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USING DATA MINING APPROACHES TO SELECT ACUPOINTS IN ACUPUNCTURE AND MOXIBUSTION FOR KNEE OSTEOARTHRITIS

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Abstract

Background: Acupuncture and moxibustion are traditional Chinese medicine therapies commonly used to treat knee osteoarthritis (KOA). Although acupoint selection affects the effectiveness of acupuncture and moxibustion, the basic rules of acupoint selection are little understood and there is a lack of guidelines regarding prescription. In this study, we used data mining approaches to investigate the principles of acupoint selection and provide a framework for formulation prescription in acupuncture and moxibustion for clinical treatment of KOA.
Materials and Methods: PubMed, Cochrane Library, Science Citation Index, Wanfang database, VIP database, and China National Knowledge Infrastructure were searched for randomized controlled clinical trials published in English or Chinese from January 1, 2009 to October 1, 2015 evaluating the effect of acupuncture and moxibustion on KOA. Databases were established. Frequency statistics and association rule were used to extract and analyze the data.
Results: A total of 876 acupuncture prescriptions and 122 acupoints were included in the analysis. Acupoints were concentrated in acupoints of fourteen meridians. The most frequently used acupoints were Dubi (ST35), Neixiyan (EX-LE4), Yanglingquan (GB34), Xuehai (SP10), Liangqiu (ST34), Zusanli (ST36), Yinlingquan (SP9), and Ashi point. The most frequently used meridian was Stomach Meridian of Foot-Yangming. Acupoints were concentrated mainly in the lower limbs. 42 acupoint pairs occurred frequently, and the top acupoint pairing was Dubi (ST35) and Neixiyan (EX-LE4).
Conclusion: Acupoint selection and formulation prescription should focus on locally affected areas, and follow the theory of meridians, which helps establish guidelines for acupuncture and moxibustion in KOA patients.

Key words: acupuncture and moxibustion, knee osteoarthritis, acupoint, data mining technology

Abbreviations: KOA, knee osteoarthritis; TCM, traditional Chinese medicine; RCT, randomized controlled trials; AR, association rule; DM, data mining; KDD, Knowledge Discover in Database; CNKI, China National Knowledge Infrastructure; SCI, Science Citation Index.

Introduction

Knee osteoarthritis (KOA), also known as degenerative arthritis, is characterized by chronic damage to the articular cartilage and new bone formation at the articulation surface – the underlying causes of three major clinical symptoms: joint pain, stiffness, and functional disorder (Adatia et al., 2012; Sinusas, 2012). Severe KOA may negatively affect a patient's function and quality of life (Yan et al., 2013). From a global perspective, the prevalence of radiographically confirmed symptomatic KOA was estimated to be 3.8% in 2010, and it was higher in women than in men (Cross et al., 2014). In the United States, KOA was the second cause of work disability in men over 50 years of age, only to be surpassed by ischemic heart disease (Arden et al., 2006).
As the world's population ages, the prevalence of KOA has increased steeply and placed a large burden on families, society, and health care systems (Liu et al., 2013). Therefore, choosing the best treatment for KOA is a major concern in modern medicine. Currently, treatment choices fall into four main categories: nonpharmacologic, pharmacologic, surgical, and complementary and alternative (Sinusas, 2012). Among complementary and alternative, acupuncture and moxibustion have been shown to have a curative effect (Corbett et al., 2013). Acupuncture and moxibustion are commonly used to reduce pain and functional dependence (Hinman et al., 2012), and have been gaining widespread acceptance among KOA patients because they are simple, convenient, safe and effective (Cohen et al., 2005; Zhang et al., 2015). However, there is a lack of guidelines regarding prescription of acupuncture . Therefore, determining the rules of acupoint selection and formulation prescription in acupuncture and moxibustion for clinical treatment of KOA is important for future research and in clinical practice. In this study, we used data mining (DM) techniques to extract and analyze literature about acupuncture and moxibustion for KOA. This paper summarizes the findings concerning the most frequently used acupoints, meridians, and the distribution of acupoints, as well as the correlating rules for selecting acupoints. The aim of this study was to investigate the principles of acupoint selection and provide a framework for formulation prescription in acupuncture and moxibustion for clinical treatment of KOA.

