75 %). The results showed that the acupoints used by acupuncture for KOA were mainly concentrated at the lower limbs, and the acupoints were mainly selected from the proximal and local parts (at, near, or around the knee joint), which reflected the rule of local acupoint selection, and conformed the principle in the theory of acupuncture that "where the acupoints are located, that are where the main treatment is concerned".

Specific results are shown in Table 4.6 and Table 4.7.

Table 4.6: The Distribution of Acupoints and Their Respective Body Parts

Part of Body	Acupoints (unit: times)
Lower Limbs	ST35 (Dubi)(2123), EX-LE4 (Neixieyan)(1977), GB34 (Yanglingquan)(1869), SP10 (Xuehai)(1755), ST36 (Zusanli)(1609), ST34 (Liangqiu)(1558), SP9 (Yinlingquan)(1374), EX-LE2 (Heding)(861), SP6 (Sanyinjiao)(363), GB33 (Xiyangguan)(337), BL40 (Weizhong)(302), KI3 (Taixi)(250), GB39 (Xuanzhong)(244), LR8 (Ququan)(160), LR3 (Taichong)(104), LR7 (Xiguan)(83), ST40 (Fenglong)(76), GB31 (Fengshi)(63), ST32 (Futu)(61), BL57 (Chengshan)(55), BL39 (Weiyang)(52), BL60 (Kunlun)(50), KI10 (Yingu)(43), GB30 (Huantiao)(23), ST31 (Biguan)(17), SP8 (Diji)(15), SP3 (Taibai)(14), KI7 (Fuliu)(13), ST44 (Neiting)(13), SP5 (Shangqiu)(13), BL36 (Chengfu)(12), BL55 (Heyang)(12), SP11 (Jimen)(12), Xixia(12), SP4 (Gongsun)(9), ST33 (Yinshi)(9), LR2 (Xingjian)(7), ST41 (Jiexi)(6), KI4 (Dazhong)(5), ST43 (Xiangu)(5), BL37 (Yinmen)(5), GB41 (Zulinqi)(5), GB40 (Qiuxu)(4), GB36 (Waiqiu)(4), LR9 (Yinbao)(4), KI6 (Zhaohai)(4), BL56 (Chengjin)(3), Siqiang(3), ST38 (Tiaokou)(3), KI1 (Yongquan)(3), GB32 (Zhongdu)(3), BL58 (Feiyang)(2), BL38 (Fuxi)(2), GB29 (Juliao)(2), KI2 (Rangu)(2), ST37 (Shangjuxu)(2), BL65 (Shugu)(2), ST39 (Xiajuxu)(2), Xiliao(2), ST42 (Chongyang)(1), SP2 (Dadu)(1), GB37 (Guangming)(1), BL64 (Jinggu)(1), KI8 (Jiaoxin)(1), EX-LE1 (Kuangu)(1), BL62 (Shenmai)(1), Xipangxue(1), GB43 (Xiaxi)(1), GB38 (Yangfu)(1), GB35 (Yangjiao)(1), LR10 (Zuwuli)(1), LR6 (Zhongdu)(1), LR4 (Zhongfeng)(1), KI9 (Zhubin)(1)
Waist and Back	BL23 (Shenshu)(269), BL17 (Geshu)(131), BL18 (Ganshu)(57), BL11 (Dazhu)(45), GV3 (Yaoyangguan)(40), BL20 (Pishu)(39), GV4 (Mingmen)(35), BL25 (Dachangshu)(17), BL12 (Fengmen)(13), BL21 (Weishu)(5), BL32 (Ciliao)(4), BL31 (Shangliao)(4), EX-B2 (Yaojiaji)(3), BL34 Xialiao(3), BL33 (Zhongliao)(3), BL54 (Zhibian)(2), BL13 (Feishu)(1), BL26 (Guanyuanshu)(1), BL28 (Pangguangshu)(1), BL22 (Sanjiaoshu)(1), BL15 (Xinshu)(1), EX-B7 (Yaoyan)(1), BL52 (Zhishi)(1)
Chest and Abdomen	CV4 (Guanyuan)(229), CV6 (Qihai)(109), CV12 (Zhongwan)(23), CV17 (Danzhong)(8), ST25 (Tianshu)(4), SP15 (Daheng)(3), CV10 (Xiawan)(3), ST24 (Huaroumen)(1), CV9 (Shuifen)(1), CV13 (Shangwan)(1), ST26 (Wailing)(1)
Upper Limbs	LI11 (Quchi)(94), LI4 (Hegu)(46), PC6 (Neiguan)(15), LI10 (Shousanli)(11), LU5 (Chize)(8), PC3 (Quze)(5), SI3 (Houxi)(4), HT3 (Shaohai)(4), TE5 (Waiguan)(3), LI12 (Zhouliao)(3), TE10 (Tianjing)(2), SI8 (Xiaohai)(2), SI6 (Yanglao)(2), TE4 (Yangchi)(2), SI5 (Yanggu)(2), LI5 (Yangxi)(2), EX-UE9 (Baxie)(1), PC7 (Daling)(1), LI15 (Jianyu)(1), LI3 (Sanjian)(1), TE9 (Sidu)(1), LI13 (Shouwuli)(1), HT7 (Shenmen)(1)
Head and Neck	GV14 (Dazhui)(71), GB20 (Fengchi)(41), GV16 (Fengfu)(6), GV20 (Baihui)(5), ST4 (Dicang)(2), BL2 (Cuanzhu)(1)、GV26 (Renzhong)(1), ST2 (Sibai)(1)

Table 4.7: The Distribution of Body Parts of Acupoints Commonly Used in the Treatment of KOA with Acupuncture

No.	Part of Body	No. of Occurrence (times)	Rate of Occurrence (%)	No. of Acupoints	Rate of Acupoints (%)
1	Lower Limbs	15638	91.78	74	53.24
2	Waist and Back	677	3.97	23	16.55
3	Chest and Abdomen	383	2.25	11	7.91
4	Upper Limbs	212	1.24	23	16.55
5	Head and Neck	128	0.75	8	5.76

3.2.5 The Analysis of the Characteristics and Special Attributes of the Acupoints Commonly Used in the KOA Treatment with Acupuncture

The 139 commonly used acupoints were classified according to the types of acupoints' special attributes (specific acupoints). Due to significant differences in the records of the "confluent points"(Confluence Acupoints, Jiaohuixue) in various historical works of literature, the names and numbers of acupoints for these "confluent points" varied greatly. Therefore, in this study, the "confluent points" were not counted and analysed. The statistical results showed that the total frequency of specific acupoints from high to low (unit: times) was: Five-shu Acupoints (Wushuxue): 36 points, used a total of 5,974 times (frequency: 35.06%); Lower-he Acupoints (Xiahexue): 6 points, used a total of 3,836 times time (frequency: 22.51%); Eight-hui Acupoints (Bahuixue): 6 points, used 2,320 times (frequency: 13.62%); Xi Acupoints (Xixue): 8 points, used 1,583 times (frequency: 9.29%); Original Acupoints (Yuanxue): 10 points, used 424 times (frequency: 2.49%); Back-shu Acupoints (Beishuxue): 9 points, used 391 times (frequency: 2.29%); Front-mu Acupoints (Muxue): 4 points, used 264 times (frequency: 1.55%); Luo-connecting Acupoints (Luoxue): 7 points, used a total of 111 times (frequency: 0.65%); Eight Confluence Acupoints (Ba mai jiao hui xue): 7 points, used a total of 41 times (frequency: 0.24%).

See Table 4.8 and Table 4.9 for details.

Among the Five-shu Acupoints, according to the total frequency of use of acupoints, from high to low, they were as follows: He Acupoints: 5,472 times (frequency: 32.12%); Shu Acupoints: 387 times (frequency: 2.27%); Jing Acupoints: 88 times (frequency: 0.52%); Xing Acupoints: 24 times (frequency 0.14%); Well Acupoints: 3 times (frequency 0.02%).

Specific results are shown in Table 4.10 and Table 4.11.

The results showed that the most used specific acupoints for acupuncture treatment of KOA were Five-shu Acupoints, followed by Lower-he Acupoints and Eight-hui Acupoints. Among the Five-shu Acupoints, the He Acupoints are the most used especially the GB34 (Yanglingquan), with total usage of 1,869 times.

Table 4.8: The Acupoints of Their Respective Specific Acupoints

Specific Acupoints	Acupoints (unit: times)
Five-shu Acupoints	GB34 (Yanglingquan)(1869), ST36 (Zusanli)(1609), SP9 (Yinlingquan)(1374), BL40 (Weizhong)(302), KI3 (Taixi)(250), LR8 (Ququan)(160), LR3 (Taichong)(104), LI11 (Quchi)(94), BL60 (Kunlun)(50), KI10 (Yingu)(43), SP3 (Taibai)(14), ST44 (Neiting)(13), SP5 (Shangqiu)(13), KI7 (Fuliu)(13), LU5 (Chize)(8), LR2 (Xingjian)(7), ST41 (Jiexi)(6), PC3 (Quze)(5), ST43 (Xiangu)(5), GB41 (Zulinqi)(5), SI3 (Houxi)(4), HT3 (Shaohai)(4), KI1 (Yongquan)(3), KI2 (Rangu)(2),

Specific Acupoints	Acupoints (unit: times)
Five-shu Acupoints	BL65 (Shugu)(2), TE10 (Tianjing)(2), SI8 (Xiaohai)(2), SI5 (Yanggu)(2), LI5 (Yangxi)(2), SP2 (Dadu)(1), PC7 (Daling)(1), LI3 (Sanjian)(1), HT7 (Shenmen)(1), GB43 (Xiaxi)(1), GB38 (Yangfu)(1), LR4 (Zhongfeng)(1)
Lower-he Acupoints	GB34 (Yanglingquan)(1869), ST36 (Zusanli)(1609), BL40 (Weizhong)(302), BL39 (Weiyang)(52), ST37 (Shangjuxu)(2), ST39 (Xiajuxu)(2)
Eight-hui Acupoints	GB34 (Yanglingquan)(1869), GB39 (Xuanzhong)(244), BL17 (Geshu)(131), BL11 (Dazhu)(45), CV12 (Zhongwan)(23), CV17 (Danzhong)(8)
Xi Acupoints	ST34 (Liangqiu)(1558), SP8 (Diji)(15), GB36 (Waiqiu)(4), SI6 (Yanglao)(2), LR6 (Zhongdu)(1), KI8 (Jiaoxin)(1), GB35 (Yangjiao)(1), KI9 (Zhubin)(1)
Original Acupoints	KI3 (Taixi)(250), LR3 (Taichong)(104), LI4 (Hegu)(46), SP3 (Taibai)(14), GB40 (Qiuxu)(4), TE4 (Yangchi)(2), ST42 (Chongyang)(1), PC7 (Daling)(1), BL64 (Jinggu)(1), HT7 (Shenmen)(1)
Back-shu Acupoints	BL23 (Shenshu)(269), BL18 (Ganshu)(57), BL20 (Pishu)(39), BL25 (Dachangshu)(17), BL21 (Weishu)(5), BL13 (Feishu)(1), BL28 (Pangguangshu)(1), BL22 (Sanjiaoshu)(1), BL15 (Xinshu)(1)
Front-mu Acupoints	CV4 (Guanyuan)(229), CV12 (Zhongwan)(23), CV17 (Danzhong)(8), ST25 (Tianshu)(4)
Luo-connecting Acupoints	ST40 (Fenglong)(76), PC6 (Neiguan)(15), SP4 (Gongsun)(9), KI4 (Dazhong)(5), TE5 (Waiguan)(3), BL58 (Feiyang)(2), GB37 (Guangming)(1)
Eight Confluence Acupoints	PC6 (Neiguan)(15), SP4 (Gongsun)(9), GB41 (Zulinqi)(5), SI3 (Houxi)(4), KI6 (Zhaohai)(4), TE5 (Waiguan)(3), BL62 (Shenmai)(1)

Table 4.9: The Specific Acupoints Used in the Treatment of KOA with Acupuncture

No.	Specific Acupoints	No. of occurrence (times)	Rate of occurrence (%)	No. of acupoints	Rate of acupoints (%)
1	Five-shu Acupoints	5974	35.06	36	25.90
2	Lower-he Acupoints	3836	22.51	6	4.32
3	Eight-hui Acupoints	2320	13.62	6	4.32
4	Xi Acupoints	1583	9.29	8	5.76
5	Original Acupoints	424	2.49	10	7.19
6	Back-shu Acupoints	391	2.29	9	6.47
7	Front-mu Acupoints	264	1.55	4	2.88
8	Luo-connecting Acupoints	111	0.65	7	5.04
9	Eight Confluence Acupoints	41	0.24	7	5.04

Table 4.10: The Acupoints of Their Respective Five-shu Acupoints

Five-shu Acupoints	Acupoints (unit: times)
He Acupoints	GB34 (Yanglingquan)(1869), ST36 (Zusanli)(1609), SP9 (Yinlingquan)(1374), BL40 (Weizhong)(302), LR8 (Ququan)(160), LI11 (Quchi)(94), KI10 (Yingu)(43), LU5 (Chize)(8), PC3 (Quze)(5), HT3 (Shaohai)(4), TE10 (Tianjing)(2), SI8 (Xiaohai)(2)
Shu Acupoints	KI3 (Taixi)(250), LR3 (Taichong)(104), SP3 (Taibai)(14), ST43 (Xiangu)(5), GB41 (Zulinqi)(5), SI3 (Houxi)(4), BL65 (Shugu)(2), PC7 (Daling)(1), LI3 (Sanjian)(1), HT7 (Shenmen)(1)
Jing Acupoints	BL60 (Kunlun)(50), SP5 (Shangqiu)(13), KI7 (Fuliu)(13), ST41 (Jiexi)(6), SI5 (Yanggu)(2), LI5 (Yangxi)(2), GB38 (Yangfu)(1), LR4 (Zhongfeng)(1)
Xing Acupoints	ST44 (Neiting)(13), LR2 (Xingjian)(7), KI2 (Rangu)(2), SP2 (Dadu)(1), GB43 (Xiaxi)(1)
Well Acupoints	KI1 (Yongquan)(3)

Table 4.11: The Distribution of Five-shu Acupoints Used in the Treatment of KOA with Acupuncture

No.	Five-shu Acupoints	No. of Occurrence (times)	Rate of Occurrence (%)	No. of Acupoints	Rate of Acupoints (%)
1	He Acupoints	5472	32.12	12	8.63
2	Shu Acupoints	387	2.27	10	7.19
3	Jing Acupoints	88	0.52	8	5.76
4	Xing Acupoints	24	0.14	5	3.60
5	Well Acupoints	3	0.02	1	0.72

4.0 Discussion

Knee Osteoarthritis (KOA) is a disease which based on primary or secondary degenerative pathological changes of knee articular cartilage (Xie et al., 2020; Xu et al., 2020). In China, the prevalence of symptomatic KOA with clear diagnosis and symptoms is about 8.1%, and continues to increase year by year with age (Peng et al., 2021; Tang et al., 2016). This disease belongs to the category of "arthritis", "Bi Syndrome", and "Bizheng" in Traditional Chinese

Medicine. It mainly manifests as knee joint swelling, pain, deformity, and dysfunction (Cao and Yang, 2019), which seriously reduces the life quality of patients, and increases the burden on the families and society (Li and Zhao, 2022).

Clinical practice and previous literature reports have shown that acupuncture has the effects of promoting Qi and Blood circulation, removing blood stasis, reducing swelling, relieving pain, dredging and activating collaterals, and relaxing tendons (Zhang, 2021). The application of acupuncture in the treatment of KOA has a clear analgesic effect, which can better relieve symptoms and reduce the frequency of recurrence, improve the range of motion of the joints, and has advantages such as long-lasting aftereffects and no significant side effects (Li et al., 2022; Zhu et al., 2021; Cheng and Ye, 2020). Based on these benefits, this study analysed and studied the RCT literatures on acupuncture treatment of KOA published in the past 15 years, and used literature search, data extraction and data analysis to screen and summarise the top ten high-frequency acupoints for acupuncture treatment of KOA; analyzed and summarized the acupoint selection rules for acupuncture treatment of KOA; and established a basic and general acupuncture prescription for acupuncture treatment of KOA, providing a reference and theoretical guidance for optimising clinical treatment of KOA.

The following analyses and discusses various aspects of the study such as the frequency of acupoints used, channel tropism (the belongings to meridians), distance, locations of distribution, and the characteristics of acupoints (specific acupoint attributes).

4.1 Frequency of Acupoints Used

4.1.1 Analysis of the Results of the Frequency of Acupoints Used

A total of 139 acupoints are commonly used for acupuncture treatment of KOA, with a total frequency of 17,038 times, and the average use of each acupoint is about 123 times. There are 17 acupoints with a frequency of use greater than the average (123 times/acupoint), with a frequency of use of 15,411 times, accounting for 90.45% of the total frequency of all acupoints used. The total frequency of use for the top 10 highly-researched acupoints is 13,826 times, accounting for 81.15% of the total frequency of all acupoints used. These 139 commonly used acupoints are arranged in descending order of frequency of use, the top 10 high-frequency acupoints are (unit: times): ST35 (Dubi) (2123), EX-LE4 (Neixieyan) (1977), GB34 (Yanglingquan) (1869), SP10 SP10 (Xuehai) (1755), ST36 (Zusanli) (1609), ST34 (Liangqiu) (1558), SP9 (Yinlingquan) (1374), EX-LE2 (Heding) (861), SP6 (Sanyinjiao) (363), and GB33 (Xiyangguan) (337).

4.1.2 Analysis of the Top 10 Highly-researched Acupoints

The specific analysis of the top 10 highly-researched acupoints are as below:

(a) "ST35 (Dubi) ", derived from *Su Wen · Qi Xue Lun (Plain Questions · Qi Acupoints Theory)* of the *Huang Di Nei Jing (Yellow Emperor's Inner Canon)* translated and annotated by Yao (2022), also known as the outer knee eye (Wai Xi Yan), and belongs to the Stomach Meridian of Foot Yangming (ST). It is located in the anterior area of the knee, in the depression lateral to the patellar ligament when the knee joint is flexed. The *Ling Shu · Ben Shu* of the *Ling Shu (the Spiritual Pivot)* edited and compiled by Tian and Liu (2005) records that "For patients whose lower limbs (knee joints) cannot be straightened after being bent, the ST35 (Dubi) can be acupunctured", indicating that this acupoint can be used to treat difficulty in knee joint flexion and extension. It has the effect of dredging meridian and activating collaterals, dispelling wind and cold, reducing swelling, relieving pain, tonifying Qi and Blood, and regulating immunity; it is mainly used to treat knee joint pain, numbness, lower limb paralysis, poor flexion and extension, difficulty in squatting and standing up flexibly (Zhang, 2020), and other lower limb and knee joint diseases (Yang et al., 2019). It is the opposite of "EX-LE4 (Neixieyan) ";

(b) “EX-LE4 (Neixieyan)” is from the book *Bei Ji Qian Jin Yao Fang (Essential Formulas Worth a Thousand Gold for Emergencies)* (Sun, Tang Dynasty) and another study (Li et al., 2021) claiming that this acupoint is recorded in "Hua Tuo Acupuncture Classic" (Hua Tuo Zhen Jiu Jing), belongs to Extra Acupoints. It is located in the area of the knee, at the central depression on the inner side of the patellar ligament in the knee. According to the book *Tai Ping Sheng Hui Fang (Peaceful Holy Benevolence Formulae)* (Wang, Northern Song Dynasty), "The four acupoints of the Xi Yan are located on both sides beneath the patella, at the center of the inner and outer depressions of the patellar ligament. They are mainly used to treat coldness and pain in the knee joint. These acupoints are not suitable for moxibustion treatment. *Wai Ke Da Cheng (The Great Compendium of Surgery)* (Qi, Qing Dynasty) states, " Xi Yan acupoints, used to treat "He Xi Feng" (KOA), located in the depression on both sides of the lower knee joint. EX-LE4 (Neixieyan) has the function of promoting blood circulation, dredging collaterals, regulating and smoothing the knee joints. It is mainly used to treat knee pain, lower limb pain, KOA, inflammation of the tissue around the knee joint of the knee, lower limb paralysis, patella osteomalacia, and other disease conditions.

Acupuncture or moxibustion on the two acupoints “ST35 (Dubi)” and “EX-LE4 (Neixieyan)” can dredge the meridians and smooth the joints, thereby reducing knee joint pain and improving knee joint mobility (Sun, 2011);

(c) "GB34 (Yanglingquan)", from the book *Ling Shu · Ben Shu* edited and compiled by Tian and Liu (2005), belongs to the Gallbladder Meridian of Foot Shaoyang, which is the place where the Qi of Gallbladder Meridian of Foot-Shaoyang (GB) gathers and confluence, it is also the Xiahexue (lower confluent point) of the gallbladder, and also is the tendon meeting point of Eight-hui Acupoints. It is located on the lateral side of the lower limb, in the depression anteriorly and lower to the head of the fibula. Acupuncture and moxibustion in GB34 (Yanglingquan) can relax meridians and activate collaterals, strengthen muscles and bones, and improve the flexion and extension function of the knee joint, so it is mainly used for swelling and pain in the knee joint, numbness of the lower limbs, muscle atrophy, etc. (Zou et al., 2018; Wang, 2020) The tendons gather in "GB34 (Yanglingquan)". Therefore, this acupoint is often selected for the treatment of KOA, and other diseases of the lower limbs;

(d) "SP10 (Xuehai)" means where the blood gathering, is recorded in *Zhen Jiu Jia Yi Jing (The A-B Classics of Acupuncture and Moxibustion)* (Huangfu, Jin Dynasty), and belongs to the Spleen Meridian of Foot Taiyin (SP). It is located in the anterior region of the thigh, 2 cun above the inner lower edge of the patella, at the site of the bulge of the vastus medialis. Studies have shown (Zhang, 2021; Lin et al., 2022; Xiao et al., 2020) that SP10 (Xuehai) point influences the supply and speed of blood flow. Acupuncture and moxibustion on this acupoint can remove blood stasis and dredge the meridian, by regulating the release of vasoactive factors, changing the shape of capillaries, accelerating the blood flow rate, and changing the hypercoagulable state of the blood (Zhao et al., 2004);

(e) "ST36 (Zusanli)", from *Ling Shu · Ben Shu* edited and compiled by Tian and Liu (2005), belongs to the Stomach Meridian of Foot Yangming (ST). It is the He acupoint (Hexue) of the Stomach Meridian of Foot-Yangming. It locates on the lateral side of the lower limb, 3 cun below ST35 (Dubi), on the line connecting ST35 (Dubi) and ST41 (Jiexi), one finger-breadth transverse to the outside of the anterior crest of the tibia. It is mainly used for the treatment of paralysis of the lower limbs. Previous studies (Zhu, 2020; Guan et al., 2020) have shown that acupuncture at ST36 (Zusanli) can moisten the tendons, dredge the meridian, and smooth the joints, and warm acupuncture at this acupoint can warm the meridians, dispel wind and dampness, replenish Qi, strengthen the body and eliminate pathogenic factors, thereby regulating the immune function of the body. Therefore, it can improve the local blood circulation of the knee joint and lower limbs, promote the absorption of inflammatory mediators, and reduce the inflammatory response of KOA (Guan et al., 2020), thereby improving knee stiffness, swelling, pain, and other symptoms;

(f) "ST34 (Liangqiu)", from *Zhen Jiu Jia Yi Jing (The A-B Classics of Acupuncture and Moxibustion)* (Huangfu, Jin Dynasty), belongs to the Stomach Meridian of Foot-Yangming (ST). It is the Xi acupoint (Xixue) of the Stomach Meridian of Foot-Yangming. It locates in the anterior region of the thigh, 2 cun above the bottom of the patella, between the vastus lateralis and the rectus femoris tendon. It is mainly used to treat diseases of the waist and knee joints, such as pain, clod and numbness of lower limbs, knees, feet and waist; joints difficulty in squatting, flexion and extension (Zou et al., 2021). *Zhen Jiu Jia Yi Jing (The A-B Classics of Acupuncture and Moxibustion)* (Huangfu, Jin Dynasty) says: "The knee joint cannot be flexed or stretched, and people cannot walk because of knee joint disease. ST34 (Liangqiu) masters it." The *Tai Ping Sheng Hui Fang (Peaceful Holy Benevolence Formulae)* (Wang, Northern Song Dynasty) records that "ST34 (Liangqiu)" can treat "cold arthralgia and knee pain." Stimulating the ST34 (Liangqiu) acupoint can loosen the rectus femoris and vastus lateralis muscles, promote blood circulation and material exchange in the knee joint, and improve local metabolism of the knee joint, so as to achieve the effects of dredging the meridians, smoothing the joints, and relieving pain (Wang, 2021; Li et al., 2021).

Acupuncture at SP10 (Xuehai), ST34 (Liangqiu), and ST36 (Zusanli) can invigorate the spleen, nourish Qi and Blood, relieve spasms and pain, moisturise and nourish tendons, smooth joints, improve the permeability of local blood vessels, regulate blood viscosity, reduce blood viscosity, effectively improve local blood circulation, promote the absorption of inflammatory mediators and inflammatory exudates, accelerate the metabolism of related cells, reduce the inflammatory response of this disease, and promote the repair of damaged tissues and the recovery of knee joint physiological functions (Tian and Lu, 2022; Zhu and Xin, 2016);

(g) "SP9 (Yinlingquan)", from *Ling Shu · Ben Shu* edited and compiled by Tian and Liu (2005), belongs to the Spleen Meridian of Foot Taiyin (SP). It is the He acupoints (Hexue) of the Spleen Meridian of Foot Taiyin. It is located in the medial region of the lower limb, in the depression between the lower border of the medial condyle of the tibial and the medial border of the tibia. Stimulating this point can reconcile Qi and Blood, balance Yin and Yang, relieve spasms, and treat diseases of the limbs, such as knee joint pain and paralysis of the lower limbs (Lin, 2016). It forms the opposite point with GB34 (Yanglingquan), and it is often used in conjunction with it. The combination of Yin and Yang has the functions of relaxing tendons and activating collaterals, expelling wind and dampness, reducing swelling and relieving pain (Luo, 2019; Zhang and Yang, 2016; Lin et al., 2020);

(h) "EX-LE2 (Heding)", was first seen in the *Yi Xue Gang Mu (Compendium of Medical Studies)* (Lou, Ming Dynasty), and it belongs to Extra Acupoints. It locates in the anterior knee region, in the depression just above the midpoint of the patella's bottom border. Acupuncture and moxibustion on this acupoint can relax and smooth the tendons, dredge the meridians, and activate the collaterals, mainly used for the treatment of knee joint pain (Zhao, 2020). It has a strong analgesic effect, thereby improving the functional activities of the patient's knee joint and improving the quality of life of the patient (Zheng et al., 2017);

(i) "GB33 (Xiyangguan)", is from *Zhen Jiu Jia Yi Jing (The A-B Classics of Acupuncture and Moxibustion)* (Huangfu, Jin Dynasty), located in the Gallbladder Meridian of Foot-Shaoyang (GB). It is located at the knee, in the depression between the biceps femoris tendon and the iliotibial tract, on the posterosuperior border of the lateral epicondyle of the femur. It is the place where the meridian Qi of the tendons of the Foot Yangming meridian and the meridian Qi of the tendons of the Foot Shaoyang Meridian converge, and can promote the flow of Qi and Blood of the knee joint, mainly used to treat knee joint swelling and pain, lower leg muscle spasm and numbness, knee arthritis, lower limb paralysis, etc. (Ma et al., 2021; Wu et al., 2020; Huang and Pan, 2019; Wu, 2019); and

(j) "SP6 (Sanyinjiao)", is from *Zhen Jiu Jia Yi Jing (The A-B Classics of Acupuncture and Moxibustion)* (Huangfu, Jin Dynasty), and is one of the frequently used acupoints of the Spleen Meridian of Foot Taiyin (SP). It is located on the medial side of the lower leg, 3 cun above the tip of the medial malleolus, on the posterior edge of the medial border of the tibia, and is the meeting point where the three Yin meridians of the kidney, liver, and spleen converge at. Stimulating this acupoint can strengthen the spleen, nourish the liver, benefit the kidney, dredge the meridian, replenish Qi and Blood, strengthen the muscles, tendons and bones, and has a better curative effect for the Bi syndrome with Qi deficiency and Blood stasis (Jin and Wang, 2017). It is mainly used to treat paralysis of the lower limbs.