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Materials and Methods

Search Methods

PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Cochrane Library (http://onlinelibrary.wiley.com/), Science Citation Index (SCI) (http://apps.webofknowledge.com/), China National Knowledge Infrastructure (CNKI) (http://www.cnki.net/), Wanfang database (http://g.wanfangdata.com.cn/), and VIP database (http://qikan.cqvip.com/) were searched for literature on acupuncture and moxibustion for KOA from January 1, 2009 to October 1, 2015. The search strategy combined the key words (i) "acupuncture" or "moxibustion" or "acupuncture points" or "acupoints", and (ii) "knee osteoarthritis" or "hyperplastic arthritis" or "degenerative arthritis" or "arthralgia" or "bone rheumatism". Language was restricted to English and Chinese.

Data Screening

Inclusion Criteria of Literature

Document Type: We included clinical research articles whose full text was available at the time of data collection.
Object: We included clinical research articles about acupuncture and moxibustion in which KOA (including hyper-plastic arthritis, degenerative arthritis, arthralgia and bone rheumatism) was diagnosed according to the diagnostic criteria of Western medicine or Chinese medicine. Patient gender, age, race and duration of disease were not limited.
Design of Clinical Trial: We included randomized controlled clinical trials (RCT).
Interventions*:* We included studies in which acupuncture (skin needle therapy, intradermal needle therapy, fire-needle, water needle therapy, electro-acupuncture, or three-edged needle therapy), moxibustion (moxibustion with moxa cone, moxibustion with moxa stick, or moxa needle therapy), or cupping therapy (blood-letting puncturing and cupping, or retaining needle and cupping) was used as a treatment alone, in combination with each other, or in combination with other treatment methods.
Outcome Assessment: Unlimited.

Exclusion Criteria of Literature

The following types of literature materials were excluded from the analysis: reviews, comments, news, guides and summaries; animal studies; studies whose main objective was the observation of the auricular needle, scalp acupuncture or acupotomology; studies in which no specific meridians and acupoints were described. If an author had several publications in different journals, only the most recent publication (in the last one year) was included.

Data Collection

All abstracts identified by the literature search were screened according to the abovementioned selection criteria to exclude those that were clearly irrelevant (e.g., studies focusing on reviews, animal trials, case reports, and so on). Full texts of all remaining references were obtained and again screened to exclude irrelevant papers. Disagreements were resolved by discussion.

Data Preprocessing

Data Entry and Databases Established

Microsoft Excel 2010 (Microsoft Corporation) was used as the development platform for the databases. Two researchers entered the data in separate data sheets and established the main database. Data entries included studies title, acupuncture prescriptions, diagnostic criteria, inclusion criteria, exclusion criteria, design of clinical trial (experimental controls, randomized design, blinded design, etc.), outcome assessment, and type of treatment. The two databases were then checked by a third party until consensus was reached. Acupuncture prescriptions were extracted from the main database, and acupoints in the acupuncture prescriptions were transformed into binary variables by PASW Statistics 18.0 (IBM Corporation). Therefore, an acupoint from a certain acupuncture prescription was defined as "1", while the other acupoints of that same prescription were automatically defined as "0". In total, data from 876 acupuncture prescriptions were collected. A database of acupuncture prescriptions for acupuncture and moxibustion treatment of KOA was constructed.

Acupoints Nomenclature

Acupoint names were adjusted according to People's Republic of China standard nomenclature and location of acupuncture points (GB/T12346-2006). For instance, tender spots, relaxing points and unfixed points were named Ashi point; Juegu was named Xuanzhong (GB39); Xiyan, depending on context, was named Dubi (ST35) and/or Neixiyan (EX-LE4); Xiyan, not otherwise specified, was named Neixiyan (EX-LE4); and Waixiyan was named Dubi (ST35).

Data Processing

Frequency statistics methods and association rule (AR) of data were used to process data with Microsoft Excel 2010, PASW Statistics 18.0, and Clementine 12.0 (IBM Corporation).

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Frequency Statistics Method

Frequency statistics were used to determine the frequency of several different values or the frequency of values falling within a designated area to understand the distribution of data.

AR

AR was developed as a technique that aimed at discovering associations, with algorithms expected to observe the frequent itemsets (Mahmood et al., 2014). AR was divided into two steps. First, we determined the frequent itemsets. Second, we used the frequent itemsets to identify strong association rules. Apriori is a classical algorithm for frequent itemset mining that is performed through an iteration method called "layer-by-layer search" (Han et al., 2007; Li et al., 2014). The Apriori algorithm involves three data objects (the transaction set [D], the candidate set [C], and the frequent set [L]) and performs three operations: counts the support by scanning D, generates C_k by joining L_{K-1} and L_{K-1}, and prunes C_k by scanning L_{K-1}. In the Apriori algorithm, the k-itemset was used to generate the (k+1)-itemset, and the frequent k-itemsets were extracted from the candidate k-itemsets. First, we identified the frequent 1-itemset and recorded it as L_1; L_1 was intended to identify the frequent 2-itemset (L_2), and L_2 for L_3, respectively. The search was continued until no more frequent k-itemset could be found. An overall scanning of the whole database was needed for every L_K. Once all the frequent itemsets were found, the strong association rules could be generated according to minimum confidence (Jin et al., 2011). Support, confidence and lift are three important indicators of the interestingness of association rules (Yu et al., 2015). For one rule "A→B", Support denotes the probability of itemset A and B to occur simultaneously, which measures the importance and universality of the rule in the entire dataset; confidence represents the probability that itemset B occurs in the case itemset A also occurs, which appraises accuracy and reliability of the rule (Li et al., 2014); lift illustrates the correlation between the rules on both sides of the property. A lift value less than 1 indicates no correlation, whereas a lift value of more than 1 indicates correlation.

Results

Overall Profile of Acupuncture Prescriptions

In total, we retrieved 6151 literatures about acupuncture and moxibustion in the clinical treatment of KOA, including 136 records in PubMed, 113 records in SCI, 20 records in Cochrane Library, 1479 records in CNKI, 3791 records in Wanfang database, and 612 records in VIP database. A total of 876 acupuncture prescriptions were identified by analysis and screening of the selected literatures.

Application of Acupoints

This analysis aimed to provide the acupoint selections and their frequencies when curing certain diseases. In the 867 acupuncture prescriptions, 122 acupoints were used. The application frequency was 5332, involving 88 acupoints of fourteen meridians, 6 extra points, 10 Dong′ s extra – point, 17 empirical points and ashi points (Table 1). The most frequently used acupoint was Neixiyan (EX-LE4) (13.37% [713/5332], 81.39% [713/876]), followed by Dubi (ST35), Yanglingquan (GB34), Xuehai (SP10), Liangqiu (ST34), Zusanli (ST36), Yinlingquan (SP9), and Aashi point (Table 2).

Application of Meridians

Meridian application analysis demonstrated how the selected acupoints in the prescription were distributed in the 14 channels, including the frequency and percentage of the acupoints on each meridian, the number and percentage of acupoints used, and the name and frequency of each acupoint. The selected acupoints were distributed among 14 meridians, including 12 regular meridians, Governor Vessel, and Conception Vessel. The most frequently used meridian was the Stomach Meridian (31.88% [1700/5332]), followed by Spleen Meridian, Gallbladder Meridian and Bladder Meridian followed. The Bladder Meridian had the highest number of acupoints (26), followed by Stomach Meridian, Spleen Meridian and Gallbladder Meridian. The frequencies for each meridian and acupoint are shown in Table 3.