4.2 Meridian Distribution (Channel Tropism) of Acupoints

The main principles of acupoints' therapeutic functions can be divided into two categories: treating according to the meridian and treating according to the local area.

Treating according to the meridian mainly refers to the use of acupoints belonging to a certain meridian to treat the corresponding diseases of the meridian pathway and the related organs. This principle is commonly known as "where the acupoints are located, and where the main treatment is concerned." This rule is particularly evident in the acupoints of the limbs. The meridian-based treatment principle occupies an important position in acupuncture and moxibustion, to the extent that some TCM practitioners or acupuncturists follow the principle of "Would rather lose its acupoints than its meridians" when treating diseases. This is a principle in acupuncture and TCM that emphasises the importance of treating along the meridian pathway rather than simply focusing on a single acupoint. This principle emphasises the importance of understanding the overall characteristics of the meridian system during treatment, rather than focusing solely on the function of a single acupoint. In clinical practice, although there are many acupoints to choose from when treating KOA with acupuncture, the acupoints that are commonly selected still reflect their meridian attributes. The three Yang meridians and the three Yin meridians of the foot all pass through the knee joint, and the site of KOA is in the knee joint, therefore, all six-foot meridians are closely related to the disease of KOA.

In the second category of treating according to the local area, acupuncture and meridian theory, is a therapeutic method commonly used for treating local diseases such as pain, swelling and inflammation. It refers to the selection of specific acupoints to treat the symptoms and lesions of a particular part of the body, based on the patient's condition and the location of the disease, rather than the meridian pathway. In clinical practice, the selection of acupoints is determined based on the patient's symptoms and pulse condition. For example, for cervical spondylosis, acupoints such as GB20 (Fengchi), GV14 (Dazhui) and BL10 (Tianzhu) are often stimulated, while acupoints such as Jianjing and

Tianzong are stimulated for treating shoulder periarthritis. The selection of these acupoints is based on the distribution of meridians and their corresponding organs and viscera, which is the theoretical basis of "treating according to the meridian".

"Treating according to the meridian" and "treating according to the local area" complement each other, and the efficacy of acupuncture treatment is closely related to the selection of acupoints. By properly applying the theories and practices of the two, various diseases and symptoms can be treated more effectively.

In this study, according to the total usage frequency of acupoints from high to low, the top 10 meridians are (unit: times, distribution %): ST Stomach Meridian of Foot Yangming (5494, 32.25%), SP Spleen Meridian of Foot Taiyin (3559, 20.89%), EX Extraordinary points (2862, 16.80%), GB Gallbladder Meridian of Foot Shaoyang (2599, 15.25%), BL Bladder Meridian of Foot Taiyang (1099, 6.45%), CV Ren Meridian (374, 2.20%), LR Liver Meridian of Foot Jueyin (361, 2.12%), KI Kidney Meridian of Foot Shaoyin (321, 1.88%), LI Large Intestine Meridian of Hand Yangming (159, 0.93%) and GV Du Meridian (158, 0.93%). Among the fourteen regular meridians, the Stomach Meridian of Foot Yangming (ST), the Spleen Meridian of Foot Taiyin (SP), and the Gallbladder Meridian of Foot Shaoyang (GB) are the main ones. This is mainly because all three meridians pass through the knee joint, and these meridians have many important acupoints distributed near the joints, such as ST35 (Dubi) (2123 times), ST34 (Liangqiu) (1558 times), ST36 (Zusanli) (1609 times) in the Stomach Meridian of Foot Yangming; SP10 (Xuehai) (1755 times), SP9 (Yinlingquan) (1374 times) in the Spleen Meridian of Foot Taiyin; GB34 (Yanglingquan) (1869 times) in the Gallbladder Meridian of Foot Shaoyang. Therefore, these meridians can be used to treat knee joint diseases. There are 10 acupoints which belong~~ing~~ to the EX Extraordinary points, and the most frequently used ones are EX-LE4 (Neixieyan) (1977 times) and EX-LE2 (Heding) (861 times).

From the perspective of the anatomical structure of the knee joint and lower limbs, the quadriceps femoris is an important muscle support and source of power for knee joint activities. As for the distribution of meridians, the Spleen meridian of Foot Taiyin and the Stomach meridian of Foot Yangming run through the location of the quadriceps femoris.

The *Huang Di Nei Jing (the Yellow Emperor's Inner Canon)* translated and annotated by Yao, C.P., 2022 states that the Stomach Meridian of Foot Yangming is a meridian of abundant Qi and Blood, which mainly nourishes the principal tendon (Zong Jin, the principal muscles governed by the main meridians), and can supplement and nourish Qi and Blood (Li et al., 2021). Zongjin governs the binding of bones and promotes joint flexibility. The spleen is the foundation of postnatal life, governing the four limbs and muscles, and playing a crucial role in producing and transforming Qi and Blood, nourishing and strengthening muscles. The Spleen Meridian of Foot Taiyin and the Stomach Meridian of Foot Yangming are the exterior and interior of each other, and are mutually complementary (Guo, 2020). Therefore, stimulating the acupoints on these two meridians can regulate the functions of the spleen and stomach, promote the absorption of nutrients, enhance metabolism, promote the generation of Qi and Blood, strengthen the vitality of the human body, facilitate the circulation of Qi and Blood, thereby nourishing the muscles, meridians, and accelerating the elimination of pathological products such as phlegm and blood stasis. It also helps to dredge the meridians, relax muscles, and relieve pain (Liu et al., 2015). The Gallbladder Meridian of Foot Shaoyang, which "exits at the knee, on the outside of the thigh," passes through the knee joint, and GB34 (Yanglingquan) is the convergence point of tendons and veins, and is located near the knee joint. Therefore, stimulating these acupoints of this meridian can promote the Qi-Blood circulation of the meridian, dredge the collaterals, relax the tendons and the muscles, and relieve pain (Huang et al., 2021). Comprehensively stimulating these meridians, can effectively alleviate or relieve local stiffness, pain, swelling, and other discomforts in the knee joint.

The total usage frequency of the two meridians the Stomach Meridian of Foot Yangming (ST) and the Spleen Meridian of Foot Taiyin (SP) is 9053 times (about 53.13%), ranking the top two, indicating that acupuncture treatment for KOA places considerable emphasis on regulating the spleen and stomach.

In summary, the acupoints with the higher frequency of use for acupuncture treatment of KOA are mainly distributed along the Stomach Meridian of Foot-Taiyin, the Spleen Meridian of Foot-Taiyin, Extraordinary acupoints, and the Gallbladder Meridian of Foot-Shaoyang, in accordance with the principle that "where the acupoints are located, and where the main treatment is concerned."

4.3 The Rule of Selecting Acupoints According to Distance

The basic principle of selecting acupoints in acupuncture prescriptions is "selecting points along the corresponding meridian". Under this guidance, the principles of selecting acupoints include selecting points at the proximal and distal ends, which meant "Selecting acupoints close to the diseased part" and "Selecting acupoints in the distance to the diseased part".

Selecting points at the proximal part refers to the method of selecting acupoints near or at the local and adjacent parts of the lesion to treat the disease, that is, where the disease is located, the acupoints are selected at or near the site, in other words, the acupoints are chosen based on the location of the disease, which involves needling at or near the affected area in all directions. It is based on the near-treatment effect of acupoints, and embodies the law of "where the acupoints are located, and where the main treatment is concerned". It has a wide range of applications and is suitable for any disease with obvious symptoms reflected on the body surface and limited lesions, acupoints can be selected for treatment according to the principle of selecting acupoints from the proximal part. For example, take Yingxiang point for nasal disease, take Taiyang point for headaches, etc. Selecting points at the proximal part can shorten the conduction distance of the stimulation, improve the intensity of the stimulation, increase the local therapeutic effect, and at the same time avoid the acupoint from being needled too deep and injuring deep and important structures. It is one of the commonly used acupuncture treatments methods.

"Selecting acupoints in the distant to the diseased part" is a method of selecting acupoints in acupuncture and moxibustion of TCM. The method refers to choosing the acupoints located at a distance far away from the lesion of the disease and treating it. According to the theory of TCM, when acupoints are far away from the diseased part, they can achieve the distant therapeutic effect of regulating the diseased part through the conduction of meridians, which is called the distant effect of acupoints. It is based on this distant treatment effect of acupoints, and conforms to the rule of "Where the meridians pass through, and where the main treatment can be reached" in the acupuncture and moxibustion theory. This method of acupoint selection is widely used. In clinical practice, acupoints at, near, or below the elbow and knee joints are usually selected for treatment. In specific applications, acupoints can be selected either from the main acupoints along the meridian to which the diseased viscera relate (primary meridians acupoint selection), or from acupoints on the superficial or interior meridians that are related to the affected organ through the theory of exterior-interior relationships (superficial and interior meridians acupoint selection), or from acupoints on meridians that share the same name as the affected organ relate to (same name meridians acupoint selection) for treatment, so as to regulate the entire meridian system and overall body function. For example, asthma can be treated with SP3 (Taibai) on the Spleen Meridian of Foot Taiyin and LU5 (Chize) on the Lung Meridian of Hand Taiyin; Low back pain can be treated with BL40 (Weizhong) on the Bladder Meridian of Foot Taiyang and SI8 (Xiaohai) on the Small Intestine Meridian of Hand Taiyang; Stomach pain can be treated with the ST36 (Zusanli) of the Stomach Meridian of Foot Yangming, and the SP4 (Gongsun) of the Spleen Meridian of Foot Taiyin.

In the treatment of diseases, the methods that acupoint selection of proximal and distal parts are not absolutely used alone, while the two methods are often used together to achieve better therapeutic effects. This is also a manifestation of the thinking of acupuncture and moxibustion based on syndrome differentiation and treatment.

In this study, 21 acupoints were selected in the proximal part, and the total frequency of acupoints use was 14,137 times (the rate of occurrence was 82.97%); while 118 acupoints were selected in the distal part, and the total frequency of use was 2,901 times (the rate of occurrence was 17.03%). The results showed that although the number of acupoints selected from the proximal part was less than that from the distal part when acupuncture was used to treat KOA, the total frequency of acupoints used near the knee joint was much higher than that of acupoints selected from the distal part. This indicates that acupuncture treatment of KOA mainly focuses on acupoints in the proximal part, and those in the distal region are used as an auxiliary treatment, which is consistent with the principle of syndrome differentiation and treatment in acupuncture.

4.4 The Rule of the Distribution of Body Parts of Acupoints

The second principle of acupoints' therapeutic functions is "treating according to the local area". This refers to the fact that all acupoints on a certain part of the body can treat a certain type of disease in that part, that is, the function that "treating according to the local area" of acupoints is related to the location and characteristics of the acupoints. The specific meaning and application examples of "treatment according to the local area" have been explained in part "4.2. Meridian Distribution (Channel Tropism) of Acupoints". This part mainly discusses and analyses the distribution of the 139 selected acupoints in the five major parts of the human body, and explores the regularities among them.

The distribution of acupoints in the five major parts of the human body was calculated according to the total frequency of acupoints used in each part. According to the total frequency of acupoints used in each part, the results are in descending order (unit: times): Lower Limbs: 74 acupoints, used a total of 15,638 times (the rate of occurrence is 91.78%); Waist and Back: 23 acupoints, used a total of 677 times (the rate of occurrence is 3.97%)); Chest and Abdomen: 11 points, used 383 times (the rate of occurrence is 2.25%); Upper Limbs: 23 points, used 212 times (the rate is 1.24%); Head and Neck: 8 points, used 128 times (the rate is 0.75) %). The results showed that the acupoints used for acupuncture treatment of KOA were mainly selected from the proximal and local parts, focusing on lower limbs, especially at, near, or around the knee joint. Due to the site of the lesion in KOA being located in the knee joint of the lower limb, local acupoints or nearby acupoints are mainly selected for acupuncture treatment, which can directly treat the affected area and better strengthen the therapeutic effects of acupuncture in relaxing tendons and collaterals, promoting blood circulation, eliminating stasis, reducing swelling, and relieving pain. It has shown that local acupoint selection is one of the acupoint selection strategies for acupuncture treatment of KOA, which embodies the principle of "where the acupoints are located, and where the main treatment is concerned" in acupuncture theory. Although most of the selected acupoints are concentrated in the lower limbs and local lesion areas, BL23 (Shenshu) located on the back and CV4 (Guanyuan) located in the abdomen are also timely used in clinical treatment, which shows that distant acupoints are also taken into consideration when selecting acupoints in actual. The above-mentioned not only reflect the proximal and distant therapeutic effects of the acupoints, but also reflect the characteristics of acupoint selection based on the combination of distant and near, syndrome differentiation and treatment, local acupoint selection as the main strategy and distal acupoint selection as the supplement.

4.5 The Characteristics of Acupoints (Specific Acupoint Attributes)

The characteristics of specific acupoints mainly refer to the specific attributes of acupoints. Specific acupoints are acupoints that simultaneously possess special therapeutic effects and properties, and are summarised by specific names among the fourteen meridian acupoints. Based on their different distribution characteristics, meanings, and therapeutic effects, they are divided into Five-shu Acupoints (Wushuxue), Lower-he Acupoints (Xiahexue), Eight-hui Acupoints (Bahuixue), Xi Acupoints (Xixue), Original Acupoints (Yuanxue), Back-shu Acupoints (Beishuxue), Front-mu Acupoints (Muxue), Luo-connecting Acupoints (Luoxue) and Eight Confluence Acupoints (Bamaijiaohuixue). Specific acupoints are mostly located where the Qi of meridians converges or where the meridians intersect. Acupuncture these acupoints can nourish the liver and tonify the kidney, nourish Qi and Blood, and regulate the meridians.

Among the 139 acupoints commonly used by acupuncture for KOA, there are 77 specific acupoints, accounting for about 55.40%. It shows that specific acupoints account for more than half of the selected acupoints, and have become the basic acupoints for acupuncture treatment of KOA. According to the total usage frequency of acupoints from high to low (unit: times): Five-shu Acupoints (5,974), Lower-he Acupoints (3,836), Eight-hui Acupoints (2,320), Xi Acupoints (1,583), Original Acupoints (424), Back-shu Acupoints (391), Front-mu Acupoints (264), Luo-connecting Acupoints (111) and Eight Confluence Acupoints (41). According to the total frequency of use, the Five-shu Acupoints, in descending order, are He Acupoints (5,472), Shu Acupoints (387), Jing Acupoints (88), Xing Acupoints (24), Well Acupoints (3). The results showed that the most used specific acupoints for acupuncture treatment of KOA were Five-shu Acupoints, followed by Lower-he Acupoints. Among Five-shu Acupoints, He Acupoints are the most used; GB34 (Yanglingquan) is the most frequently used acupoint among Five-shu Acupoints, with total usage of 1,869 times, followed by ST36 (Zusanli) (1,609) and SP9 (Yinlingquan) (1,374).

Five-shu acupoints are the important acupoints of the twelve meridians distributed below the elbow and knee joints, consisting of five key points: Jing (Well, jǐng), Xing (Spring), Shu (Stream), Jing (River, jīng), and He (Sea), collectively known as the "Five Shu." As stated in the *Ling Shu · Nine Needles and Twelve Yuan Points* edited and compiled by Tian and Liu (2005) "Jing (Well) acupoint is where Qi emerges, Xing is where it flows, Shu is where it enters, Jing (River) is where it courses, and He is where it converges." Because the Five-shu acupoints are mostly distributed below the elbow and knee joints, they are usually used as distal selection points for acupuncture; however, for local diseases of the elbow and knee joints or diseases of the limbs, these acupoints are often selected because they are located locally or near the lesion, and play a role of distant or near treatment. Compared to other specific acupoints, the Five-shu acupoints are relatively numerous in specific locations. Due to their unique location characteristics, the probability of being selected for the treatment of knee joint-related diseases is relatively high, therefore, it has the highest total frequency in this study.

The Yuan acupoints (Original Acupoints, Yuanxue) are acupoints located on the twelve meridians of the limbs where the original Qi of the Zang-Fu organs is infused, transported, and stored. Each of the twelve meridians has a Yuan Point located near the wrist or ankle joint, collectively known as the "Twelve Yuan Points" or "Shi Er Yuan." "Yuan" in Chinese refers to the original or source Qi, which is the fundamental force behind the body's life activities and the cornerstone for maintaining normal physiological function along the twelve meridians.

Lower-He acupoints (Xiahexue) are the site where Qi and Blood from the Six Fu-Organs converge into the three Yang meridians in the lower limbs. The Lower-He acupoints of the Six Fu-Organs are the parts where the meridian Qi separates from the three Yang meridians of the foot and injects into the Six Fu-

Organs, so it is closely related to the Six Fu-Organs. Abnormal sensation at the Lower-He acupoint can reflect pathological changes in the Six Fu-Organs.

Xi acupoints are the parts where the Qi of each meridian deeply converges. In Chinese, "Xi" means a gap or a seam. Each of the twelve regular meridians has a Xi acupoint, and so do the Yin Wei, Yang Wei, Yin Qiao, and Yang Qiao meridians, making a total of sixteen Xi acupoints. Except for the ST34 (Liangqiu) of the Stomach Meridian of Foot Yangming, all the Xi acupoints are located below the elbow and knee joints. In clinical practice, Xi acupoints are often used to treat acute illnesses.

Eight-Hui Acupoints are the eight acupoints in the human body where the essence and Qi of viscera, Fu-Organs, Qi, blood, tendons, blood vessel, bones, and marrow converge. *Nan Jing · Si Shi Wu Nan (Difficult Classics · Forty-Five Difficulties)* of *Nan Jing (The Classic of Difficult Issues)* (Bian, Warring States Period) states: "Why are they called the Eight Hui acupoints (Eight converge Points)? The answer is that "the essence and Qi of Fu-Organs converge at Taicang (CV12 (Zhongwan)), the essence and Qi of viscera converge at Jixie (LR13 (Zhangmen)), the essence and Qi of tendons converge at GB34 (Yanglingquan), the essence and Qi of marrow converge at Juegu (GB39 (Xuanzhong)), the essence and Qi of blood converge at BL17 (Geshu), the essence and Qi of bones converge at BL11 (Dazhu), the essence and Qi of blood vessel converge at Taiyuan, the essence of Qi converge at CV17 (Danzhong). Those with internal heat diseases should select the related Qi-converging points." Clinical applications are not limited to heat diseases, but any diseases related to the eight aspects can be treated accordingly.

He acupoint, one of the Five-Shu acupoints, is from *Ling Shu · Nine Needles and Twelve Yuan Points* edited and compiled by Tian and Liu (2005) and is located near the elbow and knee joints, where the meridian Qi penetrates deep and then converges the viscera and Fu-Organs. The He acupoint is mainly used to treat disorders caused by the reversal of the flow of Qi or the upward movement of Qi without descending, such as hiccups, belching, nausea, vomiting, and other related symptoms. The He acupoint can regulate the flow of Qi, making it smooth and thus alleviating these symptoms. In addition, the He acupoint also has a certain nourishing effect, which can strengthen the spleen and stomach, nourish the blood and promote salivation. It can also provide certain assistance in the treatment of some chronic diseases. In *Ling Shu · Shun Qi Yi Ri Fen Wei Si Shi (Ling Shu · Regulating Qi throughout a Day Divided into Four Time Periods)* edited and compiled by Tian and Liu (2005), it says, "If one's meridian channels are full of blood, and the illness is related to the stomach and caused by improper diet, then the He acupoint can be used." The above statement indicates that the He acupoint can be used to treat stomach-related diseases and all chronic diseases, and has the functions of strengthening the spleen and stomach, nourishing and promoting the generation of essential substances, and preventing diseases caused by pathogenic factors. The He acupoint is located near the elbow and knee joints, and its meridian energy is abundant and converges inward to the viscera and Fu-Organs, with the functions of tonifying the kidney, nourishing the essence and marrow, and moistening and nourishing the tendons and vessels. In acupuncture treatment of KOA, the Stomach Meridian of Foot Yangming and the Spleen Meridian of Foot Taiyin are used most frequently, when Five-Shu acupoints are used to treat KOA, the He acupoints are most used, which indirectly explains the importance of regulating the spleen and stomach, and replenishing Qi and Blood in the treatment of KOA.

5.0 Summary and Conclusion

Based on the above research study, the conclusions made are summarised as below:

(a) There were 139 acupoints commonly used for a total of 17,038 times in the treatment of KOA with acupuncture were identified out from the 2,264 papers. The top 10 high-frequency acupoints are (unit: times): ST35 (Dubi), EX-LE4 (Neixieyan), GB34 (Yanglingquan), SP10 (Xuehai), ST36 (Zusanli), ST34 (Liangqiu); SP9 (Yinlingquan), EX-LE2 (Heding), SP6 (Sanyinjiao) and GB33 (Xiyangguan);

(b) The acupoints most frequently selected to treat KOA are mainly attributed to ST Stomach Meridian of Foot Yangming, SP Spleen Meridian of Foot Taiyin, EX Extraordinary points, and GB Gallbladder Meridian of Foot Shaoyang. These conform to the rule of " Where the meridians pass through, and where the main treatment can be reached" in the acupuncture and moxibustion theory, and has showed that TCM practitioners and physicians pay more attention to regulating the spleen and stomach when they are treating KOA by using acupuncture;

(c) The acupoints used for acupuncture to treat KOA are mainly selected from the proximal and local parts (at, near, or around the knee joint), supplemented by selected from the distal part; based on local acupoint selection and symptomatic treatment. The acupoint selection is mainly concentrated on the lower limbs, especially the knee joint. These reflect the principle and characteristics of acupoints selection for KOA treatment with acupuncture, and also conform to the rule of "Where the acupoints are located, and where the main treatment is concerned". It is a direction of acupoint selection for the treatment of the disease in clinical practice. In addition, acupoints on the waist and back, chest and abdomen, upper limbs, head, and neck are also involved, which reflects the characteristics of acupuncture in the treatment of KOA by combining acupoint selection from far and near parts, and syndrome differentiation;

(d) The number of specific acupoints accounted for more than half of the commonly used acupoints in KOA treatment with acupuncture. The most frequently used specific acupoints in clinical practice are Five-Shu acupoints, among which He acupoints are used the most; GB34 (Yanglingquan) is the most frequently used among Five-Shu Acupoints, followed by ST36 (Zusanli) and SP9 (Yinlingquan). It provides a special direction for clinical acupoint selection;

(e) In overall, the selection of acupoints for KOA treatment with acupuncture follows the principles of combining “acupoints selected along the corresponding meridian” and “selection of local acupoints”, and mainly select acupoints along the meridian and from the proximal and local parts. Based on the top 10 highly-researched acupoints, the new acupoint prescription was established, while selecting local acupoints, taking into account the distal acupoints; and

(f) The new acupoint prescription can tonify the body's healthy energy while dispelling pathogenic factors, with the characteristics of combining differentiation of disease and syndrome. The combination of the 10 acupoints can have effects such as promoting blood circulation and removing blood stasis, strengthening the spleen and eliminating dampness, dispelling wind and dispersing cold, promoting the circulation of Qi and stopping pain, nourishing Qi and Blood, strengthening tendons and bones and be prescribed with taking into account both the proximal and distal acupoints. The results of the subsequent clinical research based on this acupuncture prescription have also confirmed its effectiveness, and the new prescription can be used as a guide for clinical practice.

6.0 Existing Problems and Prospects

During the literature research study, some problems were encountered:

(a) Due to the setting of restrictive search terms, it may not be comprehensive enough, should there would be possible omission during the literature search including the paper materials from newspapers and conference proceedings/abstracts. In the future, the search terms can be improved, and the literature database can be expanded, and the collection of paper documents can be increased to make the results more comprehensive and accurate;

(b) In the process of literature searching, screening, and data extraction, there would be some limitations to the people arising from biases in judgement or subjectivity. In future research, collection, screening, and proofreading methods of literature search results can be performed by multiple persons to reduce the errors; and

(c) Syndrome classification was not implemented due to limited patients and links in literatures. Syndrome is descriptive in nature, and incomplete and generalised in many research studies. Therefore, it is often not included in literatures. It is hoped that this issue can be further studied in future research.

CHAPTER 5

CLINICAL RESEARCH

CLINICAL STUDY ON TREATMENT OF NON-ACUTE KOA USING EA AT TOP TEN HIGHLY-RESEARCHED ACUPOINTS

1.0 Background

Based on the results of the previous study "Explore the Rules and Characteristics of Acupoints Selection for Acupuncture Treatment of KOA Based on Literature Research and Analysis", the top ten highly-researched acupoints were selected as the basic acupoint prescription for this clinical study. The standardised KOA clinical symptom observation scale and score indicators were utilised to evaluate the clinical treatment effects of EA, MA, and SA on KOA. The clinical effects of the highly-researched acupoints combined with different therapies were observed to scientifically evaluate the efficacy and safety of the top ten highly-researched acupoints combined with the electroacupuncture method for treating KOA, and to establish a set of standardised and clinically effective acupoint selection and acupuncture treatment plan for KOA, thereby expanding more treatment options for KOA in Malaysia. By measuring the variations in serum IL-1β and TNF-a levels before and after treatment of the patients, some of the possible internal mechanisms of electroacupuncture in treating KOA can be analysed and explored, leading to improvement in its clinical symptoms, enriching the clinical theoretical research of EA analgesia, and providing scientific theories and experimental basis for the therapy EA treatment of KOA.

2.0 Ethical Requirements and Informed Consent

2.1 Ethical Approval

This clinical trial strictly followed the Declaration of Helsinki (Wang, 2016; Yao and Fan, 2014) and was approved by the UTAR Scientific and Ethical Review Committee (SERC), and the Ethical Approval letter for Research Project was obtained before the implementation of this research project with the reference number: U/SERC/89/2020 (see Appendix A for details). The significance of obtaining the ethical approval for medical clinical research can be summarised as follows:

(a) Protecting the rights and interests of research subjects: Ethical review committees evaluate the ethical and scientific aspects of the research to ensure that it does not harm the physical, psychological, and social well-being of the research subjects. Researchers are required to adhere to ethical principles and regulations to ensure the autonomy, privacy, and confidentiality of the research subject;

(b) Improving the credibility of research results: Ethical review enhances the credibility of research by preventing unethical behavior and errors during the research process. In addition, ethics review committees can examine and evaluate aspects such as research plans, sample size, and statistical analysis to assist researchers in designing scientifically sound research protocols and methods; and

(c) Protecting the professional reputation and responsibility of researchers: Ethical review committees scrutinise research plans, procedures, and documents to ensure that researchers comply with scientific and professional ethical norms and requirements, reducing the risk of penalties and condemnation for ethical violations.