Application of Acupoints on Different Body Parts

The results of the analysis displayed the frequency and percentage of the distribution of acupoint selections in the prescriptions, the numbers and percentages of acupoints used the names and frequencies of particular acupoints, and the name and frequency of each acupoint. Acupoints on lower limbs were most frequently used, with 60 acupoints used a total of 4706 times. This was followed by acupoints on the back and lumbar (25 acupoints, used 134 times), chest and abdomen (25 acupoints, used 134 times), the upper limbs (20 acupoints, used 70 times), and the head, face, and neck (2 acupoints, used 5 times) (Table 4)

Association of Acupoint Compatibilities

The aim of the analysis was to indicate the compatibility of acupoints where the number of selected acupoints in the prescription was equal to or more than two, with the effectiveness of the compatibility measured by Support degree and confidence

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level. We analyzed the data of by using the Apriori logarithm with Clementine 12.0, and set minimum Support and minimum confidence as 0.1 and 0.5, respectively. In total, 55 rules were identified, minimum support was 10.50%, maximum support was 81.39%, minimum confidence was 50.92%, maximum confidence was 90.28%, and 2 rules had a lift value less than 1. Finally, we included 53 rules, 42 acupoint pairs. From table 5, we found the support and confidence of rule: "Dubi (ST35) →Neixiyan (EX-LE4)" were 73.17% (641/876) and 90.28% (641/710), respectively, meaning the frequency of Dubi (ST35) and Neixiyan (EX-LE4) in 876 acupuncture prescriptions occurring simultaneously was 73.17%; the frequency of Neixiyan (EX-LE4) occurring in the case of Dubi (ST35) appeared was 90.28%. Lift was different from 1 in all results, indicating that the results predicted by the rules were reliable. The combination of the acupoints Neixiyan (EX-LE4), Dubi (ST35), Yanglingquan (GB34), Xuehai (SP10), Zusanli (ST36), Yinlingquan (SP9), Ashi point, Heding (EX-LE2), Xiyangguan (GB33), Sanyinjiao (SP6), Weizhong (BL40) was used most frequently, as indicated by the support degree and confidence level meeting the minimum requirements. The 53 rules their support, confidence, and lift are shown in Table 5.

Discussion

According to traditional Chinese medicine (TCM), KOA is considered a bi-syndrome resulting from asthenia of liver, kidney as well as qi and blood, and follow-up invasion of pathogenic wind, cold and dampness (Zong et al., 2006). As written in the chapter of "Various Bi-syndromes" in the book "Recipes for Saving Lives", "the occurrence of bi-syndrome was all due to constitutional weakness, stria looseness and the follow-up invasion of pathogenic wind, cold and dampness". So far, there have been no guidelines for the treatment of KOA using TCM therapies.

DM also known as Knowledge Discover in Database (KDD), is a process that uses sophisticated analysis tools to sort through, organize, examine and combine large sets of information to reveal the implicated but useful information from massive, incomplete, noise and fuzzy data (Cui, 2006). DM techniques co uld find the core combinations from large-scale database according to characteristics of the variables with no artificial interference (Liu et al., 2013). These techniques have provided a new research direction and methods to explore the value of scientific literature. TCM data mining research has shown important results, which has practical significance for inheritance and development of TCM—at least to some extent (Jin et al., 2013; Yao et al., 2002). Some studies in particular have shown that DM can be used to extract and analyze the application characteristics and laws of acupoints from different dimensions and different levels (Zhan et al., 2014; Wu et al., 2013). The results are in line with the theory of acupuncture on the laws of acupoint selection, which could serve as a theoretical basis for the use of acupuncture and moxibustion in clinical treatment and scientific research.

In this study, we carried out preliminary studies for the inherent correlation of acupoints. This paper summarizes the findings concerning frequency, division, meridian distribution and acupoints compatibility. Overall, the results indicated that acupoints selection and formulation of the prescriptions of acupuncture and moxibustion in clinical treatment KOA were provided with consistency. At the same time, we gained some new knowledge.

The list of the most frequently used acupoints [Neixiyan (EX-LE4), Dubi (ST35), Yanglingquan (GB34), Xuehai (SP10), Liangqiu (ST34), Zusanli (ST36), Yinlingquan (SP9), and Ashi point] was consistent with general prescriptions (Cheng, 2000). ST35 and EX-LE4 are located in the knee, which can produce the coordinate effect of expelling wind and cold, removing dampness as well as dredging collaterals. The knee joint is the convergent location of all meridians. GB34 is the convergent point of tendons of the eight influential points, which can moisten and nourish tendons. Stomach meridian of foot-yangming is full of qi and blood. ST34, the Xi-Cleft point of it, is the convergent point of qi and blood of the stomach meridian. ST36, the He-Sea point of it, is the deep confluence of meridional qi. Hence, ST36 is selected to invigorate qi to nourish blood, to activate collaterals to dredge meridians, to expel wind to dissipate dampness. SP9 and SP10, the acupoints of the spleen meridian of foot-taiyin, are selected to convergent spleen to remove dampness, to eliminate cold, to stop pain, and to nourish and activate blood. Ashi point is one of the most important methods of acupoints selection theory following the principle of "the tenderness is taken as acupoint",

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Table 1: Sorts of acupoint

	Frequency		Acupoints		Acupoints (Occurrence)
	Occurrence	Percentage[%]	Number	Percentage[%]	
Acupoints of fourteen meridians	3963	74.32%	88	72.13%	Dubi (ST35) (710), Yanglingquan (GB34) (537), Xuehai(SP10) (521), Liangqiu (ST34) (477), Zusanli (ST36) (467)
Extra points	991	18.59%	6	4.92%	Neixiyan (EX-LE4) (713), Heding (EX-LE2) (271), Yaoyan (EX-B7) (1), Yintang (EX-HN3) (1)
Dong′ s extra – point	19	0.36%	10	8.20%	Jinling (3), Jinji (3), Jindou (3), Linggu (1), Dabai (1)
Empirical points	40	0.75%	17	13.93%	Xitongxue (11), Xiniao (4), Xiafengshidian (3), Qipang (2),Xizhongxue (3)
Ashi point	319	5.98%	1		

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Table 2: 30 most frequently used acupoints.

Acupoints	Occurrence	Percentage [%]	Support [%]
Neixiyan (EX-LE4)	713	13.37%	81.39%
Dubi (ST35)	710	13.32%	81.05%
Yanglingquan (GB34)	537	10.07%	61.30%
Xuehai (SP10)	521	9.77%	59.47%
Liangqiu (ST34)	477	8.95%	54.45%
Zusanli (ST36)	467	8.76%	53.31%
Yinlingquan (SP9)	364	6.83%	41.55%
Ashi point	319	5.98%	36.42%
Heding (EX-LE2)	271	5.08%	30.94%
Xiyangguan (GB33)	102	1.91%	11.64%
Weizhong (BL40)	93	1.74%	10.62%
Sanyinjiao (SP6)	92	1.73%	10.50%
Xuanzhong (GB39)	53	0.99%	6.05%
Shenshu (BL23)	49	0.92%	5.59%
Taixi (KI3)	45	0.84%	5.14%
Ququan (LR8)	39	0.73%	4.45%
Guanyuan (CV4)	36	0.68%	4.11%
Chengshan (BL57)	24	0.45%	2.74%
Qihai (CV6)	21	0.39%	2.40%
Kunlun (BL60)	21	0.39%	2.40%
Weiyang (BL39)	18	0.34%	2.05%
Taichong (LR3)	17	0.32%	1.94%
Quchi (LI11)	17	0.32%	1.94%
Xiguan (LR7)	17	0.32%	1.94%
Yingu (KI10)	15	0.28%	1.71%
Futu (ST32)	15	0.28%	1.71%
Dazhu (BL11)	14	0.26%	1.60%
Xitongxue	11	0.21%	1.26%
Ganshu (BL18)	10	0.19%	1.14%
Neiguan (PC6)	10	0.19%	1.14%

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Table 3: Meridians and acupoints used in acupuncture therapy for KOA