In summary, obtaining ethical approval is essential for medical clinical research. It not only protects the rights and interests of research subjects and improves the credibility of research results, but also safeguards the professional reputation and responsibility of researchers.

2.2 Research Project Registration

This research study with the title "Clinical Study on Treatment of Non-acute Knee Osteoarthritis (KOA) Using Electro-acupuncture at Top Ten High-selected Acupoints" had also been registered in the Chinese Clinical Trial Registry with the registration number: ChiCTR2000034783.

2.3 Informed Consent

Before the start of the clinical study, the research personnel of this trial provided and informed detailed information to all participants regarding the purpose of the study, research methods, potential risks and benefits that can be obtained, confidentiality of the personal information of participants (see Appendix B and Appendix C for details), and other relevant matters. All participants were informed that they were required to complete the examination and evaluation forms and that they had the right to withdraw from the study at any time. All participants or their legal representatives were required to fully understand the information provided and what they have been told, i.e., to obtain full informed consent, and then sign an informed consent form (see Appendix C for details). The significance of obtaining informed consent in medical clinical research can be summarised as follows:

(a) Respecting the rights and dignity of research subjects: Informed consent is a fundamental human right and ethical requirement that reflects the autonomy and dignity of research subjects. Through informed consent, research subjects can understand the purpose, methods, risks, and benefits of the research, and make their own decisions based on full information;

(b) Improving the ethical and scientific quality of research: Informed consent can ensure that the research process complies with ethical and legal requirements, reduces the risk of harm to research subjects, and enhances the credibility and scientific quality of the research; and

(c) Reducing legal liability and risk during the research process: Obtaining informed consent from research subjects can help researchers avoid violating ethical and legal requirements, and reduce their legal liability and risk during the research process.

In summary, obtaining informed consent in medical clinical research is of great significance for respecting the rights and dignity of research subjects, improving the ethical and scientific quality of research, and reducing legal liability and risk during the research process.

3.0 Clinical Information

3.1 Source of Cases

The participants in this study were mainly recruited from the Henan Province Hospital of Traditional Chinese Medicine (the Second Affiliated Hospital of Henan University of Chinese Medicine) and the Modern Medical Research Institute Hospital of Henan Province. The period of patient recruitment was from November 2020 to February 2022.

3.2 Estimation of Sample Size

The sample size estimation is based on the formula quoted from *Sample Size Calculations in Clinical Research (Second Edition)*(Chow et al., 2008), Shein-Chung Chow, Jun Shao, and Hansheng Wang. *Chapter 4. Large Sample Tests for Proportions, P92* and the results of previous literature research concluded that the efficiency rate is about 70% to 90% for KOA treated with EA (An et al., 2016; Qi, 2015; Wu, 2014). Therefore, based on these results, the estimation of the total efficiency rate in this study is 92%. The number of cases in each group is equal. Set α = 0.05, 1-β = 0.90. With the assumption that the dropout rate of no more than 10%, the following formula was used to calculate the sample size.

The formula used for sample size calculation:

$$n = \frac{\left(Z_{\frac{\alpha}{2}} + Z_{\beta}\right)^2 \left(P_1(1-P_1) + P_2(1-P_2)\right)}{\varepsilon^2}$$

Alpha (α) is the level of significance; Beta (β) is probability of Type II error; and (1-β) is power. For $\alpha = 0.05$, $Z_{\alpha/2} = 1.96$. For power = 90%, $\beta = 0.10$, $Z_{\beta} = 1.28$.

Multipliers for Conventional Values of Alpha, Two-sided	
Alpha	Multipliers
0.05	1.96
0.01	2.58

Multipliers for Conventional Values of Beta	
Beta	Multipliers
0.20	0.84
0.10	1.28
0.05	1.64
0.01	2.33

n = Sample size required for one group

$\boldsymbol{Z_{\alpha/2}}$ = Multiplier for conventional values of alpha = 1.96

$\boldsymbol{Z_{\beta}}$ = Multiplier for conventional values of beta = 1.28

$\boldsymbol{P_1}$ = The efficiency rate of control group in trials by An et al. (2016) and Qi (2015) = 0.7

$\boldsymbol{P_2}$ = The estimated efficiency rate of study group in study = 0.92

$\varepsilon = \boldsymbol{P_2 - P_1} = 0.92 - 0.7 = 0.22$

The calculation of sample size:

$$n = \frac{(1.96 + 1.28)^2 \times \big(0.7 \times (1 - 0.7) + 0.92 \times (1 - 0.92)\big)}{(0.22)^2}$$

$$= \frac{(3.24)^2 \times (0.7 \times 0.3 + 0.92 \times 0.08)}{(0.22)^2}$$

$$= \frac{(3.24)^2 \times (0.2836)}{(0.22)^2}$$

$$= 61.51 \approx 62$$

Considering a 10% dropout rate, 62 +6.2 = 68.2 ≈ 69

Therefore, sample size required is 69 patients for each group, the total sample size for 3 groups is 207.

3.3 Diagnostic Criteria

According to the research contents of this study, the Chinese and Western diagnostic criteria and the inclusion and exclusion criteria for KOA were formulated by referring to the literature such as the American College of Rheumatology clinical standards and radiological criteria in 2001 (Belo et al., 2009; Altman et al., 1986), the "*Diagnostic and Therapeutic Effect Criteria for Syndromes and Diseases in TCM*" (National Administration of Traditional

Chinese Medicine, 2012) issued by the State Administration of Traditional Chinese Medicine, the "*Guidelines for Clinical Research of Chinese Herbal Medicines as New Drugs*" issued by the Ministry of Health of the People's Republic of China (China Medical Science and Technology Press, 2002), and "*Guidelines for the diagnosis and treatment of osteoarthritis (2007 version)* (Qiu, 2007) " formulated by the Chinese Medical Association's Orthopaedics Branch.

3.3.1 Western Medicine Diagnostic Criteria

The western medicine diagnostic criteria used are as below:

(a) Repeated knee pain within 1 month;

(b) X-ray films (standing or bearing weight) indicate narrowing of joint space, subchondral bone sclerosis and/or cystic changes, and osteophyte formation at the edge of the joint;

(c) Joint fluid (at least 2 times) is clear and viscous, WBC $< 2,000$/mL;

(d) Age ≥ 38 years old;

(e) Morning joint stiffness time ≤ 30 min; and

(f) There is a feeling of bone friction and sound of the joints during the activity.

Note: Combining the clinical, laboratory, and X-Ray examinations, the patient can be diagnosed as KOA when meeting the diagnostic criteria of a+b, or a+c+e+f, or a+d+e+f.

3.3.2 Chinese Medicine Diagnostic Criteria

With reference to the diagnostic criteria for "Bone Hysteria" (Bone Bi) in the "People's Republic of China Traditional Chinese Medicine Industry Standards ▪ Diagnostic and Therapeutic Effect Criteria for Syndromes and Diseases in TCM ZY/T001.1-94" issued by the State Administration of TCM in 2012 (National Administration of Traditional Chinese Medicine, 2012), the Chinese medicine diagnostic criteria used are as below:

(a) In the beginning, the knee joints were dully painful, and the flexion and extension were unfavourable. The painfulness of the knee joints was slightly relieved with slight movement. However, the condition was aggravated by climate change, high recurrence frequency and the long course of the disease;

(b) The occurrence of the disease is often not obvious, and the course of the disease progresses slowly, which is more common among middle-aged and elderly people;

(c) The knee joint can be slightly swollen, and the joint often has a rubbing sound during the movement. In severe cases, muscle atrophy and joint deformity can be observed; and

(d) X-ray examination: osteoporosis, irregular articular surface, narrow joint space, subchondral bone sclerosis, and marginal lip-like changes with osteophyte formation.

3.4 Inclusion Criteria

The inclusion criteria are listed as below:

(a) The patient is not suffering from rheumatoid arthritis (RA), the results of the laboratory tests for rheumatoid factors are negative;

(b) The patient is not at the acute phase of KOA and has not been accompanied by inflammatory lesions in the past two weeks, has not taken antibiotics or hormonal drugs in the past two weeks;

(c) The patient must be: 40 years old ≤ Age ≤ 80 years old;

(d) The patient who meets the above diagnostic criteria;

(e) The patient has not received other related treatments within 1 month (or treatments that may affect the observation of the efficacy indicators of the study);

(f) The patient is agreeable to accept and adhere to the whole course of treatment;

(g) The patient has localized skin of the knee joint that is intact; and

(h) The patient voluntarily signed Informed Consent and Risk Notification for Acupuncture Treatment of KOA.

3.5 Exclusion Criteria

The exclusion criteria are listed as below:

(a) The patient who does not meet both diagnostic criteria and the inclusion criteria;

(b) The patient who has other relevant history of joint diseases, such as rheumatism, rheumatoid, gout disease, and any other type of arthritis or other knee painful diseases;

(c) The patient is at the acute phase of KOA and has been accompanied by inflammatory lesions in the past two weeks, and has taken antibiotics or hormonal drugs in the past two weeks;

(d) The patient's visual analogue scale (VAS) ≤ 1;

(e) The patient's knee joint disease is caused by trauma, tumor, purulent infection, etc., or has local skin of the knee joint damage or inflammation;

(f) The patient has blood, kidney, liver, and metabolic dysfunction. Or suffering mental illness or tumor;

(g) The patient has systemic or local infections or infectious diseases;

(h) The patient is a pregnancy or lactation woman;

(i) The patient suffers severe heart disease, with a cardiac pacemaker or any metal object in the body;

(j) The patient's imaging examinations show that there are a large number of osteophytes forming in the knee joint of the patients, resulting in bone bridge connection, and bony ankylosis of the knee joint;

(k) The researchers believe that there are other reasons that the patient is not suitable for clinical trials; and

(l) The patient who does not cooperate with treatment work, and the treatment measures specified in the trial protocol have not been accepted.

3.6 Removal Criteria

The patient who has been enrolled but meets one of the following conditions should be removed, but the reasons for their exclusion should be recorded in detail:

(a) The case that did not meet the inclusion criteria but was mistakenly included;

(b) The patient with poor compliance, or failure to complete the entire experimental study;

(c) The patient who used other therapies or drugs without permission, which may affect the efficacy and safety assessment;

(d) The case with serious complications or adverse reactions during the study that is not suitable for continuing the treatment and terminated the trial; and

(e) Incomplete data that cannot be used to judge efficacy or safety.

3.7 Dropout Criteria and Countermeasures

All subjects who met the enrollment conditions and signed the Informed Consent and Risk Notification Form, in accordance with the principle of voluntariness, withdraw from the trial at any time and for any reason or could not persist in completing the experiment or could not be contacted, resulting in incomplete data and inability to correctly assess the treatment effects are considered as dropout cases, including the following situations:

(a) Based on the actual number of treatments, those who received less than 90% of the prescribed times;

(b) Those who voluntarily withdraw from the study during the research process; and

(c) Those who are lost to follow-up.

When the subject drops out, the researcher should make every effort to contact the subject by means of giving phone calls, writing letters or emails, arranging follow-up visits, inquiring about the reason for dropping out, recording the time of the last treatment, and collecting as much information as possible, and completing the available evaluation items. If the patient withdraws due to adverse reactions, corresponding measures should be taken to minimise the harm to the patient. The relevant trial data for dropout cases should be properly preserved.

4.0 Research Methods

4.1 Patient Recruitment, Grouping and Collection of General Information

4.1.1 Patients Recruitment

The recruitment of the patients followed the below guidelines:

(a) Preliminary dissemination before the start of the study: Preliminary dissemination was carried out using a diverse range of means such as telephone calls, internet platforms, WeChat, distribution of promotional flyers, and physician introductions;

(b) Source of cases: Patients with KOA who mainly sought treatment at Henan Province Hospital of Traditional Chinese Medicine (the Second Affiliated Hospital of Henan University of Chinese Medicine) and the Modern Medical Research Institute Hospital of Henan Province;

(c) The recruitment period: November 2020 to February 2022;

(d) The patients who met the criteria and were willing to participate in the study were required to sign an Informed Consent and Risk Notification Form, and randomly drew a registration number as required; and

(e) Before the study began, the researchers explained to the subjects the purpose, methods, benefits, and risks of the clinical study, and informed them of their right to withdraw from the study at any time and the confidentiality of the data. The above contents were written in the Informed Consent and Risk Notification Form and the patients signed to confirm after understanding the contents of the consent.

4.1.2 Grouping Method

The randomisation process in this study referred to the book *Medical Statistics* (second edition) edited by Yan Hong, which is a textbook for 8-year and 7-year clinical medicine majors in the "Eleventh Five-Year Plan" of the Ministry of Health (Yan, 2009). Transparent Randomisation was used to randomise grouping. Before the clinical study, we numbered 1 to 207 in the order of patients' registration for the treatment. Then, we used IBM SPSS Statistics 22 software to randomise group the 207 numbers into three groups. Each number from 1-207 was finally assigned a group number (1, 2, or 3), specifying that "1 = Treatment Group, 2 = Control Group 1, 3 = Control Group 2".

The Treatment Group (TG, EA, EA with the top ten highly-researched acupoints, 69 cases), Control Group 1 (CG1, MA, MA with the top ten highly-researched acupoints, 69 cases), and Control Group 2 (CG2, SA, MA with the sham acupoints (points does not belong to the main meridians, acupoints, and pain points, 69 cases)). Patients were allocated to enter the corresponding group to receive treatment according to the group to which each patient obtained the number. Treatment was given on a one-to-one basis, with patients not knowing each other.

By using this randomised grouping method, it was intended to minimize bias and ensure that comparisons among the three groups were reliable and meaningful. The allocation ratio of 1:1:1 helped balance the number of individuals in the treatment and control groups, facilitating subsequent analyses that are both comparable and statistically significant.

4.1.3 Collection of General Information of Patients

The general information of the subjects included name, gender, ethnicity, date of birth, home address, occupation, contact information, history, current medical history, disease duration, genetic history, treatment history, food and drug allergy history.

4.2 Treatment Methods

The doctors who administer the treatment to the patients all have relevant qualifications and extensive experience in acupuncture therapy. Additionally, they had received standardized training before the start of the study. The training included the location positioning of the acupoints and non-acupoints, as well as proper and standardized needling operations.

4.2.1 The Control Group 1

4.2.1.1 Acupoints

Selection of acupoints: Based on previous literature research, the top ten highly-researched acupoints for the acupuncture treatment of KOA were summarized and selected, which were: ST35 (Dubi), EX-LE4 (Neixieyan), GB34 (Yanglingquan), SP10 (Xuehai), ST36 (Zusanli), ST34 (Liangqiu), SP9 (Yinlingquan), EX-LE2 (Heding), SP6 (Sanyinjiao) and GB33 (Xiyangguan). The locations of these acupoints were referred from *Acupoints of Meridians and Collaterals* edited by Shen Xueyong (Shen, 2016).

4.2.1.2 Treatment Equipment

Acupuncture needles: Disposable sterile acupuncture needles from Hwato (Huatuo) brand, produced by Suzhou Medical Supplies Factory Co., Ltd. with the production license number of Suzhou Food and Drug Administration Equipment Production License No. 20010020. The main specifications are: $\Phi 0.35 \times 40mm$ and $\Phi 0.35 \times 50mm$.

4.2.1.3 Specific Treatment Methods

During the MA therapy, the patient laid supine with both lower limbs flat, and a soft cushion was placed under the diseased knee joint to slightly flex the knee joint to make the patient feel comfortable. The acupuncture site was fully exposed, the acupoints were marked, and 75% ethanol medical disinfectant was used to routinely disinfect the local skin where the acupoints were located and the fingers of the operator. A disposable sterile acupuncture needle with a specification of $\Phi 0.35 \times 40mm$ or $\Phi 0.35 \times 50mm$ was selected based on the patient's physique, and the double-handed needling technique was used for the acupuncture. For ST35 (Dubi) and EX-LE4 (Neixieyan), oblique needling was performed with the ST35 (Dubi) (The acupuncture needle was inserted with an upward and inward direction) and EX-LE4 (Neixieyan) (The acupuncture needle was inserted with an upward and outward direction), and the needle should enter the joint cavity. The other acupoints were vertical needling, and the depth of insertion was about 30-40mm. The even tonification and dispersion technique were used until the local area of the needle insertion acupoint produced the feeling of De Qi, which was a composite of sensations including soreness, numbness, distention and heaviness.

Each treatment lasted for 30 minutes and was performed once a day. Six treatments made up one course of treatment, with a total of two courses of treatment. There was a one-day break between the two courses of treatment.

4.2.1.4 Precautions

Before starting the treatment, the body and handle of the acupuncture needle should be carefully checked, and acupuncture needles with burrs and bent needle bodies should be avoided.

4.2.2 The Control Group 2

4.2.2.1 Acupoints

The non-acupoint points, 1cm beside the selected acupoints of the Control Group 1 were chosen as the needling points. The selected needling points at this acupuncture site do not belong to the fourteen regular meridian points, extraordinary points, or A'shi points.

4.2.2.2 Treatment Equipment

The treatment equipment was the same as in Section 4.2.1.2.

4.2.2.3 Specific Treatment Methods

The treatment was the same as the Control Group 1 in Section 4.2.1.3 except that, the needling points beside ST35 (Dubi) and EX-LE4 (Neixieyan) were not necessary to penetrate the joint cavity, and no need to obtain the sensation of De Qi during needling.

4.2.3 The Treatment Group

4.2.3.1 Acupoints

The selection of the acupoints was the same as in Section 4.2.1.1.

4.2.3.2 Treatment Equipment

The acupuncture needles used were the same as in the Control Group 1 as in Section 4.2.1.2. The EA instrument used was Hwato (Huatuo) brand SDZ-II electronic acupuncture instrument, manufactured by Suzhou Medical Supplies

Factory Co., Ltd., with production license number: Suzhou Food and Drug Administration Medical Device (License) Letter No. 2013 2270611.

4.2.3.3 Specific Treatment Methods

During the EA therapy, based on the operation of the Control Group 1; and after the acupoints had been stimulated and had the feeling of De Qi, the Hwato (Huatuo) SDZ-II electronic acupuncture instrument was connected to the selected acupoints. The waveform was set to "sparse-dense wave", and the current intensity should be tolerable for the patient. The needle was removed after the ~~electro-acupuncture~~ EA treatment had finished.

Each treatment lasted for 30 minutes and was performed once a day. Six treatments made up one course of treatment, with a total of two courses of treatment. There was a one-day break between the two courses of treatment.

4.2.3.4 Precautions

Before each treatment, it is necessary to check whether the performance of the EA instrument is intact, whether the current output is normal, and whether the potential is at the "0" position. After having the feeling of De Qi from acupuncture, connect the EA instrument, and gradually adjust the output current to the required value, which is tolerable and comfortable for the patient. After the treatment is over, firstly, turn all the knobs of the output potential back to "0", then turn off the power, remove the wires, and pull out the acupuncture needles. When adjusting the current, it should be gradually increased from low to high, and should not be adjusted too high at the beginning, or the current should be increased suddenly, to prevent strong muscle contraction, causing bent needles, broken needles, dizziness or fainting, etc., especially the elderly and patients with weak health. When using EA, care should be taken to avoid the current loop passing through the heart. When using EA near the spinal cord and medulla oblongata, the intensity of the current should be lower to avoid accidents.

4.3 Observation Indicators

4.3.1 Observation Indicators of Clinical Effectiveness

4.3.1.1 Main Observation Indicators

The standardised KOA clinical symptom observation scale and scoring indicators were used to evaluate the changes in patients' clinical symptoms and curative effect. These scales and scoring indicators include:

(a) Subjective Quantitative Indicators:

"Quantitative Score of Knee Osteoarthritis Symptom Classification (SKSC)" in *Guidelines for Clinical Research of Chinese Herbal Medicines as New Drugs* (China Medical Science and Technology Press, 2002), Western Ontario and McMaster University Osteoarthritis Index

(WOMAC) (Bellamy et al., 1988), Lysholm Knee Scoring Scale (LKSS) (Kubiak et al., 2012), and Visual Analog Scale (VAS) (Sun and Che, 2012) (In this clinical study, if the patient has bilateral knee joint disease, the VAS score will be calculated based on the side with the most severe pain). SKSC: Please refer to Appendix D; VAS and LKSS: Please refer to Appendix E; WOMAC: Please refer to Appendix F; and

(b) Objective Quantitative Indicators:

The content and changes of IL-1β and TNF-α in serum.

4.3.1.2 Evaluation Criteria for Clinical Effectiveness

With reference to the *Diagnostic and Therapeutic Effect Criteria for Syndromes and Diseases in TCM* (National Administration of Traditional Chinese Medicine, 2012) issued by the State Administration of Traditional Chinese Medicine, combined with the Nimodipine method, the clinical effectiveness evaluation criteria were formulated, and the clinical efficacy was divided into Full Clinical Recovery, Significantly Effective (obvious recovery, obvious improvement), Effective, and Not Effective.

Quantitative Score of Knee Osteoarthritis Symptom Classification (SKSC), also known as Symptom Grading Quantitative Score Table of Knee Osteoarthritis (KOA), as shown in Appendix D and Table 5.2, is utilized to assess and score the symptoms of KOA. These scores serve as the foundation for evaluating the clinical effectiveness of treatment before and after the intervention. The clinical efficacy index is calculated using the Nimodipine method to evaluate the clinical efficacy of the treatment plans for patients (Table 5.1). Based on the recorded scores of SKSC before and after treatment, calculate the difference between the two scores (pre-treatment SKSC score minus post-treatment SKSC score), divide the difference by the pre-treatment score, and then multiply by 100% to obtain the clinical efficacy index. The Calculation formula (Nimodipine method) is "Clinical efficacy index = [(pre-treatment SKSC score - post-treatment SKSC score) ÷ pre-treatment SKSC score] × 100%".

Merge the number of cases with clinical recovery, significantly Effective, effective as the total number of effective cases and calculate the total effective rate. Total effective rate = (number of cured cases + number of significantly effective cases + number of effective cases) / total number of cases × 100%.

Table 5.1: Clinical Efficacy Evaluation Criteria

Clinical Efficacy	Evaluation Criteria	Efficacy Index
Full Clinical Recovery	Symptoms and signs disappeared, the function and activities of joint returned to normal, and the main inspection indicators were normal.	was ≥ 95%
Significantly Effective	Symptoms disappeared or the main symptoms disappeared, joint function and activities returned to normal, and the patients could participate in normal work or labor. The main indicators were basically normal.	was ≥ 70% but < 95%
Effective	The main symptoms have basically disappeared, the main joint function and activities have basically recovered or have made significant progress, patients who cannot take good care of themselves turn to be able to take care of themselves, or Work and labor capacity have recovered, which were lost before. The main inspection indicators have improved.	was ≥ 30% but < 70%
Not Effective	No change in symptoms and signs before and after treatment.	was < 30%

Table 5.2: Symptom Grading Quantitative Score Table of Knee Osteoarthritis

Symptom	Level 0 (0 score)	Level I (1 score)	Level II (2 score)	Level III (3 score)
Pain or discomfort during rest in bed at night	None	Occasional pain	Intermittent pain	Persistent pain
Morning stiffness	None or ≤1 minute	1-10 minutes	≥10minutes	≥20minutes
Morning stiffness or increased pain after getting up	None	Discomfort, disappears after a slight activity	Pain, relieved after slight movement	Pain is obvious, does not decrease after exercise
Pain or discomfort when standing from a sitting position	None	Mild pain or discomfort	Pain or discomfort is obvious, but does not require help	Pain is noticeable and needs help
Pain or discomfort while walking	None	Appears after walking > 1km	Appears when walking < 1km	Pain appears when walking, and worsens after walking
Maximum walking distance (can walk with pain)	>1km	300m-1km	300m-100m	< 100m
Squatting or knees bending	Can	Slightly difficult	Cannot exceed 90 °	Cannot squat or bend knees
Up or down the stairs	Can	Slightly difficult	Difficult	Cannot go up and down stairs
Daily activities	Normal	Occasionally difficult	Often have difficulty	Cannot

4.3.2 Laboratory Examination Indicators

4.3.2.1 Operation Procedure

Before the start of the first treatment and after the end of the two courses of treatment, about 4ml of venous blood from the three groups of patients was collected and labeled, and the blood was coagulated naturally at room temperature for 10-20 minutes, and then centrifuged at a speed of 3,000r/min in a centrifuge for 20min. The supernatant was carefully collected and stored in a -80 °C freezer before being subjected to measurement. The contents of IL-1β and TNF-α in three groups of serum samples were measured, recorded and analysed by Enzyme-linked Immunosorbent Assay (ELISA), and the effects and possible mechanisms of EA on the disease were explored by studying the changes of content before and after treatment.

4.3.2.2 Detection Indicators

The detection indicators are serum cytokine IL-1β and TNF-α content in the blood sample.

4.3.2.3 Source of Reagents

The ELISA reagents and testing kits were purchased from Shanghai Guangrui Biotechnology Co., Ltd.

4.3.3 Evaluation Time Points

The detection and measurement time of SKSC, WOMAC, LKSS, VAS scores, cytokine IL-1β and TNF-α levels were all on the day of treatment and the completion day of treatment, for a total of 2 time points.

4.3.4 Safety Observation Indicators and Adverse Events

The safety evaluation indicators and adverse events of acupuncture include:

(a) Unbearable acupuncture pain during or after acupuncture (VAS score of 8 or more);

(b) After the needle is removed, there is a long or relatively large amount of bleeding at the needle puncture site, a large area of bruising, subcutaneous hematoma, local infection, etc.;

(c) Other uncomfortable symptoms after acupuncture (post-needle pain, nausea, vomiting, palpitations, dizziness, headache, anorexia, increased or decreased blood pressure, insomnia, etc. that occur after needle prick for 1 hour or more); and

(d) Other unforeseen adverse events.

If the above situation occurs, it should be recorded in detail at all times. The above-mentioned adverse reactions that occurred during the study, whether related to treatment or not, should be recorded in detail, including the time, symptoms, signs, degree and duration of adverse reactions, laboratory test indicators, treatment methods and results, event history, follow-up time, etc., and analyse the causes of adverse reactions. The observation time point should be during each acupuncture treatment and throughout the clinical trial study.

4.4 Study Quality and Bias Control

The quality of the study and bias control during the research process can be enhanced by the following:

(a) Perform unified training for researchers and acupuncture operators; The same group of patients should be treated by the same TCM physician as much as possible;

(b) Strict establishment and enforcement of inclusion and exclusion criteria;

(c) Ensure the independence of the sample;

(d) Avoid unnecessary additional harm to patients during the trial and ensure better compliance of patients;

(e) Reduce withdrawal cases and follow up on the withdrawal cases as much as possible; and

(f) Arrange unified efficacy evaluators before and after treatment to prevent measurement deviations.

4.5 Statistical Analysis

4.5.1 Content of Statistical Analysis

The content of the statistical analysis should cover the below:

(a) Baseline Data Analysis: Compared the gender, age, clinical course (course of the disease), and pre-treatment observation indicators of the three groups of patients, and analysed whether they were balanced and comparable;

(b) Clinical Efficacy Analysis: Conducted intra-group comparisons and analysis by comparing the post-treatment observation indicators of the three groups of patients with their pre-treatment values. Analyzed if there were any differences to determine the effectiveness of the three treatment methods. and

(c) Analysis of the Differences in Therapy Methods: Conducted inter-group comparisons and analysis by comparing the changes in the various observation indicators after treatment among the three groups of patients. Analyzed whether there were differences in the extent of improvement, thereby assessing the differences among the three treatment methods.

4.5.2 Statistical Analysis Method

All observed and recorded research data were entered into the computer and analyzed using IBM SPSS Statistics 22 software. The significance level was set at $\alpha = 0.05$ (i.e., when $P < 0.05$, the difference was considered statistically significant), and the power of the test was set at $1-\beta = 0.90$. All statistical tests were two-tailed.

Age, clinical course, data values of various observed indicators, and the difference in scores (i.e., post-treatment score minus pre-treatment score) are continuous variables, belonging to quantitative data, also known as metric data. Gender (male and female) and efficacy (effective and ineffective) belong to count data or categorical data.

For continuous variables, Kolmogorov-Smirnov test is used to test normality. Normally distributed indicators are expressed as mean ± standard deviation ($\bar{x} \pm s$). One-way analysis of variance (ANOVA) is used for comparisons among the three groups. If the variances are equal, Least Significant Difference (LSD) test is used for pairwise comparisons. If the variances are unequal, Tanhane's test is used. Paired sample t-test is used for within-group comparisons before and after treatment. For non-normally distributed indicators, median and interquartile range (IQR) are used to represent the data. Kruskal-Wallis H test is used for comparisons among the three groups. Pairwise comparisons are conducted using post hoc pairwise comparison methods. Within-group comparisons before and after treatment are performed using Wilcoxon signed-rank test.

For indicators such as count data or categorical data, percentages (%) are used for representation. Chi-square test is used for comparisons among the three groups, and post hoc pairwise comparisons are conducted for pairwise comparisons.

Pairwise comparisons between groups within the three groups refer to comparisons between the Treatment Group and Control Group 1, between the Treatment Group and Control Group 2, and between Control Group 1 and Control Group 2, which are referred to as pairwise comparisons (the two-pair comparisons).

4.6 Experimental Flow Chart

The following is the Flow Chart of this Clinical Study. Please refer to Figure 5.1.

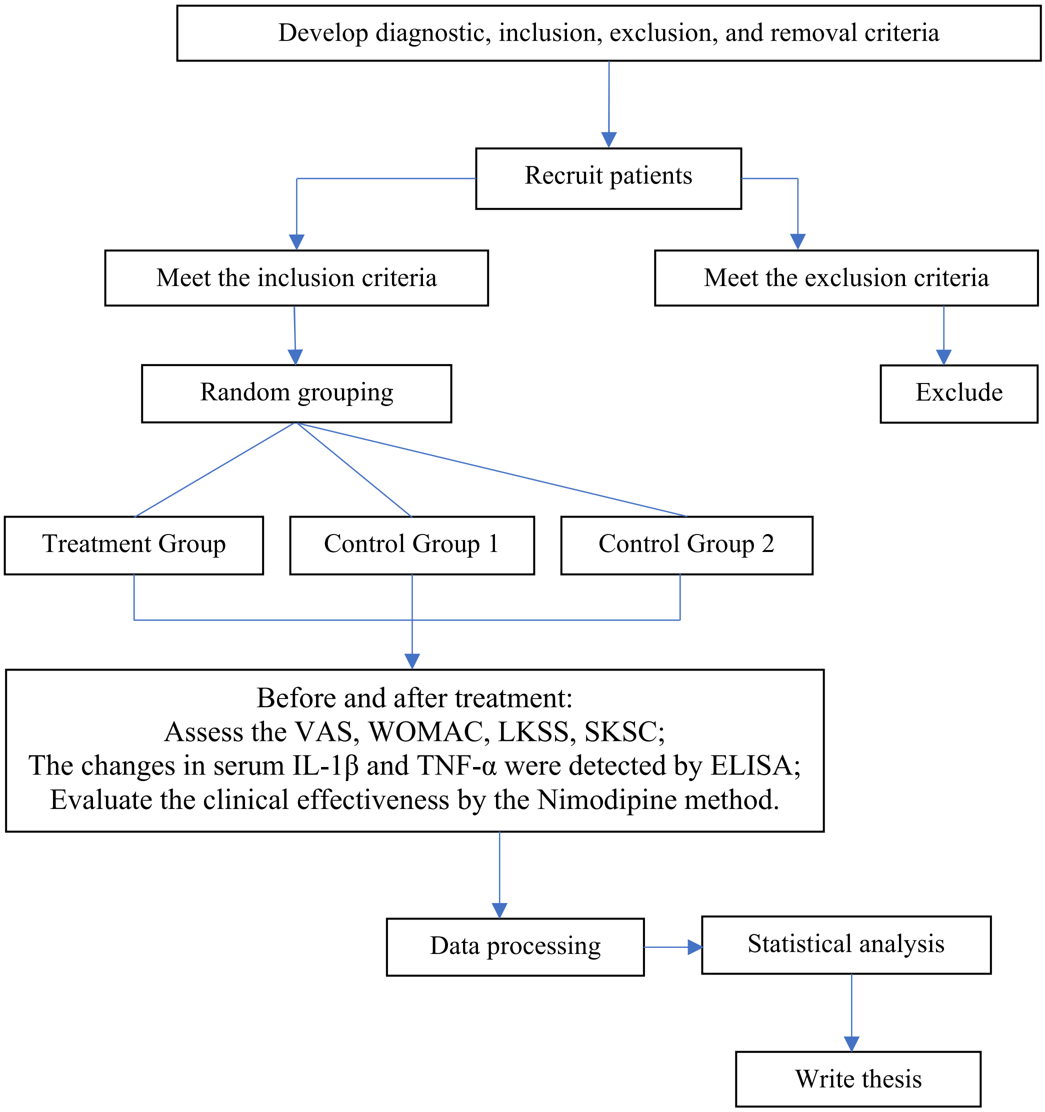

Figure 5.1: Flow Chart of Clinical Study

5.0 Results

5.1 The Completed Cases of the Study

A total of 207 cases were included in this study, with 69 cases each in the Treatment Group, Control Group 1, and Control Group 2. Some of the patients were unable to complete the treatment due to factors like the prevention and control measures of the COVID-19 pandemic such as city lockdowns, the flooding disaster in Zhengzhou, as well as other unforeseen circumstances reasons during the study period.

A total of 17 cases were dropped during the entire treatment process, of which 3 cases were in the Treatment Group (2 cases could not go out due to the city lockdown; and 1 case because he went to live with his daughter in another city). In Control Group 1, there were 5 cases of dropout (2 cases could not go out due to city lockdown; 2 cases were inconvenient to go out due to flooding; and 1 case of withdrawal due to fear of acupuncture in the later stage). In Control Group 2, there were 9 cases (3 cases could not go out due to city lockdown; 2 cases were inconvenient to go out due to flooding; 3 cases of withdrawal due to insignificant efficacy; and 1 case of withdrawal due to his family requested to use other treatments).

We had already considered the possibility of the case dropping out when calculating the sample size. Therefore, after the relaxation of pandemic control measures and overcoming the flooding disaster, with the support of our clinical study collaborating institutions, we recruited new eligible patients in the subsequent period and completed the research. With these efforts, as a result, we finally obtained experimental data from a total of 207 patients, with 69 cases in each of the three groups.

5.2 Comparison of Baseline Data of the Patients

5.2.1 Comparison of Gender among the Three Groups of Patients

Gender is a categorical variable, and the composition ratio can be expressed as a percentage (%). The Chi-Squared Test was conducted to compare the gender distribution among the three groups. The results showed that P = 0.287 > 0.05, indicating that there were no significant differences in gender distribution among the three groups. The pairwise comparisons also did not show any significant differences (P > 0.05), indicating comparable gender compositions among the three groups. Consistent with previous literature and clinical observations, the incidence of KOA is higher in females than males. The gender distribution in this study aligns with this pattern. Please refer to Table 5.3 for specific details.

Table 5.3: Comparison of the Gender Composition of the Three Groups

Group	n	Male (n, %)	Female (n, %)
Treatment Group	69	33 (47.83%)	36 (52.17%)
Control Group 1	69	24 (34.78%)	45 (65.22%)
Control Group 2	69	30 (43.48%)	39 (56.52%)
χ^2 value		2.498	
P value		0.287	

5.2.2 Comparison of Age and Clinical Course among the Three Groups of Patients

The indicators of age and clinical course were expressed as mean ± standard deviation ($\bar{x}$±s), and one-way analysis of variance (ANOVA) was used for comparison among multiple groups. The results of age and clinical course comparison were both P > 0.05 (age comparison: P = 0.621 > 0.05, clinical course comparison: P = 0.884 > 0.05). The above results indicate that there were no significant differences in age and clinical course among the three groups of patients, demonstrating comparability. Refer to Table 5.4 for specific details.

Table 5.4: Comparison of Age and Clinical Course among the Three Groups ($\bar{x} \pm s$)

Group	n	Age (years)	Clinical Course (years)
Treatment Group	69	58.51±10.48	3.52±1.52
Control Group1	69	60.12±9.12	3.46±1.51
Control Group 2	69	59.35±9.37	3.59±1.55
F value		0.478	0.123
P value		0.621	0.884

5.3 Comparison of Efficacy Evaluation Indicators - Rating Scales

The data of scoring indicators for rating scales used in this study are quantitative data, they were presented as mean ± standard deviation ($\bar{x}$±s).

5.3.1 Comparison of VAS Scores Before and After Treatment in Three Groups

Before treatment, the VAS scores were compared among the three groups, with a P-value > 0.05, indicating there was no statistical difference. The pairwise comparisons between the two groups also showed all P-values > 0.05, which indicated no statistical differences. These suggest that the VAS scores before treatment were comparable among the three groups.

After treatment, there was a statistically significant difference in the comparison among the three groups in the comparison of the VAS scores, with a P-value < 0.05. The pairwise comparisons between the two groups also showed P-values < 0.05, with statistical differences. The results indicate that the three kinds of treatment methods had different effects on the VAS scores of patients, and these differences were statistically significant.

After treatment, the differences in the VAS score (post-treatment score minus pre-treatment score) among the three groups were compared, and the results showed that the P value was less than 0.05, and there was a statistical difference. The pairwise comparisons between the two groups also showed statistically significant differences with all P-values < 0.05. Additionally, the Treatment Group exhibited a greater decrease in VAS scores compared to Control Group 1 and Control Group 2. These indicate that all three treatment methods could affect the VAS scores of patients, with the Treatment Group showing the most significant improvement, indicating Treatment Group had better treatment efficacy compared to Control Group 1 and Control Group 2 (Treatment Efficacy: Treatment Group > Control Group 1 > Control Group 2).

In intra-group comparison, the VAS scores of the same group were compared after treatment and before treatment, and the P values of the Treatment Group and Control Group 1 were both < 0.05, the differences of which were statistically significant, indicating that the two groups had a more obvious treatment effect. While the P value of Control Group 2 was > 0.05, and there was no significant difference, indicating that the score of Control Group 2 after treatment did not change much when compared with the score before treatment, and the treatment effect of this method was not obvious. The specific results are shown in Table 5.5.

Table 5.5: Comparison of the VAS Scores of the Three Groups (value, $\bar{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	6.01±1.66	3.84±1.32●	-2.17±0.82
Control Group 1	69	5.94±2.11	4.54±1.80▲●	-1.41±0.98▲
Control Group 2	69	5.77±1.51	5.72±2.18▲■	-0.04±2.40▲■
F value		0.350	19.353	32.549
P value		0.705	<0.001	<0.001

Note: a. Compared with the Treatment Group, ▲$P < 0.05$; b. Compared with the Control Group 1, ■$P < 0.05$; c. Compared with the Pre-Treatment Group, ●$P < 0.05$.

5.3.2 Comparison of WOMAC Scores Before and After Treatment in Three Groups

5.3.2.1 Comparison of WOMAC Pain Scores Before and After Treatment in Three Groups

Before treatment, the WOMAC pain scores were compared among the three groups, with a P-value greater than 0.05, indicating no statistical difference. The pairwise comparisons between the two groups also showed all P-values greater than 0.05, suggesting no statistical differences. These indicate that the WOMAC pain scores of pre-treatments were comparable among the three groups.

After treatment, the WOMAC pain scores were compared among the three groups, with a P-value less than 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values less than 0.05, with statistical differences. These suggest that the three treatment methods had different effects on the WOMAC pain scores of the patients, and these differences were statistically significant.

After treatment, the comparison of the WOMAC pain score differences (post-treatment score minus pre-treatment score) among the three groups showed a P-value less than 0.05, indicating a statistical difference. The pairwise comparisons between the two groups also showed all P-values less than 0.05, indicating statistically significant differences. Furthermore, the Treatment Group exhibited a greater decrease in the WOMAC pain scores compared to Control Group 1 and Control Group 2. These indicate that all the three treatment methods can influence the WOMAC pain scores of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

In the intragroup comparison, the WOMAC pain scores within the same group were compared before and after treatment. Both the Treatment Group and

Control Group 1 showed P-values less than 0.05, indicating statistically significant differences and demonstrating significant treatment effects. Control Group 2, on the other hand, had a P-value greater than 0.05, indicating no statistical difference and suggesting that there was minimal change in WOMAC pain scores after treatment in Control Group 2, indicating an insignificant treatment effect. The specific results are shown in Table 5.6.

Table 5.6: Comparison of WOMAC Pain Scores of the Three Groups (value, $\bar{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	13.29±3.80	8.67±2.89•	-29.61±9.23
Control Group 1	69	12.75±3.90	9.91±3.78▲•	-24.80±9.25▲
Control Group 2	69	12.22±3.92	12.22±3.77▲■	-16.83±19.85▲■
F value		1.321	18.195	15.728
P value		0.269	<0.001	<0.001

Note: a. Compared with the Treatment Group, ▲$P < 0.05$; b. Compared with the Control Group 1, ■$P < 0.05$; c. Compared with the Pre-Treatment Group, •$P < 0.05$.

5.3.2.2 Comparison of WOMAC Stiffness Scores Before and After Treatment in the Three Groups

Before treatment, the WOMAC stiffness scores were compared among the three groups, with a P-value > 0.05, indicating no statistical difference. The pairwise comparisons between the two groups also showed all P-values > 0.05, suggesting no statistical differences. These indicate that the WOMAC stiffness scores of pre-treatments were comparable among the three groups.

After treatment, the WOMAC stiffness scores were compared among the three groups, with a P-value < 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values < 0.05, with statistical differences. These suggest that the three treatment methods had different effects on the WOMAC stiffness scores of the patients, and these differences were statistically significant.

After treatment, the comparison of the WOMAC stiffness score differences (post-treatment score minus pre-treatment score) among the three groups showed a P-value < 0.05, indicating a statistical difference. The pairwise comparisons between the two groups also showed all P-values < 0.05, indicating statistically significant differences. Furthermore, the Treatment Group showed a greater decrease in the WOMAC stiffness scores compared to Control Group 1 and Control Group 2. These indicate that all the three treatment methods can influence the WOMAC stiffness scores of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

In the intragroup comparison, the WOMAC stiffness scores within the same group were compared before and after treatment. Both the Treatment Group and Control Group 1 showed that the P-values < 0.05, indicating statistically significant differences and demonstrating significant treatment effects. Control

Group 2, on the other hand, had a P-value > 0.05, indicating no statistical difference and suggesting that there was minimal change in WOMAC stiffness scores after treatment in Control Group 2, indicating an insignificant treatment effect. The specific results are shown in Table 5.7.

Table 5.7: Comparison of WOMAC Stiffness Scores of the Three Groups (value, $\overline{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	4.91±1.59	2.81±1.02•	-2.10±1.00
Control Group 1	69	4.74±1.75	3.64±1.64▲•	-1.10±1.19▲
Control Group 2	69	4.87±1.46	4.87±2.03▲■	0.00±2.72▲■
F value		0.220	28.255	23.262
P value		0.803	<0.001	<0.001

Note: a. Compared with the Treatment Group, ▲$P < 0.05$; b. Compared with the Control Group 1, ■$P < 0.05$; c. Compared with the Pre-Treatment Group, •$P < 0.05$.

5.3.2.3 Comparison of WOMAC Physical Function Scores Before and After Treatment in Three Groups

Before treatment, the WOMAC physical function scores were compared among the three groups, with a P-value greater than 0.05, indicating no statistical difference. The pairwise comparisons between the two groups also showed all P-values greater than 0.05, suggesting no statistical differences. These indicate that the WOMAC physical function scores of pre-treatments were comparable among the three groups.

After treatment, the WOMAC physical function scores were compared among the three groups, with a P-value less than 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values less than 0.05, with statistical differences. These suggest that the three treatment methods had different effects on the WOMAC physical function scores of the patients, and these differences were statistically significant.

After treatment, the comparison of the WOMAC physical function score differences (post-treatment score minus pre-treatment score) among the three groups showed a P-value less than 0.05, indicating a statistical difference. The pairwise comparisons between the two groups also showed all P-values less than 0.05, indicating statistically significant differences. Furthermore, the Treatment Group exhibited a greater decrease in the WOMAC physical function scores compared to Control Group 1 and Control Group 2. These indicate that all the three treatment methods can influence the WOMAC physical function scores of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

In the intragroup comparison, the WOMAC physical function scores within the same group were compared before and after treatment. Both the Treatment Group and Control Group 1 showed P-values less than 0.05, indicating statistically significant differences and demonstrating significant treatment effects. Control Group 2, on the other hand, had a P-value greater than 0.05, indicating no statistical difference and suggesting that there was minimal change in WOMAC physical function scores after treatment in Control Group 2, indicating the treatment effect of this therapy method was not obvious. The specific results are shown in Table 5.8.

Table 5.8: Comparison of WOMAC Physical Function Scores of the Three Groups (value, $\overline{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	47.77±12.28	36.36±9.19$^{\bullet}$	-11.41±6.88
Control Group 1	69	48.93±13.31	41.62±11.90$^{\blacktriangle\bullet}$	-7.30±6.30$^{\blacktriangle}$
Control Group 2	69	45.59±12.21	45.86±14.66$^{\blacktriangle\blacksquare}$	0.26±18.68$^{\blacktriangle\blacksquare}$
F value		1.243	10.615	16.628
P value		0.291	<0.001	<0.001

Note: a. Compared with the Treatment Group, $^{\blacktriangle}P < 0.05$; b. Compared with the Control Group 1, $^{\blacksquare}P < 0.05$; c. Compared with the Pre-Treatment Group, $^{\bullet}P < 0.05$.

5.3.2.4 Comparison of Total WOMAC Scores Before and After Treatment in the Three Groups

Before treatment, the total WOMAC scores were compared among the three groups, with a P-value > 0.05, indicating no statistical difference. The pairwise comparisons between the two groups also showed all P-values > 0.05, suggesting no statistical differences. These indicate that the total WOMAC scores of pre-treatments were comparable among the three groups.

After treatment, the total WOMAC scores were compared among the three groups, with a P-value < 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values < 0.05, with statistical differences. These suggest that the three treatment methods had different effects on the total WOMAC scores of the patients, and these differences were statistically significant.

After treatment, the comparison of the total WOMAC score differences (post-treatment score minus pre-treatment score) among the three groups showed a P-value < 0.05, indicating a statistical difference. The pairwise comparisons between the two groups also showed all P-values < 0.05, indicating statistically significant differences. Furthermore, the Treatment Group showed a greater decrease in the total WOMAC scores compared to Control Group 1 and Control Group 2. These indicate that all the three treatment methods can influence the total WOMAC scores of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

In the intragroup comparison, the total WOMAC scores within the same group were compared before and after treatment. Both the Treatment Group and Control Group 1 showed that the P-values < 0.05, indicating statistically significant differences and demonstrating significant treatment effects. Control Group 2, on the other hand, had a P-value > 0.05, indicating no statistical difference and suggesting that there was minimal change in the total WOMAC scores after treatment in Control Group 2, indicating an insignificant treatment effect. The specific results are shown in Table 5.9.

Table 5.9: Comparison of Total WOMAC Scores of the Three Groups (value, $\bar{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	65.97±15.11	47.84±11.07$^{\bullet}$	-18.13±7.53
Control Group 1	69	66.42±16.47	55.17±14.97$^{\blacktriangle\bullet}$	-11.25±6.61$^{\blacktriangle}$
Control Group 2	69	62.68±13.78	62.94±15.63$^{\blacktriangle\blacksquare}$	0.26±20.14$^{\blacktriangle\blacksquare}$
F value		1.251	19.976	35.330
P value		0.288	<0.001	<0.001

Note: a. Compared with the Treatment Group, $^{\blacktriangle}P < 0.05$; b. Compared with the Control Group 1, $^{\blacksquare}P < 0.05$; c. Compared with the Pre-Treatment Group, $^{\bullet}P < 0.05$.

5.3.3 Comparison of LKSS Scores Before and After Treatment in the Three Groups

Before treatment, the LKSS scores were compared among the three groups, with a P-value > 0.05, indicating no statistical difference. The pairwise comparisons between the two groups also showed all P-values > 0.05, suggesting no statistical differences. These indicate that the LKSS scores of pre-treatments were comparable among the three groups.

After treatment, the LKSS scores were compared among the three groups, with a P-value < 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values < 0.05, with statistical differences. These suggest that the three treatment methods had different effects on the LKSS scores of the patients, and these differences were statistically significant.

After treatment, the comparison of the LKSS score differences (post-treatment score minus pre-treatment score) among the three groups showed a P-value < 0.05, indicating a statistical difference. The pairwise comparisons between the two groups also showed all P-values < 0.05, indicating statistically significant differences. Moreover, the increase in the LKSS scores of the Treatment Group was greater than that of the Control Group 1 and the Control Group 2. These indicate that all the three treatment methods can affect the LKSS scores of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

In the intragroup comparison, the LKSS scores within the same group were compared before and after treatment. Both the Treatment Group and Control Group 1 showed that the P-values < 0.05, indicating statistically significant differences and demonstrating significant treatment effects. Control Group 2, on the other hand, had a P-value > 0.05, indicating no statistical difference and suggesting that there was minimal change in the LKSS scores after treatment in Control Group 2, indicating an insignificant treatment effect. The specific results are shown in Table 5.10.

Table 5.10: Comparison of LKSS Scores of the Three Groups (value, $\bar{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	53.91±15.87	70.19±14.59$^{\bullet}$	16.28±9.17
Control Group 1	69	48.91±17.08	59.46±16.05$^{\blacktriangle\bullet}$	10.55±6.76$^{\blacktriangle}$
Control Group 2	69	53.00±13.61	53.10±17.23$^{\blacktriangle\blacksquare}$	0.10±18.85$^{\blacktriangle\blacksquare}$
F value		2.014	20.122	28.712
P value		0.136	<0.001	<0.001

Note: a. Compared with the Treatment Group, $^{\blacktriangle}P < 0.05$; b. Compared with the Control Group 1, $^{\blacksquare}P < 0.05$; c. Compared with the Pre-Treatment Group, $^{\bullet}P < 0.05$.

5.3.4 Comparison of SKSC Scores Before and After Treatment in the Three Groups

Before treatment, the SKSC scores were compared among the three groups, with a P-value greater than 0.05, indicating no statistical difference. The pairwise comparisons between the two groups also showed all P-values greater than 0.05, suggesting no statistical differences. These indicate that the SKSC scores of pre-treatments were comparable among the three groups.

After treatment, the SKSC scores were compared among the three groups, with a P-value less than 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values less than 0.05, with statistical differences. These suggest that the three treatment methods had different effects on the SKSC scores of the patients, and these differences were statistically significant.

After treatment, the comparison of the SKSC score differences (post-treatment score minus pre-treatment score) among the three groups showed a P-value of less than 0.05, which indicates a statistical difference. The pairwise comparisons between the two groups also showed all P-values are less than 0.05, indicating statistically significant differences. Furthermore, the Treatment Group exhibited a greater decrease in the SKSC scores compared to Control Group 1 and Control Group 2. These indicated that all three treatment methods can influence the SKSC scores of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

In the intragroup comparison, the SKSC scores within the same group were compared before and after treatment. Both the Treatment Group and Control Group 1 showed P-values of less than 0.05, which indicates statistically significant differences and demonstrates the significant treatment effects. The Control Group 2, on the other hand, had a P-value of greater than 0.05, which indicates that there was no statistical difference and suggests that when compared with before treatment, the SKSC scores of Control Group 2 after treatment did not change much, and the treatment effect of Control Group 2 was not obvious. The specific results are shown in Table 5.11.

Table 5.11: Comparison of SKSC Scores in the Three Groups (value, $\bar{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	62.65±10.69	37.26±10.80$^{\bullet}$	-25.39±10.51
Control Group 1	69	62.70±12.97	42.46±11.22$^{\blacktriangle\bullet}$	-20.23±7.44$^{\blacktriangle}$
Control Group 2	69	62.45±10.73	62.43±11.94$^{\blacktriangle\blacksquare}$	-0.01±12.63$^{\blacktriangle\blacksquare}$
F value		0.009	94.964	114.412
P value		0.991	<0.001	<0.001

Note: a. Compared with the Treatment Group, $^{\blacktriangle}P < 0.05$; b. Compared with the Control Group 1, $^{\blacksquare}P < 0.05$; c. Compared with the Pre-Treatment Group, $^{\bullet}P < 0.05$.

5.4 Comparison of Efficacy Evaluation Indicators - Laboratory Indicators

5.4.1 Comparison of IL-1β Content Before and After Treatment in the Three Groups

Before treatment, the serum IL-1β contents of the three groups were compared, with a P-value > 0.05, indicating that there was no statistical difference. The pairwise comparisons between the two groups also showed all P-values > 0.05, suggesting no statistical differences. These indicate that before treatment the serum IL-1β contents of the three groups were comparable.

After treatment, the serum IL-1β contents of the three groups were compared, with a P-value < 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values < 0.05, with statistical differences. These results suggest that the three treatment methods had different effects on the serum IL-1β contents of the patients, and these differences were statistically significant.

After treatment, the comparison of the serum IL-1β content changes (post-treatment score minus pre-treatment score) among the three groups showed a P-value < 0.05, indicating a statistical difference. The pairwise comparisons between the two groups also showed all P-values < 0.05, indicating statistically significant differences. Moreover, the Treatment Group showed a greater decrease in the serum IL-1β content when compared to those of Control Group 1 and Control Group 2. The results indicate that all the three treatment methods can influence the serum IL-1β content of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

The intra-group comparison was conducted by comparing the serum IL-1β contents before and after treatment in the same group. Both the Treatment Group and Control Group 1 showed P-values less than 0.05, indicating statistically significant differences and showing that this therapy method had significant treatment effects on KOA. Control Group 2, on the other hand, had a P-value > 0.05, indicating there was no statistical difference and suggesting that there was minimal change in the serum IL-1β content after treatment, with an insignificant treatment effect. The specific results are shown in Table 5.12.

Table 5.12: Comparison of Serum IL-1β Content of the Three Groups (pg/mL, $\bar{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	14.23±4.10	8.56±3.67●	-5.67±1.97
Control Group 1	69	13.37±4.79	10.34±4.81▲●	-3.03±2.30▲
Control Group 2	69	13.19±4.25	13.17±4.83▲■	-0.01±4.39▲■
F value		1.107	18.753	58.484
P value		0.332	<0.001	<0.001

Note: a. Compared with the Treatment Group, ▲$P < 0.05$; b. Compared with the Control Group 1, ■$P < 0.05$; c. Compared with the Pre-Treatment Group, ●$P < 0.05$.

5.4.2 Comparison of TNF-α Content Before and After Treatment in the Three Groups

Before treatment, the serum TNF-α contents of the three groups were compared, with a P-value > 0.05, indicating that there was no statistical difference. The pairwise comparisons between the two groups also showed all P-values > 0.05, suggesting no statistical differences. These indicate that before treatment the serum TNF-α contents of the three groups were comparable.