Meridians	Frequency	Percentage [%]	Number	Percentage [%]	Acupoints (Selected acupoints and their frequencies)
Stomach Meridian	1700	31.88%	14	11.48%	Dubi (ST35)（710), Liangqiu (ST34) （477), Zusanli (ST36) (467), Futu (ST32) (15), Wailing (ST26) (5)
Spleen Meridian	990	18.57%	9	7.38%	Xuehai (SP10) (521), Yinlingquan (SP9) (364), Sanyinjiao (SP6) (92), Daheng (SP15) (4), Jimen (SP11) (3)
Gallbladder Meridian	703	13.18%	7	5.74%	Yanglingquan (GB34) (537), Xiyangguan (GB33) (102), Xuanzhong (GB39) (53), Huantiao (GB30) (4), Fengshi (GB31) (4)
Bladder Meridian	271	5.08%	26	21.31%	Weizhong (BL40) (93), Shenshu (BL23) (49), Chengshan (BL57) (24), Weiyang (BL39) (18), Kunlun (BL60) (21)
Liver Meridian	77	1.44%	6	4.92%	Taichong (LR3) (17), Ququan (LR8) (39), Xiguan (LR7) (17), Xingjian (LR2) (1), Zhongfeng (LR4) (2)
Conception Meridian	78	1.46%	7	5.74%	Guanyuan (CV4) (36), Zhongwan (CV12) (9), Qihai (CV6) (21), shenque (CV8) (5), shuifen(CV9) (4)
Kidney Meridian	72	1.35%	5	4.10%	Taixi (KI3) (45), Yingu (KI10) (15), Fuliu (KI7) (8), Zhaohai (KI6) (2), Shuiquan (KI5) (2)
Large Intestine Meridian	28	0.53%	4	3.28%	Quchi (LI11) (17), Hegu (LI4) (6), Shousanli (LI10) (3), Zhouliao (LI12) (2)
Governor Meridian	25	0.47%	4	3.28%	Yaoyangguan (GV3) (9), Dazhui (GV14) (4), Mingmen (GV4) (8), Baihui (GV20) (4)
Pericardium Meridian	10	0.19%	1	0.82%	Neiguan (PC6) (10)
Lung Meridian	3	0.06%	2	1.64%	Chize (LU5) (2), Lieque (LU7) (1)
Heart Meridian	3	0.06%	1	0.82%	Shaohai (HT2) (3)
Triple Energizer Meridian	2	0.04%	1	0.82%	Waiguan (TE5) (2)
Small Intestine Meridian	1	0.02%	1	0.82%	Zhizheng (SI7) (1)

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Table 4: The frequencies and numbers of acupoints on different body parts

Division	Frequency	Percentage [%]	Number	Percentage [%]	Acupoints (Selected acupoints and their frequencies)
Upper limbs	20	16.39%	70	1.31%	Quchi (LI11) (17), Neiguan (PC6) (10), Hegu (LI4) (6), Shaohai (HT2) (3), Shousanli (LI10) (3)
Lower limbs	60	49.18%	4706	88.26%	Dubi (ST35) (710), Neixiyan (EX-LE4) (713), Yanglingquan (GB34) (537), Xuehai (SP10) (521), Liangqiu (ST34) (477)
Head, face, and neck	2	1.64%	5	0.09%	Baihui (GV20) (4), Yintang (EX-HN3) (1)
Chest and abdomen	14	11.48%	98	1.84%	Guanyuan (CV4) (36), Qihai (CV6) (21), Zhongwan (CV12) (9), Wailing (ST26) (5), shenque (CV8) (5)
Back and lumbar	25	20.49%	134	2.51%	Shenshu (BL23) (49), Dazhu (BL11) (14), Ganshu (BL18) (10), Yaoyangguan (GV3) (9), Mingmen (GV4) (8)

Table 5: Statistics of the 10 most frequently used acupoint combinations.

Consequent	Antecedent	Support [%]	Confidence [%]	Rule support [%]	Lift
Neixiyan (EX-LE4)	Dubi (ST35)	81.05	90.282	73.174	1.109
Dubi (ST35)	Neixiyan (EX-LE4)	81.393	89.902	73.174	1.109
Neixiyan (EX-LE4)	Yanglingquan (GB34)	61.301	84.171	51.598	1.034
Yanglingquan (GB34)	Neixiyan (EX-LE4)	81.393	63.394	51.598	1.034
Dubi (ST35)	Xuehai (SP10)	59.475	85.221	50.685	1.051
Xuehai (SP10)	Dubi (ST35)	81.05	62.535	50.685	1.051
Dubi (ST35)	Yanglingquan (GB34)	61.301	81.378	49.886	1.004