After treatment, the serum TNF-α contents of the three groups were compared, with a P-value < 0.05, indicating that there was a statistically significant difference. The pairwise comparisons between the two groups also showed P-values < 0.05, with statistical differences. These results suggest that the three treatment methods had different effects on the serum TNF-α contents of the patients, and these differences were statistically significant.

After treatment, the comparison of the serum TNF-α content changes (post-treatment score minus pre-treatment score) among the three groups showed a P-value < 0.05, indicating a statistical difference. The pairwise comparisons between the two groups also showed all P-values < 0.05, indicating statistically significant differences. Moreover, the Treatment Group showed a greater decrease in the serum TNF-α content when compared to those of Control Group 1 and Control Group 2. The results indicate that all the three treatment methods can influence the serum TNF-α content of the patients, with the Treatment Group showing the most significant improvement, suggesting that the therapeutic effect of the Treatment Group was superior to that of Control Group 1 and Control Group 2 (Treatment Effect: Treatment Group > Control Group 1 > Control Group 2).

The intra-group comparison was conducted by comparing the serum TNF-α contents before and after treatment in the same group. Both the Treatment Group and Control Group 1 showed P-values less than 0.05, indicating that there were statistically significant differences, and showing that the two therapy methods had significant treatment effects on KOA. While the result of Control Group 2 was P-value > 0.05, indicating there was no statistical difference and suggesting that the serum TNF-α content of Control Group 2 did not change much when compared with before treatment, and the treatment effect of Control Group 2 was not obvious. The specific results are shown in Table 5.13.

Table 5.13: Comparison of Serum TNF-α Content in Three Groups (pg/mL, $\bar{x} \pm s$)

Group	n	Before Treatment	After Treatment	Difference
Treatment Group	69	161.45±97.03	84.03±67.18•	-77.42±40.27
Control Group 1	69	137.28±89.48	108.13±77.38▲•	-29.15±19.43▲
Control Group 2	69	138.08±70.51	138.07±63.08▲■	-0.01±72.04▲■
F value		1.743	10.479	44.024
P value		0.178	<0.001	<0.001

Note: a. Compared with the Treatment Group, ▲$P < 0.05$; b. Compared with the Control Group 1, ■$P < 0.05$; c. Compared with the Pre-Treatment Group, •$P < 0.05$.

5.5 Comparison of Clinical Efficacy in the Three Groups

The nimodipine calculation method was used to calculate the clinical efficacy index by using the Quantitative Score of Knee Osteoarthritis Symptom Classification (Symptom Grading Quantitative Score Table of Knee Osteoarthritis), and the clinical efficacy of the three treatments on patients was evaluated.

Clinical efficacy was treated as ordinal data and analyzed using the non-parametric rank sum test, and the result was Z = 109.106, with P < 0.05. The number of clinically cured, significantly effective, and effective cases were combined as the total effective cases, and the total effective rate was calculated. The transformed data were then categorized into effective and ineffective variables, and analyzed using the Chi-square test, and the result was $\chi^2 = 113.690$, with P < 0.05. The aforementioned results indicate that there are significant differences in clinical efficacy among the three groups, and these differences are statistically significant. When comparing the total effective rates between each pair of groups, all the P-values were < 0.05, indicating that they all had statistically significant differences. The Treatment Group had a total effective rate of 89.9%, close to 90%, while Control Group 1 had a rate of 75.36%, and Control Group 2 had a rate of 5.8%. These results suggest that both the Treatment Group and Control Group 1 had significant therapeutic effects on the disease, but the Treatment Group showed better therapeutic outcomes, while Control Group 2 had poor efficacy. The specific results are shown in Table 5.14.

Table 5.14: Comparison of Clinical Efficacy of Three Groups

Group	Full Clinical Recovery	Significantly Effective	Effective	Not Effective	Total Clinical Efficacy
Treatment Group	0(0.0%)	7(10.1%)	55(79.7%)	7(10.1%)	62(89.9%)
Control Group1	0(0.0%)	3(4.3%)	49(71.0%)	17(24.6%)	52(75.4%)▲
Control Group2	0(0.0%)	0(0.0%)	4(5.8%)	65(94.2%)	4(5.8%)▲■
Z/χ^2 value	109.106				113.690
P value	<0.001				<0.001

Note: a. Compared with the Treatment Group, ▲$P < 0.05$; b. Compared with the Control Group 1, ■$P < 0.05$.

5.6 Safety Evaluation

During the entire treatment process, all cases did not experience adverse reactions such as dizziness from needling, needle breakage, large areas of bruising, subcutaneous hematoma, or local infection.

6.0 Discussion

6.1 Western Medicine's Understanding of KOA

6.1.1 Definition of KOA in Western Medicine

KOA, also known as Osteoarthrosis of the Knee, is the definition used by Western medicine for KOA. It is a disease caused by local knee joint damage, inflammation and chronic strain, primarily characterized by degenerative changes in the articular cartilage. The condition affects the bone, synovium, joint capsule and surrounding structures, leading to symptoms such as adhesion of surrounding tissues, synovitis and cartilage destruction. KOA has a relatively high prevalence in the population, particularly among middle-aged and elderly individuals, and is more common in females than males (Chen, 2020; Dziedzic et al., 2014; McGrory et al., 2016).

This definition emphasizes that KOA is a chronic degenerative disease, with the main impact being the destruction of the articular cartilage. Additionally, it involves damage to other joint-related tissues and structures, such as bone, synovium, and joint capsule.

The understanding of KOA in Western medicine also includes the knowledge of its incidence and risk factors, as well as a range of diagnostic and treatment methods, such as medication, physical therapy, surgical intervention and rehabilitation measures (detailed in Chapter 2). The selection of these methods depends on the severity of the condition and the individual circumstances of the patient.

6.1.2 Research on Knee Joint Anatomy and Biomechanics in Western Medicine

Extensive research has been conducted in Western medicine on the anatomy and biomechanics of the knee joint.

6.1.2.1 Anatomical Structure of Knee Joint

The knee joint is one of the largest joints in the human body. It is a hinge joint that allows flexion and extension, enabling movements such as walking and bending of the leg. Its anatomical structure mainly includes:

(a) Bones: The knee joint is primarily composed of the distal end of the femur, the proximal end of the tibia and the patella. The knee joint can be divided into two parts: the tibiofemoral joint (the femoral-tibial joint) and the patellofemoral joint (the femoral-patellar joint). The distal end of the femur has two condyles, the medial condyle and the lateral condyle, which respectively articulate with the medial and lateral tibial condyles, forming the tibiofemoral joint. The patella is located in front of the distal femur, forms the patellofemoral joint, a femoral-patellar joint with the femur and tibia, and is connected to the femur through the patellar ligament;

(b) Articular Cartilage: The articular surfaces of the knee joint are covered with articular cartilage, which has a smooth surface that better reduces friction between the bones and provides protection during knee joint movement;

(c) Meniscus: The meniscus is a fibrocartilaginous plate, belonging to the cartilaginous structure. The meniscuses of the knee joint are located between the femoral and tibial condyles and are divided into the medial meniscus and lateral meniscus. The meniscuses help to distribute the weight of the upper body, provide shock absorption, reduce friction, and minimize the impact on the articular surfaces. They also contribute to increasing the depth of the joint socket and enhancing the stability and flexibility of the knee joint (Li et al., 2020);

(d) Ligaments: There are four important ligaments within and around the knee joint, including the anterior cruciate ligament (ACL), the posterior cruciate ligament (PCL), the medial collateral ligament (MCL), and the lateral collateral ligament (LCL). These ligaments provide stability to the knee joint, preventing excessive extension or twisting. The ACL and PCL, by firmly attaching and connecting to the femur and tibia, can restrict the forward and backward sliding of the tibia relative to the femur. When the knee joint is in extension, the ACL provides maximal tension to prevent anterior displacement of the tibia, while the PCL provides maximal tension in flexion of the knee joint to prevent posterior displacement of the tibia. The MCL and LCL are located on the medial and lateral sides of the knee joint respectively, reinforcing the stability of the knee joint and preventing excessive extension of the joint (Zheng et al., 2022);

(e) Muscle Groups: The muscle groups surrounding the knee joint (muscles and tendons such as quadriceps femoris muscle, semitendinosus muscle and semimembranosus muscle) play a crucial role in the stability and movement of the joint and have a significant impact on the biomechanical characteristics of the knee joint. The quadriceps femoris is the main muscle responsible for extending the knee joint, while the semitendinosus and semimembranosus are the primary muscles responsible for flexing the knee joint. The contraction and relaxation of these muscles and tendons generate forces in different directions, thereby controlling the movement of the knee joint, especially flexion and extension. These structures work together to enable normal knee joint motion and stability. However, pathological changes such as muscle atrophy and weakness, particularly in the quadriceps femoris, can affect the knee joint's buffering capacity, and increase pressure on the articular cartilage, when the pressure load exceeds the compensatory range, it can lead to degeneration and damage to the articular cartilage, resulting in KOA (Thomas et al., 2010; Ye et al., 2023); and

(f) Nerves: The knee joint is innervated by multiple nerves, including sciatic nerve, tibial nerve, common fibular nerve, saphenous nerve, etc. These nerves provide sensory feedback and influence motor function in the knee joint. They are responsible for transmitting information related to pain, pressure, and proprioception and also control muscle contraction and relaxation.

Through in-depth research on the anatomy of the knee joint, Western medicine has gained a better understanding of its structure and function, providing a foundation for the diagnosis and treatment of knee-related diseases. These research findings also serve as an important basis for the development of treatment methods for knee joint disorders, including methods such as total knee replacement surgery.

6.1.2.2 Biomechanics of the Knee Joint

The knee joint is one of the crucial joints in the human body for weight-bearing and body support. It experiences forces of various directions and magnitudes during movement, making its biomechanical characteristics vital for normal motion and joint stability.

The anatomical structure of the knee joint determines that the primary movement of the knee joint is flexion and extension along the sagittal plane, including bending and straightening. Flexion refers to the bending of the knee, while extension refers to the straightening of the knee. During flexion, the femur slides backward and allows rotational movement and a limited passive valgus movement within a small range. During extension, the femur slides forward. The knee joint maintains both static and dynamic stability through the combined actions of its bony structure, meniscus, joint capsule and accessory ligament structures mentioned above. When the knee joint is fully extended, it undergoes a locking mechanism to achieve maximum joint stability. This locking occurs because, in full extension, the femur internally rotates on the tibia. Conversely, in excessive flexion, the femur externally rotates. This mechanism increases joint stability through the occlusion of the articular surfaces and the braking effect of the cruciate ligaments. Additionally, at the femur-patella joint, the muscular strength of the quadriceps increases with knee flexion (He et al., 2019; Cai et al., 2017).

The forces acting on the knee joint primarily involve three directions: anterior-posterior forces, medial-lateral forces and torque. Ligaments and muscles of the knee joint help to disperse and absorb these forces, thereby reducing stress and wear on the joint's articular cartilage and bones. During daily activities such as walking and running, the knee joint experiences the weight of the body and the ground reaction forces. When the knee joint flexes, the two condyles at the distal end of the femur come into contact with the platform at the proximal end of the tibia, resulting in a relatively small contact area, and the pressure which bears is relatively high. To alleviate this pressure, the meniscuses play a crucial role by dispersing the force over a wider area and providing cushioning during knee flexion and extension.

In conclusion, studying the anatomy and biomechanics of the knee joint is of great significance for understanding its structure, function, as well as the treatment and prevention of knee joint diseases. By gaining a deeper understanding of the biomechanical characteristics of the knee joint, we can develop better treatment, rehabilitation, and exercise training programs, thereby improving the treatment efficacy of knee joint disease, and enhancing the quality of life for patients.

6.1.3 Research on the Pathogenesis of KOA in Western Medicine

KOA is a common degenerative joint disease characterised by progressive cartilage deterioration, osteophyte formation and synovial inflammation. Extensive research has been conducted in Western medicine to understand its etiology and pathogenesis, which can be attributed to several factors, primarily involves the following aspects:

(a) Biomechanical Imbalance

Long-term high-load activities, repetitive movements and poor posture can lead to abnormal stress on the knee joint, resulting in a series of changes including cartilage degeneration, bone hyperplasia, soft tissue strain and contraction around the joint. During high-load activities, the knee joint is subjected to excessive forces, causing pressure and shear stress on the cartilage. Over time, this excessive load can disrupt the structure of the cartilage matrix, and interfere with its normal metabolic balance. As a result, micro-damage may occur on the surface of the cartilage, gradually progressing into cartilage wear (Chen and Wang, 2023). These changes disrupt the normal stress balance, leading to abnormal joint function;

(b) Cytokines and Inflammatory Response

Research conducted by Wang et al. (2017) suggests that although the pathogenesis of KOA is not fully understood, inflammatory cytokines play a significant role in the occurrence and progression of KOA, and can serve as biological markers for KOA pain and disease severity. Cytokines are small soluble peptides or glycoproteins produced by innate and adaptive immune cells through autocrine or paracrine secretion (Liu et al., 2021). These cytokines exert their effects on KOA. KOA is accompanied by the inflammatory response of the joint capsule and synovium, where inflammatory cells release various inflammatory and cytokine factors, accelerating the degradation of articular cartilage and the progression of bone hyperplasia. In KOA, IL-1β, IL-6, and TNF-α are considered pro-inflammatory cytokines and early inflammatory factors that have destructive effects on cartilage cells and can also influence bone metabolism (Li et al., 2019). TNF-α can enhance the production of receptor activators of nuclear factor-kB ligand (RANKL) by bone cells, further promoting the generation of osteoclasts, and contributing to joint destruction (Marahleh et al., 2019). TNF-α selectively inhibits the production of collagen and proteoglycans in cartilage, promotes the degradation of proteoglycans, and stimulates cartilage-degrading enzymes to act on endothelial cells, leading to local tissue inflammation, edema, and infiltration of inflammatory cells. Tissue inhibitors of metalloproteinase-1 (TIMP-1) and matrix metalloproteinase-3 (MMP-3) are cytokines involved in the pathogenesis of KOA. They are closely associated with the degradation of the cartilage matrix in the knee joint and exist in a dynamic balance. TIMP-1 can inhibit the activity of MMP-3, thereby reducing the degradation of the cartilage matrix (Zhao et al., 2020).

Studying these cytokines helps to enhance our understanding of the pathogenesis of KOA and can provide a basis for the development of treatment strategies. Therefore, further research is needed to explore the specific mechanisms of action of these cytokines in KOA and evaluate their potential value as biomarkers;

(c) Genetic Factors

Genetic factors play a significant role in the pathogenesis of KOA, although the specific genetic variations and related genes have not been fully elucidated. Research conducted by Wang (2008) indicates that multiple genes may be associated with genetic susceptibility to KOA, including genes related to articular cartilage metabolism, inflammatory response, bone metabolism and cell apoptosis. Certain gene mutations may increase the risk of articular cartilage degradation and osteophyte formation. In everyday life, it is common to observe an increased probability of KOA in offspring when parents are affected by KOA, particularly in female offspring.

Furthermore, genetic factors may interact with environmental factors, jointly influencing the risk of KOA. For instance, the interaction between genetic factors and environmental factors such as obesity, excessive joint use and joint injury may contribute to the occurrence and progression of KOA.

Understanding the role of genetic factors in KOA is crucial for prevention, early diagnosis and personalized treatment. However, further research is needed to identify and validate genetic factors associated with KOA and delve into their underlying mechanisms;

(d) Osteoporosis

Studies conducted by Qing (2019) and Zhao (2014) have shown a significant association between KOA and osteoporosis, with a higher likelihood of concurrent occurrence of osteoporosis in KOA patients. Osteoporosis is considered one of the environmental risk factors for KOA.

In the early stages of KOA and osteoporosis, these two conditions exhibit a negative correlation. This suggests that in the early stages, the presence of osteoporosis may have a protective effect on the development of KOA. However, when microfractures occur in trabecular bone, osteoporosis and KOA mutually promote and accelerate each other's progression. This indicates that microfractures may play a crucial role in the development of KOA, further expediting the disease's evolution.

Another study conducted by Lin (2005) examining lumbar spine X-ray bone density in KOA patients found that osteoporosis is likely to be one of the causes of bone-joint disease. This suggests a close relationship between osteoporosis and KOA.

(e) Hormone Levels

Tao (2021) and Li (2017) conducted the Studies, which have indicated that the peri-menopausal and post-menopausal periods, particularly post-menopause, are periods of increased prevalence of KOA, primarily due to the decline in estrogen levels.

Estrogen plays a protective role in bone health. It promotes increased bone density, prevents osteoporosis, and reduces the degradation of articular cartilage. Therefore, as women enter menopause and their ovaries gradually stop producing estrogen, the level of estrogen in the body declines. The decrease in estrogen level causes a series of physiological changes, such as osteoporosis, cardiovascular diseases and metabolic syndrome. The reduction in estrogen leads to decreased bone density, making the bones more susceptible to damage, and it may also contribute to the deterioration of articular cartilage. The decline in estrogen also affects the functioning of the immune system and exacerbates inflammatory responses, and inflammatory reactions can promote the infiltration of inflammatory cells and accelerate the degradation of articular cartilage, playing a significant role in the pathological process of KOA. These may contribute to the occurrence and progression of arthritis (Duan and Wei, 2007; Liu, 2012); and

(f) Cartilage Degeneration

Cartilage is a smooth and resilient tissue that covers the ends of bones, playing a crucial role in reducing friction and protecting the bones. However, with age and a range of factors such as excessive exercise, obesity and injury, the cartilage tissue gradually deteriorates. This leads to surface wear and cracks in the articular cartilage, resulting in loss of smoothness and symptoms such as pain and stiffness.

As cartilage degeneration progresses, chondrocytes, the cells within the cartilage, start to secrete large amounts of enzymatic substances, accelerating the degradation process of cartilage. This causes a narrowing of the joint space, exacerbating the mutual friction between bones and further intensifying the inflammation and pain associated with arthritis. Under the influence of pathological factors, inflammatory cytokines mediate the increased expression of various proteinases in the articular cartilage and synovium. The activity of these proteinases leads to the degradation of collagen fiber network and proteoglycans in the cartilage matrix. Ultimately, these changes result in cartilage degeneration. Additionally, subchondral bone loss and subchondral bone absorption are closely associated with the development of osteoarthritic cartilage lesions. This implies that during the process of cartilage degeneration, not only is the cartilage itself damaged, but there is also concurrent loss and absorption of bone.

Therefore, cartilage degeneration is a significant factor in the development of osteoarthritis. As cartilage degeneration worsens, joint function deteriorates, and symptoms of inflammation and pain increase. Understanding the mechanisms of cartilage degeneration and the associated pathological factors is crucial for comprehending the progression of osteoarthritis and providing a scientific basis for its prevention and treatment.

In conclusion, the pathogenesis of KOA is a complex process involving multiple factors and mechanisms, including degenerative changes in articular cartilage, osteophyte formation, excessive loading, inflammatory response, and genetic factors. The interaction of these factors can lead to the occurrence and progression of KOA. Understanding these pathological factors and the mechanisms of onset is of significant importance for the prevention and treatment of KOA.

6.2 Understanding of KOA in TCM

6.2.1 Definition of KOA in TCM

In TCM, there is no specific or explicit term to name KOA. While according to the symptoms and signs exhibited by this disease, TCM classifies it into the category of such as "arthralgia syndrome", "flaccidity syndrome", "bone impediment", "muscle impediment", "bone flaccidity", "muscle flaccidity", "arthralgia syndrome", etc. (in Chinese, the names are Bi Zheng (痹证), Gu Bi (骨痹), Jin Bi (筋痹), Gu Wei (骨痿), Jin Wei (筋痿), Wei Zheng (痿证), etc.). Also known as "crane knee wind" (He Xi Feng), "knee arthralgia" (Xi Bi Bing), "arthralgia of the knee" (Xi Bi Bing), and so on (Hu, 2022; Wang and Gao, 2021; Tan et al., 2018).

KOA is a disease that involves pathological changes in the muscles, bones and joints, with symptoms such as muscle atrophy, muscle weakness, arthralgia, joint stiffness and restricted movement of the joint (lesions involve tendons, muscles, and bones, and atrophy syndrome and arthralgia syndrome exist simultaneously). In 1997, the Disease section of the *Traditional Chinese Medicine Clinical Diagnosis and Treatment Terminology* issued by the State Administration of Traditional Chinese Medicine unified the term used to describe this condition as "Xi Bi" (National Administration of Traditional Chinese Medicine, 1997).

6.2.2 Documentary Records of KOA in TCM

TCM has rich literature records on KOA, the following are some of them:

(a) *Su Wen · Chang Ci Jie Lun* translated and annotated by Yao (2022) states: "When the disease is in the bones, you will feel that the bones are too heavy to lift, the bone marrow will be sore and pain, and the body will feel cold, which is called Bone Flaccidity (Bone Impediment, Bone Bi).";

(b) *Zhu Bing Yuan Hou Lun (Treatise on the Origins and Symptoms of Various Diseases)* (Chao, Sui Dynasty) says: "The arthralgia is caused by the combination of wind, cold, and dampness, which combine to form arthralgia. Its main symptom is muscle stiffness or pain.";

(c) *Jing Yue Quan Shu (Complete Works of Jing Yue)* (Zhang, Ming Dynasty) says: "Arthralgia is blocked by stagnation, Qi and Blood are paralysed by pathogenic factors, and cannot pass through, which leads to disease." KOA is mostly caused by old age and frailty, muscle and bone strain, plus external wind-cold-damp pathogens blocking the meridians, or injury from falls and blood stasis blocking the meridians;

(d) *Su Wen · Bi Lun* translated and annotated by Yao (2022) says: "When the disease invades the bones, the joints will be heavy and sore；The disease lies in the tendons, and the flexion does not stretch."

(e) *Su Wen · Chang Ci Jie Lun* translated and annotated by Yao (2022) says: "The disease is in the tendons, and there will be muscle spasms, joint pains, and symptoms of inability to walk and move, which are called tendon flaccidity (Jin Bi).";

(f) *Su Wen · Wei Lun Pian* translated and annotated by Yao (2022) says: "Zong Tendon plays the role of restraining bones and making joints flexible.";

(g) *Zhang Shi Yi Tong (The Comprehensive Medicine of Zhang)* (Zhang, Qing Dynasty) says: "The knee is the mansion of the tendons, and all knee pain is always caused by liver and kidney deficiency.";

(h) *Yan Shi Ji Sheng Fang (Yan's Formulas for Saving Lives)* (Yan, Southern Song Dynasty) also states that "the three qi of wind, cold and dampness mix and become stagnant, they cause arthralgia due to the physical weakness and emptiness of the pores. This is caused by the invasion of wind, cold, and dampness."; and

(i) *Su Wen Xuan Ji Yuan Bing Shi (Original Disease Patterns in the Yellow Emperor's Inner Canon)* (Liu, Jin Dynasty) says: "Atrophy (Wei) means that the hands and feet are flaccid and weak, and they are unable to move."

From the above excerpts from the ancient TCM records about KOA, we can see that KOA has the characteristics of flaccidity syndrome (Wei syndrome) and arthralgia syndrome (Bi syndrome) at the same time.

6.2.3 Understanding of the Etiology and Pathogenesis of KOA in TCM

In TCM theory, the etiology and pathogenesis of KOA mainly include the following aspects:

(a) Deficiency of Qi and Blood, disharmony between the Ying-nutrients and Wei-defence, and deficiency of liver and kidney are the internal factors that cause disease in KOA.

In the pathogenesis of KOA, the deficiency of healthy Qi (the body's defensive Qi) plays a decisive role as an internal factor. The prerequisite for the occurrence of KOA is the insufficiency of Qi, blood, essence, and body fluid in the human body, which leads to the decreased regulation function of the human body, and the weakened ability to prevent external pathogenic factors. As stated in the *Su Wen · Ci Fa Lun* translated and annotated by Yao (2022) "When the healthy Qi is abundant inside the body, and the external pathogenic factors cannot invade the body." *Su Wen · Ping Re Bing Lun* translated and annotated by Yao (2022) also states, "The reason why pathological factors can gather is that its healthy Qi must be deficient." When the healthy Qi in the body is insufficient, external pathogenic factors such as wind, cold, dampness and heat can take advantage of the deficiency to invade the limbs, joints and muscles of the body, causing meridians obstruction and the onset of Bi syndrome with symptom as numbness, pain, stiffness, etc.

(i) Deficiency of Qi and Blood

Patients with severe KOA, especially among the elderly, have a higher proportion of females than males. The main reason is that most women have blood deficiency after menstruation and giving birth. Because of the co-existence and mutual transformation of Qi and Blood, it leads to Qi deficiency, the deficiency of Ren and

Chong Meridians, and pathogenic factors such as wind, cold and dampness take the opportunity to invade the human body, leading to the occurrence of this disease;

(ii) Disharmony Between the Ying-nutrients and Wei-defence

It is a pathological state of lack of coordination between the Ying-nutritive Qi (Ying Qi) and Wei-defensive Qi (Wei Qi). Ying-nutrient circulates within the vessels and turns into the blood to nourish the whole body; while Wei-defence circulates outside the vessels and meridians to protect the whole body and prevent external pathogenic factors from invading. *Lei Zheng Zhi Cai · Bi Lun* (Lin, Qing Dynasty) said: "All kinds of Bi Syndromes (Arthralgia Syndrome, Flaccidity Syndrome, Bone Impediment, etc.) are primarily caused by the deficiency of Ying-nutrient Qi and Wei-defensive Qi, the skin and muscles are not dense, and the wind, cold and dampness take advantage of the deficiency to attack the interior. The healthy Qi is hindered by pathogenic factors, and it cannot run smoothly, so it stagnates. If Qi and Blood do not move forward, it will cause stagnation, and after a long time, the original disease will be formed." When the Ying-nutrient Qi is deficient, it is unable to nourish the entire body, and when the Wei-defensive Qi is deficient, its defensive and warming functions are weakened, disharmony between Ying and Wei which will lead to the loss of nourishment of the tendons and bones, making it easier for pathogenic factors such as wind, cold, and dampness to invade the body, thus leading to the Bi syndrome with numbness, pain, and so on; and

(iii) Deficiency of Liver and Kidney

The liver stores blood and governs the tendons, while the kidneys store essence and govern the bones and marrow. Deficiency of the liver and kidney leads to insufficient essence and blood, which is unable to moisten and nourish the tendons and meridians, resulting in joint discomfort and not smooth, and tendon spasms. In addition, invasion of wind, cold and dampness pathogenic factors taking advantage of the deficiency to invade can exacerbate the condition, making it an important internal cause of arthralgia (Bi Syndrome). According to *Zhang Shi Yi Tong* (Zhang, Qing Dynasty), "The knee is the mansion of the tendons, and all knee pain is always caused by liver and kidney deficiency. If there is a deficiency, wind, cold and dampness will invade. " The *Zhong Zang Jing (The Internal Canon of Medicine)* (Hua, Eastern Han Dynasty) also points out that "The reason why Bone Bi occurs is mainly because of not knowing how to control desires and excessive indulgence, which damages the kidneys and leads to the loss of kidney Qi leading to the gradual exhaustion of essence Qi, then pathogenic Qi begins to hurt people and invade recklessly. Ling Shu · Wu Xie *(Lingshu · Five pathogenic factors)* edited and compiled by Tian and Liu (2005) says: "Pathogenic Qi in the kidney causes bone pain" (If pathogenic factors invade the kidneys, bone pain will occur). *Su Wen · Mai Yao Jing Wei Lun* translated and annotated by Yao (2022) says: "The waist is the mansion of the kidneys, if the waist cannot rotate, turn and shake, it means that the kidney Qi is about to be exhausted; The knee is the mansion of the tendons, if the knees cannot be flexed or extended, it means that the tendon and muscle are about to degenerate and be flaccid; The bone is the mansion of the marrow, if one cannot stand for a long time, and tremble when walk, it means that the bone is about to decline." It can be seen that although KOA is related to both tendons and bones, it is closely related to the liver and kidneys.

(b) External injuries, overuse, and external pathogenic factors of wind, cold, dampness and heat, are the external conditions which causing the disease.

As stated in Chapter 43 of the *Su Wen · Bi Lun Pian Di Si Shi San* translated and annotated by Yao (2022), "The wind, cold and dampness are mixed together to form arthralgia (Bi syndrome)." If the body is usually Yang deficient (deficient in Yang energy), the Yang Qi will be damaged even more when the disease recurs, and cold arthralgia and asthenia arthralgia (deficient-type Bi syndrome) will appear. If the Yang energy is relatively strong at ordinary times, and there is internal heat in the body, when the wind, cold and dampness pathogenic factors invade the human body, which can be turned into fiery heat over time due to the excess Yang Qi; or wind-cold-damp arthralgia persists for a long time, and it can also accumulate and turn into heat; fiery manifestations can also occur due to direct experience of wind, dampness and heat pathogenic factors. External injuries and overuse can also cause stagnation of Qi and Blood in the meridians, and blood stasis stays in the body, leading to Bi syndrome. For example, *Su Wen · Xuan Ming Wu Qi* translated and annotated by Yao (2022) said: "Long-term viewing damages the blood, long-term lying damages Qi, long-term sitting damages the flesh, and long-term walking damages the tendons." It shows that long-term chronic overuse or strain is one of the main causes of degenerative joint disease. The spleen is responsible for the transportation and transformation of fluids in the body, which is the source of the production of Qi and Blood. It supplies nutrients to the muscles of the limbs. Deficiency of the spleen leads to malnourishment of the muscles, bones, and tendons, causing muscle weakness. External pathogenic factors invasion is the external cause of this disease: due to the deficiency of Qi and Blood in the liver and kidney, the muscles and bones are malnourished, and the skin's defense function is reduced, making the body susceptible to external pathogens such as wind, cold and dampness, affecting the muscles and bones, and causing muscle spasms, stiffness, and limited range of motion in the joints; and

(c) The main pathogenesis of this disease is the stagnation of Qi and Blood in the meridians and collaterals, and the intertwining of phlegm and blood stasis.

The main pathogenesis of this disease is the obstruction of pathogenic Qi in the meridians and the stagnation of the flow of Qi and Blood, with the key factor being "stagnation and obstruction". "Stagnation" means that the Qi and Blood in the meridians are disturbed by pathogenic Qi, leading to poor circulation, even blockage. If Qi and Blood are blocked, it will cause pain. *Jing Yue Quan Shu* (Zhang, Ming Dynasty) says: "Bi

Syndrome refers to the condition of obstruction and blockage, mainly caused by the obstruction and besieged of Qi and Blood by pathogenic factors, resulting in the inability of smooth circulation and running, leading to the appearance of the disease. As the *Su Wen · Wu Zang Sheng Cheng* translated and annotated by Yao (2022) explains: "The foot receives blood and can walk, the palm receives blood and can grasp, and the finger receives blood and can grip and pinch. *Nan Jing · Er Shi Er Nan* (Bian, Warring States Period) summarises the important functions of blood on the viscera, Fu-organs and tissues of the whole body as "Blood dominates moistening". This demonstrates that the muscles and bones are nourished by Qi and Blood, which produces the limb functions of walking, grasping, gripping and pinching. Stagnation of Qi and Blood leads to a lack of nourishment in the knee bones, causing pain when it is not properly nourished. During the Qing dynasty, Wang Qingren also proposed the theory that the stasis of blood causes Bi Syndrome disease. Qi and Blood stagnate, phlegm and blood stasis intertwine, meridian Qi and Blood flow not smoothly, muscles and joints lose nourishment, resulting in damage to the joint structure and appearing degenerative changes. KOA is more common in middle-aged and elderly populations due to insufficiency of Qi and Blood, deficiency of liver and kidney, and invasion of external pathogenic factors, leading to poor circulation of Qi and Blood, pathogenic factors stay in the meridians and joints, with long-term illness, phlegm and blood stasis intertwine, finally forming Bi Syndrome. Therefore, the treatment should focus on promoting dredge in the meridians, regulating the flow of Qi, and activating blood circulation.

The internal basis for the onset of this disease is deficiency of healthy Qi and failure of Wei-defensive Qi to stay firmly on guard. Suffering from external pathogenic factors is the external condition that causes the disease. Wind, cold, dampness heat and other pathogenic factors, stay in the tendons, joints and muscles of the human body, resulting in blockage of tendons and meridians, Qi stagnation and Blood stasis, and phlegm and blood stasis intertwined, thereby causing symptoms such as pain due to blockage, and problems of joint movement. In general, invasion by wind, cold and dampness, deficiency of liver and kidney, loss of nourishment to the muscles, tendons and bones, deficiency of spleen with phlegm retention, dampness and stasis obstruction, obstruction and blockage of meridians are the pathogenic mechanisms of this disease (Zhao, 2022; Shen, 2022).

Modern medical research believes that the main pathological changes of osteoarthritis are the degenerative changes in cartilage and the formation of osteophytes. Scholars such as Wu (2018) believe that there is a pattern of "softening first, atrophy and weakness first" (cartilage and muscle degeneration) and "stiffening later, osteosclerosis later" (osteophytes formation), and that for KOA, "Jin Bi" is a necessary stage, and "Gu Bi" is the ultimate manifestation. This means that for KOA commonly seen in clinical practice, the manifestations of KOA in the early stages are mainly joint stiffness, pain, and swelling, followed by an imbalance of the musculoskeletal system (tendon-bone system) around the joints, and the final manifestations are joint deformity and loss of joint activities function.

For the clinical treatment of KOA, it is important to differentiate and treat according to the syndrome differentiation. The main treatment principles include nourishing the liver and tonifying kidneys, expelling wind and dispelling cold, clearing heat and removing dampness, promoting Qi and Blood circulation, eliminating swelling and relieving pain, dredging meridians and activating collaterals, and improving joint movement. If the disease persists or for a long-term illness, it will consume Qi and Blood, so attention should be paid to regulating Qi and nourishing Blood, tonifying the liver and kidneys. If phlegm and blood stasis are intertwined, the treatment should focus on resolving phlegm and removing blood stasis, and dredging the meridians.

6.3 Reasons for Choosing EA for KOA

6.3.1 The Advantages of EA and Comparison with Other Acupuncture Treatments for KOA

The basis for the EA treatment of KOA includes acupuncture theory, clinical practice experience and scientific research evidence.

The theoretical basis for EA treatment of KOA primarily comes from the theory of acupuncture in TCM. According to acupuncture theory, KOA is caused by poor circulation of Qi and Blood, leading to joint obstruction. Through acupuncture, the meridians can be dredged, Qi and Blood can be regulated, and joint function can be improved.

EA is a special type of acupuncture method, enhances the stimulation of acupoints by applying a low-level electric current on top of traditional acupuncture with "De Qi". This technique produces a series of physiological effects and has therapeutic effects on various diseases and symptoms. The main aspects of its functions include the following (Cao et al., 2005; Yu, 2016; Wu, 2021):

(a) One of the primary effects of EA is to enhance blood circulation and improve the local microenvironment. By stimulating with electric current, it promotes blood circulation, increases local oxygen supply, and facilitates the delivery of nutrients, which is beneficial for tissue repair and metabolic regulation;

(b) Additionally, EA can reduce intraosseous high pressure in subchondral bone and promote the circulation, metabolism, and absorption of inflammatory mediators. This is particularly significant for inflammatory conditions like KOA, as it can alleviate inflammation, relieve pain, and reduce swelling;

(c) EA has analgesic, sedative and effects on promoting Qi and Blood circulation, and adjusting muscle tension. It can modulate the function of the nervous system, reduce pain perception, and improve overall comfort. Additionally, EA can influence muscle tone and range of motion, aiding in the restoration of normal muscle function; and

(d) EA also has a role in regulating immune function. It can modulate the activity of immune cells, enhance their functionality, and regulate the release of inflammatory factors, thereby suppressing inflammatory responses and alleviating symptoms of arthritis.

In summary, EA can effectively regulate the body's physiological functions, achieving therapeutic goals such as dredging meridian, reducing swelling, alleviating pain, relieving stiffness, increasing mobility, and facilitating disease tissue repair.

The scope of application of EA is basically similar to that of traditional acupuncture, so EA has a relatively wide range of applications. In clinical practice, it is widely used in various pain disorders, Bi syndromes, and functional disorders of organs such as the heart, stomach, intestines, bladder, uterus, and so on. Furthermore, it can be used in the treatment of musculoskeletal injuries involving muscles, ligaments and joints, and it can produce certain therapeutic effects on symptoms like mania.

EA has regulatory effects on the symptoms, etiology and pathogenesis of KOA. The mechanism of action of EA mainly includes direct effects on the nervous and muscular systems, improving local blood circulation, enhancing tissue metabolism and immune function, thereby achieving analgesic, detumescence, anti-inflammatory, antispasmodic, tonic and support healthy Qi, etc. (Li et al., 2014; Tang, 2020). EA directly acts on the nervous system by stimulating acupoints and nerve endings. It can modulate nerve conduction and the release of neurotransmitters, resulting in analgesic and sedative effects. EA can also improve muscle tone, relieve muscle spasms, and alleviate pain and stiffness. Studies in recent years have also confirmed the therapeutic effect of EA on KOA. For example, a systematic review (Lin et al., 2016) found that EA can significantly relieve pain and joint dysfunction in patients with KOA, and also has a significant effect on improving their quality of life. The studies conducted by Huang (2022) and Tang (2012) have found that EA therapy can better dredge meridians and collaterals, promote the smooth flow of Qi and Blood, dilate blood vessels, improve local blood circulation, inhibit the release of free radicals, regulate inflammatory factors, reduce muscle atrophy, and have a favorable effect on relieving pain and swelling in the knee joint, and play a possible role in repairing damaged cartilage tissue.

Compared to other acupuncture methods such as WNA Therapy and FN Therapy, EA offers several advantages and characteristics in the treatment of KOA:

(a) Ease of Operation: EA enables automated and quantitative operations, reducing human errors and ensuring more accurate and reliable treatment compared to manual methods like warm needle acupuncture therapy and fire needle therapy;

(b) Reduced Patient Panic: Acupuncture methods such as WNA therapy and FN therapy carry potential risks of burns and scalds, which can easily cause panic in patients. In contrast, EA is less painful and less likely to induce fear and discomfort, making it more suitable for elderly patients；

(c) Strong Controllability: EA allows for the adjustment of parameters such as current intensity and frequency based on the patient's specific condition and response level. This personalised approach enhances treatment efficacy and safety;

(d) Stable Efficacy: Multiple studies have demonstrated that EA effectively and consistently alleviates pain and improves joint dysfunction in KOA.

Its therapeutic effects are long-lasting and less prone to recurrence (Wu, 2022; Tan, 2014); and

(e) High Safety: EA carries lower treatment risks and side effects compared to methods like WNA therapy and FN therapy (Lin et al., 2016). Especially when performed by skilled healthcare professionals following standardised procedures, EA is considered safer.

Therefore, due to its ease of operation, reduced patient panic, strong controllability, stable efficacy, and high safety, EA is regarded as an ideal method for treating KOA.

6.3.2 Current Status of EA Application for the Treatment of KOA in Malaysia

Through the previous questionnaire research, we found that the application of EA in Malaysia is not very prevalent, and there is a certain gap in terms of popularity compared to China. Considering the purpose of this study, which is to enrich the treatment methods for KOA in Malaysia and to evaluate the effectiveness of EA combined with the top ten highly-researched acupoints, we have chosen EA as the primary treatment method for this clinical research.

6.4 Reasons and Basis for Choosing the "Sparse-Dense Waveforms"

6.4.1 Characteristics and Applicable Scope of Three Waveforms

In clinical practice, EA is commonly used with three main waveforms: continuous wave, intermittent wave and sparse-dense wave. Each waveform has its own characteristics, different functions, as well as advantages and disadvantages. Choosing the appropriate waveform of EA is important in the treatment of KOA to enhance treatment effectiveness and safety.

(a) Continuous Wave: Also known as an adjustable wave, it is a form of waveform composed of multiple individual pulses combined in different ways. It can be adjusted at different frequencies, typically ranging from several tens of times per minute to several hundreds of times per second. Among them, the fast continuous wave (50-100Hz) is called dense wave or high-frequency continuous wave, usually ranging from 50-100 times per second, while the slow continuous wave (2-5Hz) is called sparse wave or low-frequency continuous wave, typically ranging from 2-5 times per second. The frequency can be adjusted using a knob to select the desired sparse or dense waveform.

High-frequency continuous wave has inhibitory effects and can suppress sensory and motor nerves. It is commonly used for pain relief, sedation, and relief of muscle and vascular spasms. Low-frequency continuous wave has pronounced excitatory effects. Short-term application can stimulate muscles, while long-term use can suppress sensory and motor nerves. It is often used to treat flaccidity syndrome, various muscle, ligament, and tendon injuries, as well as chronic pain symptoms.

In general, continuous waveforms typically have higher frequencies, which can quickly stimulate nerve and muscle tissues, enhance local blood circulation, and alleviate pain and muscle stiffness. However, due to the higher intensity of stimulation, it may cause discomfort and muscle fatigue for patients (Luo et al., 2022). Therefore, it is necessary to control the current intensity and treatment time to ensure safe and effective treatment;

(b) Intermittent Wave: It is a waveform that rhythmically interrupts and resumes. Within a cycle, there is an interval of no pulse output, typically around 1.5 seconds, followed by a period of dense continuous wave for 1.5 seconds. The intermittent waveform is not easily adapted by the body and has a strong motivation and dynamic effect. It can increase the excitability of muscle tissue and provide good stimulation and contraction effects on striated muscles (Wang and Xi, 2019; Hu et al., 2007). Therefore, it is commonly used for the treatment of flaccidity syndrome, paralysis and similar symptoms.

However, due to the strong tremor and shaking sensation it generates in the body, the intermittent wave is not easily accepted by patients, and its therapeutic efficacy is relatively inferior compared to sparse-dense waves and continuous waves (Huang et al., 2020). Therefore, when used in clinical practice, attention should be given to the comfort and acceptance level of the patients; and

(c) Sparse-dense Wave: It is an electrical current pattern where sparse waves and dense waves alternate automatically. Sparse waves refer to a situation where the frequency of electrical pulses is low, typically between 1 and 15 Hz, while dense waves refer to a higher frequency of electrical pulses, generally between 30 and 300 Hz (Wu, 2009). The duration of sparse waves and dense waves is approximately 1.5 seconds each. By alternating between the two, strong and gentle stimulation can be produced simultaneously in a short period, overcoming the disadvantage of adaptability associated with a single waveform.

Sparse-dense waves have a powerful and significant dynamic effect, with a predominance of excitatory effects during treatment. Therefore, they are commonly used in the treatment of conditions such as hemorrhage, sprains, bruises, periarticular inflammation, osteoarthritis, disorders of Blood and Qi circulation, sciatica, facial paralysis, myasthenia (muscle weakness), and local frostbite.

In recent years, with the advancement of physical therapy and the continuous research by rehabilitation medicine practitioners, sparse-dense waves have been frequently applied in the rehabilitation treatment of osteoarthritis as a form of physical therapy (Lin and Wu, 2016).

6.4.2 Research on the Treatment of KOA with " Sparse-Dense Wave "

Studies indicate that the stimulation of sparse-dense waves is closer to the body's bioelectricity, and applying sparse-dense waves for EA treatment helps promote local blood circulation, increase tissue metabolism, improve tissue nutrition, reduce the release of inflammatory factors, eliminate inflammatory edema, and alleviate pain and muscle stiffness (Sun et al., 1998; Shen and Shen, 2003; Chen et al., 2020; Li et al., 2020). In TCM, sparse-dense waves are considered equivalent to the "tonification" method and have a significant therapeutic effect on KOA. Studies conducted by Luo et al. (2022) and Huang et al. (2020) have also shown that the use of sparse-dense waves in the treatment of KOA can significantly improve knee joint function, effectively regulate inflammatory factors, and produce good clinical outcomes. Sparse-dense waves are superior to intermittent waves in alleviating pain, joint swelling, and instability of joint.

Based on studies by Zhao et al. (2015), Jiang et al. (2021) and Pan et al. (2019) on pain-relieving effect of sparse-dense waves, the waves have a relieving effect on joint, muscle, and nerve pain. The underlying mechanism may involve the activation of opioid receptors to inhibit chronic inflammatory pain. Sparse-dense waves also exert immediate inhibitory effects and delayed inhibitory effects on sensory and motor nerves. They have excellent analgesic effects with a prolonged duration and they will not easily develop the treatment resistance by patients.

Additionally, Zhang et al. (2019), Ban et al. (2021) and Wang et al. (2019) conducted studies about treating KOA with EA, which has also shown that sparse-dense waves have an inhibitory effect on cartilage matrix degradation and chondrocyte apoptosis in the treatment of KOA. The sparse-dense waves can protect and improve the morphological structure of cartilage, promote chondrocyte differentiation, suppress the expression of related effusion fragments, and inhibit the expression of inflammatory factors. As a result, the sparse-dense waves can slow down the progression of cartilage degeneration and alleviate the development of KOA.

Sparse-dense waves possess the advantages mentioned above, which are not present in intermittent waves and continuous waves. Therefore, stimulating with sparse-dense wave EA can be considered as a preferred approach for the clinical treatment of KOA.

In conclusion, considering the characteristics of the three waveforms and the nature of KOA, we have chosen sparse-dense waves as the waveform for EA treatment.

6.5 Analysis of Acupuncture Acupoint Prescription

6.5.1 Acupoint Analysis

The top ten acupoints used in this study were obtained through literature search, data extraction and data analysis, and they are the top ten acupoints in terms of frequency. The selected acupoints are mainly from the Stomach Meridian of Foot Yangming and the Spleen Meridian of Foot Taiyin, and also include acupoints from the Gallbladder Meridian of Foot Shaoyang and Extraordinary Points. The three meridians of the Stomach, Spleen, and Gallbladder all pass through the knee joint, which reflects the theories and rules of acupuncture that "Where the meridians pass through, and where the main treatment can be reached" and

"Where the acupoints are located, and where the main treatment is concerned." At the same time, it also reflects the emphasis on regulating and tonifying the spleen and stomach, replenishing Qi and nourishing blood, moistening the tendons and nourishing meridians in the treatment of KOA, in order to better improve the conditions such as weakness of lower limb muscles and limited mobility in the lower limbs.

For the specific and detailed analysis of the top ten highly-researched acupoints, please refer to the discussion part of the fourth section of chapter four: "4.1.2 Analysis of the Top 10 Highly-researched Acupoints ". The below is a brief discussion and analysis of the top 10 highly selected acupoints:

(a) "ST35 (Dubi) ", has the functions of dispelling dampness, eliminating cold, promoting joint movement, activating collaterals, and relieving pain (Zhang, 2020). It is mainly used to treat diseases of the lower limbs and knee joints, such as knee pain, limited flexion and extension, and lower limb paralysis (Yang et al., 2019);

(b) "EX-LE4 (Neixieyan)", has the function of promoting blood circulation, dredging collaterals, regulating and smoothing the knee joints. It is mainly used to treat knee pain, lower limb pain, KOA, inflammation of the tissue around the knee joint of the knee, lower limb paralysis, patella osteomalacia, et al.(Wang et al., 2023)

    "ST35 (Dubi)" and "EX-LE4 (Neixieyan)" are at the opposite location. The two acupoints form a relative point pair. The combination of these two acupoints can relieve knee joint pain and improve the range of motion of the knee joint. They are commonly used in the treatment of swelling and pain in knee joints, poor flexion and extension of knee joints, and paralysis of the lower limbs (Sun, 2011). Furthermore, the two acupoints are located on the external and internal of the knee joint, which is in line with the principle of acupoint selection based on syndrome differentiation and the theory of "Where the acupoints are located, and where the main treatment is concerned.";

(c) "SP10 (Xuehai)", has the effects of regulating blood, nourishing blood, and promoting blood circulation, invigorating the spleen and removing dampness, and expelling wind. Acupuncture and moxibustion on this acupoint can remove blood stasis and dredge the meridian, by regulating the release of vasoactive factors, changing the shape of capillaries, accelerating the blood flow rate, and changing the hypercoagulable state of the blood (Zhao et al., 2004). This may be the reason why “Hui Yuan Zhen Jiu Xue” states that SP10 (Xuehai) can be used to treat "swelling of the knee and calf, numbness of the foot.";

(d) "GB34 (Yanglingquan)", has the functions of soothing the liver and promoting bile flow, strengthening the waist and knees, relaxing tendons and activating collaterals, dispelling wind and relieving pain, etc. It is an empirical acupoint for treating KOA. It can dredge the Qi and Blood of the local meridians around the knee joint, improve the symptoms of KOA such as pain, stiffness, and poor function of flexion and extension; this acupoint is mainly used for swelling and pain of the knee joint, numbness of the lower limbs, muscle atrophy, etc. (Zou et al., 2018; Wang, 2020) Acupuncture on this acupoint can improve the flexion and extension function of the knee joint. Therefore, this acupoint is often selected for the treatment of KOA, and other diseases of the lower limbs;

(e) "ST34 (Liangqiu)", is the Xi acupoint (Xixue) of the Stomach Meridian of Foot-Yangming. Due to its acupoint characteristics, it has a good therapeutic effect on pain and is located at the knee joint, so it is often used to treat knee joint swelling, pain, poor function of flexion and extension of lower limbs (Zou et al., 2021);

(f) "ST36 (Zusanli)", is the main acupuncture point for treating lower limb flaccidity. As the theory of acupuncture and moxibustion states that “treat the disease manifested as muscle weakness, atrophy and flaccidity, just need to select the acupoints belonging to Yangming Meridian”, ST36 (Zusanli) is mainly used for the treatment of paralysis of the lower limbs.

Moreover, the Foot Yangming Meridian has the characteristics of abundant Qi and Blood. Stimulating ST36 (Zusanli) can better tonify Qi and nourish Blood, enhance the body's immune function, and provide sufficient nutrients and energy to tissues such as muscles, ligaments, cartilage, and bone, thus reducing muscle atrophy and strengthening muscle strength (Zhu, 2020; Guan et al., 2020).

Acupuncture at SP10 (Xuehai), ST34 (Liangqiu), and ST36 (Zusanli) can invigorate the spleen, nourish Qi and Blood, relieve spasms and pain, moisturise and nourish tendons, smooth joints, improve the permeability of local blood vessels, regulate blood viscosity, reduce blood viscosity, effectively improve local blood circulation, promote the absorption of inflammatory mediators and inflammatory exudates, accelerate the metabolism of related cells, reduce the inflammatory response of this disease, and promote the repair of damaged tissues and the recovery of knee joint physiological functions;

(g) "SP9 (Yinlingquan)", is often used in conjunction with GB34 (Yanglingquan). The combination of Yin and Yang has the functions of relaxing muscles and tendons, activating collaterals, expelling wind and dampness, reducing swelling and relieving pain. The meridian Qi of the Spleen Meridian of Foot Taiyin is gathering at the SP9 (Yinlingquan). Stimulating this point can invigorate the spleen and expel dampness, remove blood stasis and resolve stagnation (Luo, 2019; Zhang and Yang, 2016; Lin et al., 2020). It is often used to treat knee joint pain and paralysis of the lower limbs;

(h) "EX-LE2 (Heding)”, has the effect of dredging the local Qi and Blood of the knee joint, smoothing the joint movement, and has a strong analgesic effect. It is often used to treat knee joint pain, weakness of the lower limbs, paralysis of the lower limbs and other diseases (Zhao, 2020). Acupuncture at the EX-LE2 (Heding) can better improve the functional activities of the knee joint and improve the quality of life of the patients (Zheng et al., 2017);

(i) "GB33 (Xiyangguan)", is the place where the meridian qi of the tendons of the Foot Yangming meridian and the meridian qi of the tendons of the Foot Shaoyang Meridian converge. It has the functions of dredging Qi and Blood, dispelling wind and dampness, and is mainly used to treat knee joint swelling, pain, lower leg muscle spasm and numbness, KOA, paralysis of lower limbs, etc. (Ma et al., 2021; Wu et al., 2020; Huang and Pan, 2019; Wu, 2019); and

(j) "SP6 (Sanyinjiao)", is the meeting point where the three Yin meridians of the kidney, liver, and spleen converge. The three Yin meridians run through the lower limbs. The spleen governs the limbs and muscles, the liver governs the tendons, and the kidney governs the bones. Therefore, SP6 (Sanyinjiao) can treat paralysis of the lower limbs and hemiplegia. Stimulating this acupoint can invigorate the spleen, nourish the liver, tonify the kidney, dredge the meridians, replenish Qi and Blood, strengthen tendons and bones, and has a good curative effect for the Bi syndrome with Qi deficiency and Blood stasis type (Jin and Wang, 2017).

6.5.2 Acupoints Selection Ideas Reflected in Acupuncture Prescription

Below are the considerations in selecting the top 10 highly-researched acupoints:

(a) Focus on local acupoint selection: The lesion site of KOA is located at the knee joint, with the main symptoms of knee joint pain, swelling, stiffness and dysfunction of functional activity. The main principles of treatment are promoting Qi and Blood circulation, removing blood stasis, reducing swelling and relieving pain, dredging meridians and activating collaterals, and smoothing and promoting joint movement. Acupoints such as ST35 (Dubi), EX-LE4 (Neixieyan), GB34 (Yanglingquan), SP10 (Xuehai), ST34 (Liangqiu), SP9 (Yinlingquan), EX-LE2 (Heding), GB33 (Xiyangguan), and are all located around the knee joint. Selecting and combining these acupoints allows for direct stimulation of the meridians and tissues around the knee joint, regulating the Qi and Blood circulation of local meridians and collaterals. This direct therapeutic effect on the affected area helps to maximize the near-therapeutic effects of the acupoints;

(b) Consider local anatomy: Considering the anatomical structure of the knee joint, the Stomach Meridian of Foot-Yangming and the Spleen Meridian of Foot-Taiyin respectively run along the outer and inner sides of the knee joint. By selecting the acupoints located on these two meridians at the local area of the knee joint, it is possible to directly stimulate the local meridians and promote Qi and Blood circulation in the affected area. This helps to release local adhesions, better restore the balance of stress in the outer and inner muscles and tendons, and correct or eliminate certain triggering factors that cause damage to local soft tissues, bones, and joints, as well as local cartilage; and

(c) Supporting the healthy factors and eliminating pathogenic factors, seeking the root cause of the disease when conducting the treatment: The combination application of the above-mentioned acupoints can promote blood circulation, eliminate blood stasis, invigorate the spleen and eliminate dampness, dispel wind and scatter cold, regulate and dredge meridians and collaterals, alleviate pain, tonify Qi and nourish the Blood, strengthen tendons, and invigorate bones, etc. It takes into account the principles of both supporting the body's healthy factors and eliminating pathogenic factors, thereby achieving the treatment for the etiology and pathogenesis of KOA.

6.6 Analysis of Research Results

6.6.1 Baseline Data Analysis

Baseline data primarily includes the patient's age, gender, clinical course, pre-treatment WOMAC, VAS, LKSS and SKSC scores, as well as the measurement of IL-1β and TNF-α levels in the patient's serum before treatment.

The results of the statistical analysis of these data showed that there was no statistically significant difference among the three groups ($P > 0.05$), indicating that the baseline characteristics of the three groups had no statistical differences and were comparable.

In terms of gender distribution, the number of female patients in all three groups was higher than that of male patients. This is consistent with the results expressed in previous literature studies (Wang et al., 2021; Zhao, 2016) and the actual situation seen in clinical practice, as well as the epidemiological characteristics of KOA (Yu et al., 2005). The main possible reasons for the fact that the higher prevalence of KOA in female patients compared to males may be the following:

(a) Genetic Factors: Genetic factors have a significant influence on the occurrence and development of KOA. A study has demonstrated that females have a higher susceptibility to KOA, which may be attributed to genetic factors (Blacher et al., 2019);

(b) Hormonal Factors: It has been reported in previous literature (Fan, 2018) that hormonal imbalance, particularly involving endocrine hormones like leptin and estrogen, can contribute to weight gain. Estrogen being a protective hormone for joint articular cartilage, aids in the growth and repair of chondrocytes (cells responsible for cartilage matrix production). Estrogen deficiency can lead to cartilage degeneration and the development of KOA. Post-menopausal women experience a decline in estrogen levels thereby increasing the risk of KOA;

(c) Biomechanical Factors: Women exhibit different bone structures and biomechanical characteristics compared to men, making their hip and knee joints more prone to injuries. Compared to men, sprains, impacts and ligament injuries much more easily affect women's hips and knee joints can contribute to the development of KOA; and

(d) Physical Activity Level: Women often prioritize appearance and weight management compared to men, potentially engaging in more activities focused on weight loss and body shaping. This increased physical stress and strain on the knee joints can raise the risk of the occurrence and development of KOA.

In conclusion, the higher incidence and prevalence of KOA in females, as compared to males, can be attributed to a combination of multiple factors. Understanding these risk factors can help individuals take appropriate preventive measures and reduce the likelihood of developing KOA.

On age distribution, the patients in all three groups were predominantly between the ages of 50 and 70, consistent with the results of our previous survey questionnaire. This aligns with the reported age of onset for the disease reported in the literature, as KOA is more commonly observed among middle-aged and elderly individuals.

6.6.2 Analysis of Observation Indicators

In the preceding literature review, it was observed that different studies employed diverse evaluation methods to assess the efficacy of treatment for KOA, without the presence of a uniform and standardised approach. Furthermore, previous investigations have indicated a lack of universally recognised criteria for evaluating KOA by far (Zhou et al., 2011). In this study, we have primarily focused on selecting several highly and frequently employed observation indicators, which have been categorised into subjective and objective evaluation criteria (refer to Section 3.1.1). The objective is to comprehensively and scientifically evaluate the therapeutic effects of the three treatment methods on KOA. The following section provides a detailed analysis and discussion of these observation indicators.

6.6.2.1 Visual Analog Scale (VAS)

The Visual Analog Scale (VAS) is a widely utilised subjective assessment tool for evaluating various subjective experiences, including pain intensity, disease symptoms and severity of physical discomfort. First introduced to evaluate pain intensity by Woodforde and Merskey (1972) in 1972, this scale consists of a 10-

centimeter straight line or ruler, with "No pain" and "Worst possible pain" or corresponding extremes of symptoms labeled at the ends. The scale incorporates 10 markings, with each centimeter representing one point on a continuum ranging from 0 (indicating no pain) to 10 (indicating the worst possible pain). Patients are provided with a comprehensive explanation of the scale's purpose, significance and usage. They are then asked to mark the point on the scale that reflects their current pain intensity, with the distance from 0 to the marked point representing their pain level. The evaluation criteria for VAS are as follows: 0 denotes no pain, scores below 3 (below 3 cm) indicate mild pain, scores between 4 and 6 (4-6 cm) indicate moderate pain, and scores between 7 and 10 (7-10 cm) indicate severe pain.

The VAS is widely utilised as a subjective evaluation indicator in various fields such as clinical research, clinical diagnosis and treatment, disease prevention, health management, and other scientific research domains, particularly in the assessment of clinical pain. It offers several advantages:

(a) Simplicity and Practicality: VAS rating is a straightforward assessment method where patients simply mark a point on a continuous line or scale to indicate their subjective perception of symptoms or discomfort. This rating method is easy to administer and imposes minimal cognitive and execution burdens on patients;

(b) Rapid Data Acquisition: VAS rating allows for the swift acquisition of information. Patients can quickly convert their sensations into a specific numerical or marked value, providing immediate assessment results; and

(c) Ease of Understanding: VAS rating employs a simple visual analog scale that enables patients to intuitively comprehend and express their sensations. This rating method does not require complex explanations or guidance, thus reducing communication barriers between patients and assessors.

VAS is considered the "gold standard" for evaluating pain and other subjective experiences. Studies conducted by Snow and Kirwan (1988) and Wang (2019) have shown that VAS accurately captures percentage differences between visual analog scale measurements obtained from multiple time points or independent individual samples, effectively quantifying pain intensity and changes. Research on pain intensity assessment among Chinese adults has indicated that VAS exhibits good reliability, validity and sensitivity, displaying favorable correlations with other scales (Li et al., 2007; Gao and Wang, 2013). Therefore, VAS can assist physicians and researchers in more accurately assessing the intensity and changes in patient symptoms, monitoring treatment effectiveness, and providing a basis for formulating the treatment plan.

The primary aim of this study was to observe and assess the amelioration of key symptoms associated with KOA after treatment. This evaluation aimed to gauge the clinical effectiveness of various treatment approaches, in conjunction with novel acupoint prescriptions for KOA. Pain serves as the central symptom of KOA and represents the primary motive for patients seeking medical attention. Considering the alignment between the study objectives and the VAS score's utility in pain assessment, we selected the VAS as one of the evaluation indicators.

The initial VAS scores of the three groups did not exhibit significant differences and were comparable ($P > 0.05$). In post-treatment, all three groups demonstrated a decrease in VAS scores compared to pre-treatment values. The Treatment Group exhibited the most prominent reduction, followed by Control Group 1, while the change in Control Group 2 was not statistically significant. When comparing the VAS scores after treatment among the three groups, the P-value was < 0.05. For each two group comparisons, all the P-values were < 0.05, indicating statistically significant differences. Additionally, within-group comparisons revealed that both the Treatment and Control Group 1 exhibited P-values < 0.05, indicating a statistically significant difference between post-treatment and pre-treatment VAS scores. However, the P-value for Control Group 2 was > 0.05, suggesting no statistically significant difference. Moreover, the difference in VAS scores before and after treatment among the three groups was statistically significant ($P < 0.05$), with the Treatment Group demonstrating superior improvement.

The aforementioned results suggest the following:

(a) There is a noteworthy disparity in the VAS scores after treatment among the three groups. A comparison of the means and standard deviations indicates that the Treatment Group exhibited superior efficacy compared to Control Groups, 1 and 2. Control Group 2, on the other hand, demonstrated relatively less effectiveness; and

(b) Both the Treatment Group and Control Group 1 have experienced significant pain relief and treatment efficacy for KOA. However, the pain relief effect achieved through EA in combination with the top ten highly-researched acupoints is notably superior to that of MA therapy.

6.6.2.2 Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

The VAS serves as a valid tool for evaluating subjective experiences. However, its subjective nature implies that the results may be influenced by various factors, such as the patient's emotions, attitudes and cultural background. Consequently, when utilising the VAS score, it is crucial to carefully consider these factors and complement them with other objective assessment methods to ensure the accuracy and reliability of the evaluation outcomes. Moreover, it is important to note that the VAS solely captures the pain symptoms experienced by KOA patients and does not provide a comprehensive assessment of functional activity and knee joint stiffness. In order to more comprehensively evaluate changes in symptoms and signs of patients before and after treatment, and to address the limitations of the VAS, we incorporated the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which is widely employed in clinical studies focusing on KOA. The WOMAC score allows for a more holistic evaluation of the subjects' condition and compensates for the limited scope of the VAS.

The WOMAC scale is specifically designed and used to evaluate the disease status of patients with hip and knee conditions (Bellamy et al., 1988). It is a tool developed and recommended by the American Rheumatoid Arthritis Clinical Research Group, primarily used to measure joint pain, stiffness and functional impairment (Bellamy et al., 1997). The scale is widely employed for assessing the condition and treatment outcomes and effects of individuals with osteoarthritis. The scoring system encompasses three sections, each comprising different sets of questions, resulting in a total of 24 questions. These sections include Pain (consisting of 5 questions), Stiffness (comprising 2 questions), and Physical Function (consisting of 17 questions). Each question is assigned a score ranging from 0 to 4, leading to a total score ranging from 0 to 96 (Sun et al., 2022).

The WOMAC scale assesses the symptoms and functional activities of patients with KOA across three distinct dimensions, providing a comprehensive evaluation of knee joint function from multiple perspectives:

(a) The Pain section primarily focuses on assessing the level of pain experienced by KOA patients during their daily activities involving the knee joint;

(b) The Stiffness section evaluates the degree of stiffness felt in the joint when the knee joint is changed after maintaining a specific position or posture for a period. It also considers the duration of stiffness experienced throughout the day; and

(c) The Physical Function section is primarily designed to assess the individual's ability to perform specific activities, such as standing up from a seated position, walking, ascending and descending stairs, putting on socks, etc.

The WOMAC scale serves as a quantitative measure to assess the impact of KOA on an individual's well-being and functional abilities. Patients self-assess their condition and provide ratings based on their own condition and experiences. By summing up the scores, one can derive the scores for each of the three sections of the WOMAC scale (pain, stiffness and physical function), as well as the overall total score. Lower scores on the scale indicate lower severity of symptoms or physical disability, indicating less pain, stiffness and functional limitations. Conversely, higher scores on the scale indicate higher levels of pain, stiffness and functional limitations, indicating a more severe condition.

In conclusion, the WOMAC score has undergone rigorous psychometric validation and has proven to be a reliable and effective assessment tool for evaluating symptoms of osteoarthritis. It is widely utilised in clinical trials, and clinical diagnosis and treatment. Previous studies have further confirmed the reliability and validity of the Chinese version of the WOMAC scale (Symonds et al., 2015; Xie et al., 2008). Moreover, WOMAC has gained recognition and endorsement from esteemed organizations such as the Osteoarthritis Research Society International (OARSI) and Outcome Measures in Rheumatology Clinical Trials (OMERACT), as well as various regulatory bodies. The WOMAC can provide a more comprehensive index to evaluate the symptoms and disease progression in patients with osteoarthritis, provide reliable data to guide medical decisions, and help patients gain a better understanding of their disease conditions. It is particularly valuable and helpful for doctors, enabling them to more comprehensively evaluate the condition and severity of patients with KOA, provide guidance in formulating and adjusting treatment plans, and assess treatment effectiveness.

There were no significant differences in the pain, stiffness, physical function and total scores of WOMAC among the three groups before treatment, indicating that they were comparable ($P > 0.05$). After treatment, all four WOMAC-related scores showed a decrease compared to the pre-treatment values in all three groups, with the Treatment Group showing the most significant decrease, followed by Control Group 1, while the change in Control Group 2 was not significant. The comparison of the four scores among the three post-treatment groups showed P values < 0.05, indicating statistical differences. The pairwise comparison between groups also showed P values < 0.05, indicating statistically significant differences. When comparing the four scores within the same group before and after treatment, both the Treatment Group and Control Group 1 showed P values < 0.05, indicating statistically significant differences, while the Control Group 2 had P values > 0.05, indicating no statistical difference. The differences in the four WOMAC-related scores between pre-treatment and post-treatment in all three groups were statistically significant ($P < 0.05$), and the Treatment Group showed the greatest improvement.

The above results indicate that:

(a) There are significant differences in the four WOMAC-related scores among the three groups after treatment. Comparing the mean values and standard deviations, it can be observed that the Treatment Group has better effects compared to Control Groups 1 and 2, while the efficacy of Control Group 2 is poor; and

(b) The treatment methods used in the Treatment Group and Control Group 1 have a relieving and therapeutic effect on the pain, stiffness, and physical function of KOA. However, the combination of EA and the top ten highly-researched acupoints yields better improvements in the symptoms of pain, stiffness, and physical dysfunction associated with KOA. In different evaluation dimensions, EA consistently demonstrates better clinical efficacy compared to MA.

6.6.2.3 Lysholm Knee Scoring Scale (LKSS)

The Lysholm Knee Scoring Scale (LKSS) is a widely used tool for assessing knee joint function and the degree of recovery in knee-related injuries and conditions. It was initially proposed by Lysholm and Gillquist (1982) in 1982 for evaluating ligamentous knee injuries. Over time, the scale has been continuously improved and gradually expanded in its applicability. It is now used to assess the severity of knee joint injuries, monitor the recovery of injuries after treatment, and evaluate the clinical treatment outcomes of various knee joint diseases (Bengtsson et al., 1996; Kocher et al., 2004).

The scale primarily consists of eight components: limping, use of supports, locking sensation, joint stability, pain, swelling, stair climbing, and squatting.

Each component has corresponding scoring criteria, with scores ranging from 0 to 100. Patients rate each item based on their own condition, and an overall score is obtained. Higher scores indicate better function of the knee joint, a higher degree of recovery, and better clinical efficacy (Tegner and Lysholm, 1985).

Pain and joint stability are the two most important components of the LKSS, as they carry the highest proportion of the total score. This implies that pain and joint stability have a significant impact on evaluating knee joint function and the degree of recovery.

Previous research has shown that the LKSS conforms to modern psychometric measurement standards and is not influenced by factors such as patient gender or physician bias (Fu et al., 2018). It can be used to assess joint mobility, knee joint stability, and various pathological symptoms of the knee joint, and it is characterized by simplicity, comprehensiveness, and reliability (Hao et al., 2016). The scale demonstrates good reliability and meets the standards for Patient-Reported Outcome Measures (PROM) (also known as patient-reported clinical outcomes), making it suitable for evaluating conditions such as pain in KOA or disorders of the patellofemoral joint (Ma et al., 2016). The combined use of LKSS and the knee joint activity scale enhances a more comprehensive assessment of clinical efficacy in knee-related diseases, especially those predominantly involving ligamentous injuries of the knee joint.

In summary, the LKSS provides a simple, straightforward and comprehensive assessment of the patient's functional perception of daily activities. And, it also allows for a preliminary assessment of the level of motor function of patients when performing exercises of different intensities. By providing a numerical score that corresponds directly to the patient's activity and joint function, it provides a clear picture of the patient's degree of dysfunction (Yan, 2010), allowing both the patient and the physician to clearly understand the patient's current condition, which can help the physician to assess the patient's knee joint function and degree of impairment more accurately, and thus provide a more personalised treatment plan for the patient. In addition, the scale allows each content parameter of the assessment system to reflect the treatment process. Therefore, it can also be used to assess the effectiveness of treatment, monitor changes in the patient's knee joint function, and evaluate the effectiveness and safety of the treatment plan.

There were no significant differences in the LKSS scaores among the three groups before treatment, indicating comparability ($P > 0.05$). After treatment, all three groups showed an improvement in LKSS scores compared to before treatment, with the Treatment Group showing the most significant improvement, followed by Control Group 1, while Control Group 2 showed minimal changes. The comparison of scores among the three post-treatment groups showed P values < 0.05, indicating statistical differences. The pairwise comparison between groups also showed P values < 0.05, indicating statistically significant differences. When comparing the scores within the same group before and after treatment, both the Treatment Group and Control Group 1 had P values < 0.05, indicating statistically significant differences, while Control Group 2 had P values > 0.05, indicating no statistical difference. The comparison of score differences before and after treatment among the three groups also showed statistical significance ($P < 0.05$), with the Treatment Group showing the greatest improvement.

Based on the above results, it shows that:

(a) There are significant differences in the LKSS scores among the three groups after treatment. Comparing the mean values and standard deviations, it can be observed that the Treatment Group has better effects compared to Control Groups 1 and 2, while the efficacy of Control Group 2 is poor; and

(b) Evaluating the results of three different methods for treating KOA from multiple perspectives suggests that both the treatment methods of Treatment Group and Control Group 1 have a relieving and therapeutic effect. However, the combination of EA and the top ten highly-researched acupoints demonstrates better improvement in the symptoms associated with KOA, highlighting the superior clinical efficacy of EA over MA.

6.6.2.4 Quantitative Score of Knee Osteoarthritis Symptom Classification (SKSC)

The Quantitative Score of Knee Osteoarthritis Symptom Classification (SKSC) in the *Guidelines for Clinical Research of Chinese Herbal Medicines as New Drugs*, also known as the Symptom Severity Grading and Quantification Scale for Knee Osteoarthritis, is a commonly used assessment tool for evaluating the symptoms and severity of KOA in patients. This scale allows for the classification of symptoms into different levels according to the patient's symptomatology and the quantitative assessment of the patient's symptoms according to the points awarded for each level.

This quantitative assessment scale can help physicians more accurately evaluate the symptoms and severity of patients, thus providing a more personalised treatment plan for the patient. In clinical research on new Chinese herbal medicines or novel treatment approaches, this assessment scale can be used to observe the improvement of symptoms in KOA patients with the new medicine or treatment method, providing a reference for the development of new drugs or therapies. Additionally, this assessment scale can also be used for evaluating the effectiveness of treatment, monitoring changes in patients' symptoms, and assessing the effectiveness and safety of treatment plans.

There were no significant differences in the SKSC among the three groups before treatment, indicating comparability ($P > 0.05$). After treatment, all three groups showed a decrease in the SKSC compared to before treatment, with the Treatment Group showing the most significant decrease, followed by Control Group 1, while Control Group 2 showed minimal changes. The comparison of scores among the three post-treatment groups showed P values < 0.05, indicating statistical differences. The pairwise comparison between groups also showed P values < 0.05, indicating statistically significant differences. When comparing the scores within the same group before and after treatment, both the Treatment Group and Control Group 1 had P values < 0.05, indicating statistically significant differences, while Control Group 2 had P values > 0.05, indicating no statistical difference. The comparison of score differences before and after treatment among the three groups also showed statistical significance ($P < 0.05$), and the improvement was better in the Treatment Group.

Based on the above results, it shows that:

(a) There are significant differences in the SKSC among the three groups after treatment. Comparing the mean values and standard deviations, it can be observed that the Treatment Group has better effects compared to Control Groups, 1 and 2, while the efficacy of Control Group 2 is poor; and

(b) The results suggest that both the Treatment Group and Control Group 1's treatment methods have an alleviating and therapeutic effect on KOA. However, EA combined with the top ten highly-researched acupoints can better improve the symptoms associated with KOA, reflecting that EA has better clinical efficacy than MA.

6.6.2.5 TNF-α

KOA is a prevalent joint disease characterized by joint pain, stiffness and functional impairment. Contemporary research suggests that KOA involves an inflammatory response mediated by multiple inflammatory factors (Liu, 2018). These factors have a significant impact on the anabolic and catabolic processes of articular cartilage tissue, with Tumor Necrosis Factor-alpha (TNF-α) being one such influential inflammatory mediator.

TNF-α, an inflammatory cytokine synthesised by immune cells, assumes a pivotal role in inflammation and immune responses. It stimulates the release of protease activity from prostaglandins (PG) and matrix metalloproteinases (MMPs), impedes the synthesis of proteoglycans and type II collagen, disrupts the equilibrium between chondrocyte matrix and cartilage extracellular matrix (CECM), initiates a peroxidative reaction in osteocytes, and subsequently affects the process of cartilage matrix degradation and bone resorption (Wang and Zhang, 2021; Wang and He, 2018; Mueller and Tuan, 2011; Nees et al., 2019; Liu and Niu, 2008). These destructive processes exacerbate the damage and degeneration of cartilage and bone tissue, consequently eliciting a range of symptoms in individuals with KOA. Studies have revealed that patients with KOA exhibit elevated serum levels of TNF-α, with significantly higher levels observed in both serum and synovial fluid compared to healthy individuals (Ma et al., 2017; Jiang, 2009). Moreover, TNF-α levels exhibit a positive correlation with the severity of KOA, being markedly higher in patients with severe symptoms as opposed to those with milder manifestations. These findings underscore the crucial role played by TNF-α in the pathogenesis, progression, and development of KOA.

Animal experiments conducted by Neidel et al. (1996) have yielded results that demonstrate the positive staining of TNF-α and its receptors in cartilage matrix and cells, with the intensity and extent of staining corresponding to the severity of osteoarthritis. TNF-α actively promotes the degradation of proteoglycans, inhibits their synthesis, and selectively suppresses cartilage collagen production (Jia, 2020). Furthermore, TNF-α stimulates cartilage-degrading enzymes to act on vascular endothelial cells, thereby increasing vascular permeability, exacerbating local tissue inflammatory edema and infiltration of inflammatory cells, leading to knee joint swelling and pain, and ultimately influencing the functional activities of KOA patients.

To summarise, TNF-α can induce apoptosis of articular chondrocytes and cartilage destruction, stimulate the production of inflammatory mediators by synovial cells, and activate bone-resorbing cells, thereby contributing to osteoporosis and osteoarticular destruction. Additionally, TNF-α promotes the generation and persistence of pain, exacerbating the symptoms and discomfort experienced by KOA patients. Consequently, there exists a correlation between serum TNF-α levels and KOA, whereby elevated TNF-α levels may exacerbate symptom severity and disease progression. Accordingly, reducing TNF-α levels may alleviate inflammation and improve disease outcomes. Thus, monitoring changes in serum TNF-α levels can serve as an objective indicator and basis for evaluating the efficacy of KOA treatments (Matsukawa et al., 1997).

There were no significant differences in the serum TNF-α contents among the three groups before treatment, indicating comparability ($P > 0.05$). After treatment, the serum TNF-α contents of all three groups decreased compared with before treatment, and the Treatment Group decreased the most, followed by Control Group 1, however, Control Group 2 did not change significantly. The comparison of serum TNF-α levels among the three post-treatment groups showed P values < 0.05, indicating statistical differences. The pairwise comparison between groups also showed P values < 0.05, indicating statistically significant differences. When comparing within the same group before and after treatment, both the Treatment Group and Control Group 1 had P values < 0.05, indicating statistically significant differences, while Control Group 2 had P values > 0.05, and there was no significant difference. The comparison of differences in serum TNF-α levels before and after treatment among the three groups also showed statistical significance (P < 0.05), and the improvement was greatest in the Treatment Group.

The above results indicate that:

(a) There are significant differences in serum TNF-α levels among the three groups after treatment. Comparing the mean values and standard deviations, it can be observed that the Treatment Group has better effects compared to Control Groups, 1 and 2, while Control Group 2 is less effective;

(b) The results suggest that both the Treatment Group and Control Group 1's treatment methods have a relieving and therapeutic effect on KOA. However, EA combined with the top ten highly-researched acupoints demonstrates better downregulation of serum TNF-α levels, reflecting that EA has superior clinical efficacy than MA; and

(c) One of the mechanisms of action of EA in treating KOA may be through the downregulation of serum TNF-α levels and reduction of the pathway of pro-inflammatory cytokines.

6.6.2.6 IL-1β

Inflammatory factors have an important role to play in KOA and are closely associated with the disease (Liu et al., 2020; Giordano et al., 2020; He et al., 2019). One of the commonly observed inflammatory factors in clinical practice and most trials is interleukin-1 beta (IL-1β).

IL-1β is an inflammatory factor mainly secreted by leukocytes, can participate in blood circulation, and plays an important role in the inflammatory and immune response. IL-1β can be seen in various pathological injury processes of the human body, such as the destruction of articular cartilage and the formation of edema (Zhou et al., 2018), which has an important correlation with pathological degeneration of joint morphology (Zhang et al., 2021). As an important pro-inflammatory factor, IL-1β can mediate the secretion of various inflammatory cytokines, promote the release of MMP-1, MMP-3, etc., up-regulate cyclooxygenase 2 (COX-2), and inhibit type II and IX collagen, leading to the apoptosis and decomposition of chondrocytes, which in turn changes the structure and function of chondrocytes and causes cartilage damage, which affects the generation and progression of knee osteoarthritis (Su et al., 2017; Fang et al., 2022).

IL-1β and TNF-α are pro-inflammatory cytokines that play significant roles in the pathogenesis of KOA. These cytokines promote cartilage matrix degradation and accelerate cartilage destruction within the knee joint. Multiple studies conducted by Bemeur et al. (2008) and Xiong et al. (2023) have demonstrated a positive correlation between the levels of IL-1β and TNF-α and the severity of KOA. Higher levels of these inflammatory factors typically indicate a more severe condition of KOA in patients. This suggests that the production and release of IL-1β and TNF-α contribute to the progression of cartilage damage and the overall degenerative changes in the knee joint. One study completed by Yu et al. (2022) examined the relationship between MRI synovial thickness, serum inflammatory cytokines (IL-1β and TNF-α), and KOA combined with synovitis. The findings of this study revealed a positive correlation between synovial thickness and the levels of IL-1β and TNF-α in the serum. Additionally, MRI cartilage thickness was found to be negatively correlated with the levels of IL-1β and TNF-α. These results support the notion that IL-1β and TNF-α can promote cartilage destruction, alter the synovial structure, and contribute to knee swelling and pain. Studies conducted by Blom et al. (2007) and Dai and Qu, (2023) have shown that IL-1β plays a critical role in the regulation of inflammation and is considered a key mediator in the overall inflammatory process. It acts as an initial factor in triggering the inflammatory response and subsequently initiates a cascade of inflammatory reactions. By activating various signaling pathways, IL-1β can induce the production of other pro-inflammatory cytokines and further perpetuate the inflammatory process.

The study conducted by Wang Kexin et al. (2020) suggested that acupuncture therapy could have beneficial effects on KOA by exerting anti-inflammatory and antioxidant effects, promoting local blood circulation in the knee joint, and accelerating the downregulation of IL-1 (including IL-1β) and TNF-α levels in patients for therapeutic purposes. By reducing the levels of these inflammatory factors, acupuncture may help alleviate inflammation, which is a major contributor to the progression of KOA. This downregulation of IL-1β levels may contribute to an alleviation of inflammation, a reduction in cartilage degradation, and a potential improvement in the disease process. The changes in IL-1β levels can serve as an objective indicator and basis for evaluating the effectiveness of treatment for KOA. Monitoring the levels of IL-1β throughout acupuncture therapy can provide insights into the therapeutic response and the impact of treatment on the inflammatory processes involved in KOA.

There were no significant differences in the serum IL-1β levels among the three groups before treatment, indicating which were comparable ($P > 0.05$). After treatment, all three groups showed a decrease in serum IL-1β levels compared to before treatment, with the Treatment Group showing the most significant decrease, followed by Control Group 1, while Control Group 2 did not change significantly. The comparison of serum IL-1β levels among the three post-treatment groups showed P values < 0.05, indicating statistical differences. The pairwise comparison between groups also showed P values < 0.05, indicating statistically significant differences. When comparing within the same group before and after treatment, both the Treatment Group and Control Group 1 had P values < 0.05, indicating statistically significant differences, while Control Group 2 had P values > 0.05, indicating there was no significant difference. The comparison of differences in serum IL-1β levels before and after treatment among the three groups also showed statistical significance ($P < 0.05$), with the Treatment Group showing the greatest improvement.

Based on the above results, it shows that:

(a) There are significant differences in serum IL-1β levels among the three groups after treatment. Comparing the mean values and standard deviations, it can be observed that the Treatment Group has better effects compared to Control Group 1 and Control Group 2, while the efficacy of Control Group 2 is poor;

(b) The results suggest that both the treatment methods of the Treatment Group and Control Group 1 have a relieving and therapeutic effect on KOA. However, the combination of EA with the top ten highly-researched acupoints can better downregulate the serum IL-1β levels, reduce the inflammatory response of KOA, and improve its symptoms, highlighting the superior clinical efficacy of EA over MA; and

(c) One of the mechanisms of action of EA in the treatment of KOA may be achieved by the downregulation of serum IL-1β levels and reduction of pro-inflammatory cytokines.

Overall, IL-1β and TNF-α are related to the pathogenesis of KOA, particularly in promoting cartilage degradation and affecting synovial inflammation. Targeting these inflammatory factors may have potential therapeutic value in controlling the progression of KOA and alleviating related symptoms.

6.6.3 Analysis of Clinical Efficacy

The clinical efficacy analysis revealed that at the end of the treatment session, the Treatment Group had a total effective rate of 89.9%, which is close to 90%. Control Group 1 achieved a total effective rate of 75.4%, while Control Group 2 had a significantly lower total effective rate of 5.8%. After statistical analysis, it was determined that there were significant differences in the clinical efficacy and total effective rate among the three treatments for KOA, and all the differences were statistically significant ($P < 0.05$). The results indicate that both the Treatment Group and Control Group 1 demonstrated significant therapeutic effects for KOA. The Treatment Group showed a better treatment effect when compared to Control Group 1, while Control Group 2 exhibited poor therapeutic effects.

Therefore, it can be concluded that the treatment methods employed in both the Treatment Group and Control Group 1 have significant therapeutic effects on KOA. The Treatment Group demonstrated superior efficacy, suggesting that it is a more effective treatment option. Control Group 2 has a low total effective rate, indicating the use of a placebo does not lead to substantial improvements in KOA.

7.0 Conclusion

Based on the above, we concluded that:

(a) Both EA and MA combined with the top ten highly-researched acupoints have therapeutic effects on KOA. The two treatment methods both effectively improve clinical symptoms and signs of patients while reducing serum levels of inflammatory cytokines, including IL-1β and TNF-α;

(b) EA yields better clinical efficacy compared to MA. EA not only improves clinical symptoms but also enhances patients' quality of life;

(c) Acupuncture treatment at the points does not belong to the main meridians, acupoints and pain points, is not effective in treating KOA, and sham acupuncture does not exhibit a significant placebo effect, resulting in poorer clinical outcomes;

(d) One of the proposed mechanisms of action for EA in treating KOA is its ability to regulate serum levels of IL-1β and TNF-α, ultimately reducing pro-inflammatory cytokines;

(e) The results of the clinical research have validated the clinical efficacy and scientific basis of the acupuncture prescription used in the study, as well as the significant clinical efficacy of combining it with EA; and

(f) The combination of EA with the top ten highly-researched acupoints is a simple, convenient, effective treatment method for KOA. It is a safer, more efficient and easily implemented KOA acupuncture treatment, making it worthy of promotion in Malaysia, and can be extended to countries outside China.

8.0 Existing Problems and Prospects

Below are the existing challenges and proposals to mitigate and further improve the study:

(a) This study would have been done with larger samples and a longer period if there were no limitations in funding, personnel and pandemic controls. In the future, when conditions such as funds and personnel permit, the sample size will be expanded as much as possible, and the observation period will be extended to better evaluate the long-term efficacy of EA;

(b) For homogeneity analysis of the baseline information, consideration of influencing factors, such as body mass index and disease stage have not been done in this study. Statistical measurements of these factors can improve the conformity and the test results; and

(c) Due to the particularity of acupuncture therapy, true double-blindness cannot be achieved during the trial process, and the particularity of the implementation of acupuncture intervention in the study did not strictly implement the principle of double-blindness.

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APPENDIX A

Ethical Approval from UTAR Scientific and Ethical Review Committee (SERC)

UNIVERSITI TUNKU ABDUL RAHMAN
Wholly Owned by UTAR Education Foundation (Company No. 578227-M)

Re: U/SERC/89/2020

29 June 2020

Dr Te Kian Keong
Department of Chinese Medicine
Faculty of Medicine and Health Sciences
Universiti Tunku Abdul Rahman
Jalan Sungai Long
Bandar Sungai Long
43000 Kajang, Selangor

Dear Dr Te,

Ethical Approval For Research Project/Protocol

We refer to your application which was circulated for consideration of the UTAR Scientific and Ethical Review Committee (SERC). We are pleased to inform that your application for ethical approval of your research project (PhD student's project) involving human subjects has been approved by SERC.

The details of the project are as follows:

Research Title	Clinical Study on Treatment of Non-acute Knee Osteoarthritis (KOA) Using Electro-acupuncture at Top Ten High-selected Acupoints
Investigator(s)	Dr Te Kian Keong Yu, Shichao (UTAR Postgraduate Student)
Research Area	Science
Research Location	1. The Second Affiliated Hospital of Henan University of TCM (Henan Province Hospital of TCM) 2. The Third Affiliated Hospital of Henan University of TCM
No of Participants	156 participants (Age: 45 - 80)
Research Costs	UTAR Research Fund 2019 Cycle 1
Approval Validity	29 June 2020 - 28 June 2021

The conduct of this research is subject to the following:

(1) The participants' informed consent be obtained prior to the commencement of the research.

(2) Confidentiality of participants' personal data must be maintained; and

(3) Compliance with procedures set out in related policies of UTAR such as the UTAR Research Ethics and Code of Conduct, Code of Practice for Research Involving Humans and other related policies/guidelines.

Kampar Campus : Jalan Universiti, Bandar Barat, 31900 Kampar, Perak Darul Ridzuan, Malaysia
Tel: (605) 468 8888 **Fax**: (605) 466 1313
Sungai Long Campus : Jalan Sungai Long, Bandar Sungai Long, Cheras, 43000 Kajang, Selangor Darul Ehsan, Malaysia
Tel: (603) 9086 0288 **Fax**: (603) 9019 8868
Website: www.utar.edu.my

Should you collect personal data of participants in your study, please have the participants in the research signed the attached Personal Data Protection Statement for your records.

The University wishes you all the best in your research.

Thank you.

Yours sincerely,

Professor Ts Dr Faidz bin Abd Rahman
Chairman
UTAR Scientific and Ethical Review Committee

c.c Dean, Faculty of Medicine and Health Sciences
Director, Institute of Postgraduate Studies and Research

Kampar Campus : Jalan Universiti, Bandar Barat, 31900 Kampar, Perak Darul Ridzuan, Malaysia
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Website: www.utar.edu.my

APPENDIX B

Personal Data Protection Statement

PERSONAL DATA PROTECTION STATEMENT

Please be informed that in accordance with Personal Data Protection Act 2010 ("PDPA") which came into force on 15 November 2013, Universiti Tunku Abdul Rahman ("UTAR") is hereby bound to make notice and require consent in relation to collection, recording, storage, usage and retention of personal information.

Notice:

1. The purposes for which your personal data may be used are inclusive but not limited to:-
   - For assessment of any application to UTAR
   - For processing any benefits and services
   - For communication purposes
   - For advertorial and news
   - For general administration and record purposes
   - For enhancing the value of education
   - For educational and related purposes consequential to UTAR
   - For the purpose of our corporate governance
   - For consideration as a guarantor for UTAR staff/ student applying for his/her scholarship/ study loan

2. Your personal data may be transferred and/or disclosed to third party and/or UTAR collaborative partners including but not limited to the respective and appointed outsourcing agents for purpose of fulfilling our obligations to you in respect of the purposes and all such other purposes that are related to the purposes and also in providing integrated services, maintaining and storing records. Your data may be shared when required by laws and when disclosure is necessary to comply with applicable laws.

3. Any personal information retained by UTAR shall be destroyed and/or deleted in accordance with our retention policy applicable for us in the event such information is no longer required.

4. UTAR is committed in ensuring the confidentiality, protection, security and accuracy of your personal information made available to us and it has been our ongoing strict policy to ensure that your personal information is accurate, complete, not misleading and updated. UTAR would also ensure that your personal data shall not be used for political and commercial purposes.

Consent:

1. By submitting this form you hereby authorise and consent to us processing (including disclosing) your personal data and any updates of your information, for the purposes and/or for any other purposes related to the purpose.

2. If you do not consent or subsequently withdraw your consent to the processing and disclosure of your personal data, UTAR will not be able to fulfill our obligations or to contact you or to assist you in respect of the purposes and/or for any other purposes related to the purpose.

3. You may access and update your personal data by writing to us at ____________________.

Acknowledgment of Notice

[ ] I have been notified by you and that I hereby understood, consented and agreed per UTAR above notice.

[ ] I disagree, my personal data will not be processed.

....
Name:
Date:

APPENDIX C
Informed Consent and Risk Notification for Acupuncture Treatment of KOA (English)

Informed Consent and Risk Notification for Acupuncture Treatment of KOA

Serial Number: ____

Name:	**Age:**	☐**Male** ☐**Female**
Telephone:	**Profession:**	☐**Single** ☐**Married** ☐**Divorced**
Address:		

Informed Consent and Risk Notification for Treatment:

1. I have understood the clinical study on acupuncture treatment (Include electro-acupuncture) for knee osteoarthritis and voluntarily agree to participate in it.
2. The clinical research on acupuncture treatment of knee osteoarthritis is carried out under the guidance of relevant qualified experts and professors in hospitals with nationally recognized qualifications. It has reliable security and professionalism. I understand and agree with this.
3. Personal information and other data of the participants will be strictly kept confidential during the study and any unauthorized disclosure is prohibited.
4. This study will involve randomized controlled trials, and I have understood the significance, purpose, and specific research methods of this clinical study.
5. I have been informed about the potential risks during the treatment process, such as pain, bleeding, infection, as well as adverse reactions such as acupuncture accidents and fainting, and the methods for managing them appropriately. In case of any related harm, timely and effective treatment and assistance can be provided.
6. I have the right to have any questions regarding this study answered at any time and the right to withdraw from the study at any point. It should be ensured that I can still receive alternative treatment methods after withdrawal and will not be treated unfairly.
7. Other unpredictable accidents.

Signature:

Date:___ (D) ___ (M) 202___

APPENDIX C

Informed Consent and Risk Notification for Acupuncture Treatment of KOA (Mandarin)

针灸治疗膝关节骨性关节炎知情同意及风险告知书

序号：_____

姓名：	年龄：	□男 □女
电话：	职业：	□未婚 □已婚 □离异

治疗知情同意及风险告知：

1. 我已经了解针灸（包括电针）治疗膝关节骨性关节炎病的临床研究，且自愿参加之。

2. 针灸治疗膝关节骨性关节炎的临床研究是在国家认可的具有资质的医院的有关专家和教授的指导下进行的，安全性和疗效性可靠，我对此表示理解和认同。

3. 受试者的个人资料等信息在研究过程中将受到严格保密，严禁外泄。

4. 本研究将采取随机分组对照，我对本次临床研究的意义、目的和具体研究方法已经了解。

5. 治疗过程中可能发生的疼痛、出血、感染等风险以及针刺事故和晕厥等不良反应和对症处理的方法确认已告知，如发生相关的损害时，本人可获得及时有效的治疗。

6. 我有对在本研究中的疑问获得随时解答、在任何时间节点退出本研究的权力，应当确保我在退出后仍可采用其他方法进行治疗，不会受到不公平之待遇。

7. 其他不可预知的意外。

签名：

日期：202__年__月__日

APPENDIX D

Quantitative Score of Knee Osteoarthritis Symptom Classification (SKSC)

Name:____________ Gender: Male ( ), Female ( ) Age:_____ (years old)

Quantitative Score of Knee Osteoarthritis Symptom Classification (SKSC)

(Symptom Grading Quantitative Score Table)

Symptom	Level 0 (0 score)	Level I (1 score)	LevelII (2 score)	LevelIII (3 score)
Pain or discomfort during rest in bed at night	None	Occasional pain	Intermittent pain	Persistent pain
Morning stiffness	None or ≤1 minute	1-10 minutes	≥10minutes	≥20minutes
Morning stiffness or pain increased after getting up	None	Discomfort, disappears after a slight activity	Pain, relieved after slight movement	Pain is obvious, does not decrease after exercise
Pain or discomfort when standing from a sitting position	None	Mild pain or discomfort	Pain or discomfort is obvious, but does not require help	Pain is noticeable and needs help
Pain or discomfort while walking	None	Appears after walking> 1km	Appears when walking <1km	Pain appears when walking, and worsens after walking
Maximum walking distance (can walk with pain)	＞1km	300m-1km	300m-100m	＜100m
Squatting or knees bending	Can	Slightly difficult	Cannot exceed 90 °	Cannot squat or bend knees
Up or down the stairs	Can	Slightly difficult	Difficult	Cannot go up and down stairs
Daily activities	Normal	Occasionally difficult	Often have difficulty	Cannot

膝骨关节炎症状分级量化积分表

症状	0 级（0 分）	I 级（1 分）	II 级（2 分）	III 级（3 分）
夜间卧床休息时疼痛或不适	无	偶有疼痛	间断疼痛	持续疼痛
晨僵	无或≤1 分钟	1-10 分钟	≥10 分钟	≥20 分钟
晨僵或起床后疼痛加重	无	有不适感，稍活动后消失	疼痛，稍活动后减轻	疼痛明显，活动后不减轻
从坐位站立时疼痛或不适	无	轻度疼痛或不适	疼痛或不适明显，不需帮助	疼痛明显，需要帮助
行走时疼痛或不适	无	＞1km 后出现	＜1km 出现	一行走即痛，行走后疼痛加重
最大步行距离（可伴疼痛行走）	＞1km	300m-1km	300m-100m	＜100m
蹲下或屈膝	能	略感困难	不能超过 90°	不能下蹲或屈膝
上下楼梯	能	略感困难	艰难步行	不能上下楼梯
日常活动	正常	偶有困难	时有困难	不能

Total score (总分): ______

Date(日期): ____(D)____(M) 2022___

APPENDIX E

Lysholm Knee Scoring Scale (LKSS) & Visual Analog Scale (VAS)

(English)

LYSHOLM KNEE SCORING SCALE (LKSS)

This questionnaire is designed to give your Physical Therapist information as to how your knee problems have affected your ability to manage in everyday life Please answer every section and mark only the ONE box which best applies to you at this moment.

Reference for Score: Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries[J]. Clinical Orthopaedics and Related Research (1976-2007), 1985, 198: 42-49.

SECTION 1 - LIMP

☐ I have no limp when I walk. (5)
☐ I have a slight or periodical limp when I walk. (3)
☐ I have a severe and constant limp when I walk. (0)

SECTION 2 - Using support (cane or crutches) to bear weigh

☐ I do not use a cane or crutches. (5)
☐ I use a cane or crutches with some weight-bearing. (2)
☐ Putting weight on my hurt leg is impossible. (0)

SECTION 3 - Locking sensation in the knee

☐ I have no locking and no catching sensation in my knee. (15)
☐ Have catching sensation but no locking sensation in knee.(10)
☐ My knee locks occasionally. (6)
☐ My knee locks frequently. (2)
☐ My knee feels locked at this moment. (0)

SECTION 4 - Giving way sensation from the knee

☐ My knee never gives way. (25)
☐ My knee rarely gives way, only during athletics or vigorous activity. (20)
☐ My knee frequently gives way during athletics or other vigorous activities. In turn I am unable to participate in these activities. (15)
☐ My knee occasionally gives way during daily activities. (10)
☐ My knee often gives way during daily activities. (5)
☐ My knee gives way every step I take. (0)

SECTION 5 – PAIN

☐ I have no pain in my knee. (25)
☐ I have intermittent or slight pain in my knee during vigorous activities. (20)
☐ I have marked pain in my knee during vigorous activities. (15)
☐ I have marked pain in my knee during or after walking more than 1 mile. (10)
☐ I have marked pain in my knee during or after walking less than 1 mile. (5)
☐ I have constant pain in my knee. (0)

SECTION 6 – SWELLING

☐ I have no swelling in my knee. (10)
☐ I have swelling in my knee only after vigorous activities. (6)
☐ I have swelling in my knee after ordinary activities. (2)
☐ I have swelling constantly in my knee. (0)

SECTION 7 – CLIMBING STAIRS

☐ I have no problems climbing stairs. (10)
☐ I have slight problems climbing stairs. (6)
☐ I can climb stairs only one step at a time. (2)
☐ Climbing stairs is impossible for me. (0)

SECTION 8 – SQUATTING

☐ I have no problems squatting. (5)
☐ I have slight problems squatting. (4)
☐ I cannot squat beyond a 90 degree-bend in my knee. (2)
☐ Squatting is impossible because of my knee. (0)

Total: _____

Visual Analogue Scale for Pain (VAS)

A 10cm-long ruler is marked at both ends with "no pain" and "severe pain", a total of 10 scales, each 1cm is a scale, representing 1 point, 0 is "no pain", 10 points for "severe pain", ask the patient to mark a score on the ruler that reflects the level of pain at the time (or in the past 24 hours).

0 1 2 3 4 5 6 7 8 9 10

No pain at all **Worst possible pain**

Total:_____

Name: __________ Gender: Male( ), Female( ) Age:______ (years old) Date: ___(D)___(M) 202__

APPENDIX E

Lysholm Knee Scoring Scale (LKSS) & Visual Analog Scale (VAS)

(Mandarin)

膝关节 LYSHOLM 评分量表

LYSHOLM KNEE SCORING SCALE

(LKSS)

本量表旨在向您的医师/物理治疗师提供有关您的膝关节问题如何影响您的日常生活管理能力的信息。 请回答每个部分，并仅在目前最适合您的一个方框中打勾。

第一部分-跛行

- ☐ 走路时无跛行。(5)
- ☐ 走路时轻微或偶尔跛行。(3)
- ☐ 走路时严重或持续跛行。(0)

第二部分-需要使用支撑物（手杖或拐杖）负重

- ☐ 不使用手杖或拐杖。(5)
- ☐ 负重时需使用手杖或拐杖。(2)
- ☐ 患膝不能负重。(0)

第三部分-膝关节绞锁

- ☐ 膝关节没有绞锁和卡顿的感觉。(15)
- ☐ 膝关节有卡顿的感觉但没有绞锁。(10)
- ☐ 膝关节偶尔发生绞锁。(6)
- ☐ 膝关节经常发生绞锁。(2)
- ☐ 膝关节此时正在发生绞锁。(0)

第四部分-膝关节不稳定

- ☐ 稳定，从不打软腿。(25)
- ☐ 体育运动或其他剧烈活动时极少会不稳。(20)
- ☐ 体育运动或其他剧烈活动时经常出现膝关节不稳，从而导致不能参加这些活动。(15)
- ☐ 日常生活活动中偶尔出现膝关节不稳。(10)
- ☐ 日常生活活动中经常出现膝关节不稳。(5)
- ☐ 每走一步均出现膝关节不稳。(0)

第五部分-疼痛

- ☐ 膝关节无疼痛。(25)
- ☐ 剧烈/用力活动时膝关节有时轻微疼痛。(20)
- ☐ 剧烈/用力活动时膝关节明显疼痛。(15)
- ☐ 步行超过1英里（约1.6公里）后，膝关节明显疼痛。(10)
- ☐ 步行不到1英里（约1.6公里），膝关节明显疼痛。(5)
- ☐ 膝关节持续性疼痛。(0)

第六部分-肿胀

- ☐ 膝关节无肿胀。(10)
- ☐ 剧烈活动后膝关节发生肿胀。(6)
- ☐ 日常活动时膝关节发生肿胀。(2)
- ☐ 膝关节持续肿胀。(0)

第七部分-爬楼梯

- ☐ 没有困难。(10)
- ☐ 有轻微困难。(6)
- ☐ 一次只能上一级台阶。(2)
- ☐ 不能爬楼梯。(0)

第八部分-下蹲

- ☐ 没有问题。(5)
- ☐ 稍微有困难。(4)
- ☐ 下蹲时屈膝不能超过90度。(2)
- ☐ 无法下蹲。(0)

总分:______

视觉模拟评分法

Visual Analogue Scale for Pain

(VAS)

在一根10cm长的尺子两端分别标有“无痛”和“剧痛”，每1cm为一个刻度（共10个刻度），代表1分，起点0分为“无痛”，终点10分为“重痛”，请您在尺子上标出反映当时（或过去 24 小时内）疼痛程度的分数。

0 1 2 3 4 5 6 7 8 9 10

无痛 剧痛

总分:_____

姓名:____________ 性别：男（）、女（） 年龄:_____（岁） 日期: 202__年___月___日

APPENDIX F

Western Ontario and McMaster Universities Osteoarthritis Index

(WOMAC)

(English)

WESTERN ONTARIO AND MCMASTER UNIVERSITIES OSTEOARTHRITIS INDEX (WOMAC)

Name:_____________ Gender: Male ( ), Female ( ) Age:_____ (years old)

RATE YOUR PAIN WHEN…	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	Part 1: Pain
Walking	0	1	2	3	4	
Climbing stairs	0	1	2	3	4	
Sleeping at night	0	1	2	3	4	
Resting	0	1	2	3	4	
Standing	0	1	2	3	4	TOTAL
RATE YOUR STIFFNESS IN THE…	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	**Part 2: Stiffness**
Morning	0	1	2	3	4	
Evening	0	1	2	3	4	TOTAL
RATE YOUR DIFFICULTY WHEN…	NONE	SLIGHT	MODERATE	SEVERE	EXTREME	**Part 3: Physical Function**
Descending stairs	0	1	2	3	4	
Ascending stairs	0	1	2	3	4	
Rising from sitting	0	1	2	3	4	
Standing	0	1	2	3	4	
Bending to floor	0	1	2	3	4	
Walking on even floor	0	1	2	3	4	
Getting in/out of car	0	1	2	3	4	
Going shopping	0	1	2	3	4	
Putting on socks	0	1	2	3	4	
Rising from bed	0	1	2	3	4	
Taking off socks	0	1	2	3	4	
Lying in bed	0	1	2	3	4	
Getting in/out of bath	0	1	2	3	4	
Sitting	0	1	2	3	4	
Getting on/off toilet	0	1	2	3	4	
Doing light domestic duties (cooking, dusting)	0	1	2	3	4	
Doing heavy domestic duties (moving furniture)	0	1	2	3	4	TOTAL

Instructions: Please rate the activities in each category according to the above-mentioned scale of difficulty and circle the appropriate rating for each item.

WOMAC TOTAL SCORE: ______ / 96 = _______%

Date: _____ （D） ______ （M） 202_____

APPENDIX F

Western Ontario and McMaster Universities Osteoarthritis Index

(WOMAC)

(Mandarin)

西安大略和麦克马斯特大学骨关节炎指数量表

WESTERN ONTARIO AND MCMASTER UNIVERSITIES OSTEOARTHRITIS INDEX

(WOMAC)

姓名:____________ 性别：男（）、女（） 年龄:_____（岁）

疼痛程度	没有疼痛	轻微的疼痛	中等的疼痛	严重的疼痛	非常严重的	**第一部分：疼痛**
在平地行走的时候	0	1	2	3	4	
上下楼梯的时候	0	1	2	3	4	
晚上在床上睡觉的时候	0	1	2	3	4	
坐着或躺着休息的时候	0	1	2	3	4	
站立的时候	0	1	2	3	4	评分：____

僵硬程度	没有僵硬	轻微的僵硬	中等的僵硬	严重的僵硬	非常严重的	**第二部分：僵硬**
在早晨刚醒起床时，膝关节的僵硬程度	0	1	2	3	4	
在之后的时间里，坐、躺或休息后，关节僵硬程度	0	1	2	3	4	评分：____

在以下各种情况下，您感觉困难程度如何	没有困难	轻微的困难	中等的困难	严重的困难	非常严重的	**第三部分：躯体功能**
下楼梯	0	1	2	3	4	
上楼梯	0	1	2	3	4	
从坐着的椅子上站起来的时候	0	1	2	3	4	
站立	0	1	2	3	4	
弯腰	0	1	2	3	4	
在平地行走	0	1	2	3	4	
上下汽车	0	1	2	3	4	
逛街、购物	0	1	2	3	4	
穿袜子	0	1	2	3	4	
起床站起来	0	1	2	3	4	
脱袜子	0	1	2	3	4	
上床躺着	0	1	2	3	4	
进、出浴缸的时候	0	1	2	3	4	
坐着	0	1	2	3	4	
在卫生间蹲（坐）下马桶或者站起来的时候	0	1	2	3	4	
干比较轻的家务活的时候(做饭、扫地)	0	1	2	3	4	
干比较重的家务活的时候 (搬动家具等)	0	1	2	3	4	评分：____

使用说明：请根据上述每项活动的难度等级对每个类别中的活动进行评分，并圈出每个项目的相应评分分值。

WOMAC 总分: ______ / 96 = _______%

日期: 202__年___月___日

APPENDIX G
The Application of Traditional Chinese Medicine Therapies in the Treatment of Knee Osteoarthritis Patients
(English)

The Application of Traditional Chinese Medicine Therapies in the Treatment of Knee Osteoarthritis Patients

Questionnaire Introduction:
Greetings, this is a questionnaire research project conducted by the Department of Chinese Medicine, Universiti Tunku Abdul Rahman (UTAR).
This survey aims to understand the application of Traditional Chinese Medicine therapies in the treatment of Knee Osteoarthritis (KOA) patients in Malaysia and China, including the Chinese medicine approaches employed during treatment and the age distribution of patients seeking treatment for KOA.
We sincerely appreciate your valuable time in participating in this survey amidst your busy schedules.

1. TCM Therapy Methods Used in the Treatment of KOA (in no particular order) [allow **multiple selection**]

☐ Traditional Acupuncture
☐ Massage
☐ Cupping
☐ Moxibustion
☐ Bloodletting
☐ Electro acupuncture
☐ Chinese herbs (internal or external use)
☐ Lamp lighting up therapy/TDP therapy
☐ Traditional indigenous therapy
☐ Others (self-supplemented by respondents)

2. Age Range of the Patients (years) [allow **multiple selection**]

☐ 18-29
☐ 30-39
☐ 40-49
☐ 50-59
☐ 60-69
☐ 70-79
☐ 80-

APPENDIX G

The Application of Traditional Chinese Medicine Therapies in the Treatment of Knee Osteoarthritis Patients

(Mandarin)

中医疗法在膝关节骨性关节炎患者治疗中的应用情况

问卷说明：

您好，这是 UTAR 中医系的一项问卷研究项目。

本调研旨在了解中医疗法在马来西亚/中国膝关节骨性关节炎患者治疗中的应用情况，问卷内容包括：治疗时采取的中医方法、就诊膝骨关节炎患者的年龄分布。

感谢您百忙之中抽出宝贵的时间进行填写。

1. 膝骨关节炎的中医治疗方法（排名不分先后）**（可多选）**

☐ 传统针刺

☐ 推拿

☐ 拔罐

☐ 艾灸

☐ 放血

☐ 电针

☐ 中药（内服、外用）

☐ 神灯/TDP

☐ 传统土著疗法

☐ 其它（自行补充）

2. 患者的年龄范围（可多选）

☐ 18-29

☐ 30-39

☐ 40-49

☐ 50-59

☐ 60-69

☐ 70-79

☐ 80-