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Yanglingquan (GB34)	Dubi (ST35)	81.05	61.549	49.886	1.004
Neixiyan (EX-LE4)	Xuehai (SP10)	59.475	83.685	49.772	1.028
Xuehai (SP10)	Neixiyan (EX-LE4)	81.393	61.15	49.772	1.028
Neixiyan (EX-LE4)	Zusanli (ST36)	53.311	84.154	44.863	1.034
Zusanli (ST36)	Neixiyan (EX-LE4)	81.393	55.119	44.863	1.034
Dubi (ST35)	Zusanli (ST36)	53.311	83.084	44.292	1.025
Zusanli (ST36)	Dubi (ST35)	81.05	54.648	44.292	1.025
Yanglingquan (GB34)	Xuehai (SP10)	59.475	74.28	44.178	1.212
Xuehai (SP10)	Yanglingquan (GB34)	61.301	72.067	44.178	1.212
Yanglingquan (GB34)	Zusanli (ST36)	53.311	75.375	40.183	1.23
Zusanli (ST36)	Yanglingquan (GB34)	61.301	65.549	40.183	1.23
Zusanli (ST36)	Xuehai (SP10)	59.475	64.491	38.356	1.21
Xuehai (SP10)	Zusanli (ST36)	53.311	71.949	38.356	1.21
Yanglingquan (GB34)	Yinlingquan (SP9)	41.553	88.187	36.644	1.439
Yinlingquan (SP9)	Yanglingquan (GB34)	61.301	59.777	36.644	1.439
Neixiyan (EX-LE4)	Yinlingquan (SP9)	41.553	83.791	34.817	1.029
Dubi (ST35)	Yinlingquan (SP9)	41.553	82.418	34.247	1.017

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Xuehai (SP10)	Yinlingquan (SP9)	41.553	78.846	32.763	1.326
Yinlingquan (SP9)	Xuehai (SP10)	59.475	55.086	32.763	1.326
Dubi (ST35)	Ashi point	36.416	84.326	30.708	1.04
Neixiyan (EX-LE4)	Ashi point	36.416	83.699	30.479	1.028
Yinlingquan (SP9)	Zusanli (ST36)	53.311	54.39	28.995	1.309
Zusanli (ST36)	Yinlingquan (SP9)	41.553	69.78	28.995	1.309
Neixiyan (EX-LE4)	Heding (EX-LE2)	30.936	89.299	27.626	1.097
Dubi (ST35)	Heding (EX-LE2)	30.936	87.823	27.169	1.084
Yanglingquan (GB34)	Ashi point	36.416	66.144	24.087	1.079
Xuehai (SP10)	Ashi point	36.416	65.831	23.973	1.107
Yanglingquan (GB34)	Heding (EX-LE2)	30.936	70.849	21.918	1.156
Zusanli (ST36)	Ashi point	36.416	54.232	19.749	1.017
Zusanli (ST36)	Heding (EX-LE2)	30.936	63.1	19.521	1.184
Xuehai (SP10)	Heding (EX-LE2)	30.936	62.362	19.292	1.049
Yinlingquan (SP9)	Heding (EX-LE2)	30.936	50.923	15.753	1.225
Neixiyan (EX-LE4)	Xiyangguan (GB33)	11.644	87.255	10.16	1.072
Dubi (ST35)	Xiyangguan (GB33)	11.644	83.333	9.703	1.028
Zusanli (ST36)	Sanyinjiao (SP6)	10.502	88.043	9.247	1.652

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Yanglingquan (GB34)	Sanyinjiao (SP6)	10.502	85.87	9.018	1.401
Yanglingquan (GB34)	Xiyangguan (GB33)	11.644	76.471	8.904	1.247
Dubi (ST35)	Sanyinjiao (SP6)	10.502	82.609	8.676	1.019
Neixiyan (EX-LE4)	Weizhong (BL40)	10.616	81.72	8.676	1.004
Neixiyan (EX-LE4)	Sanyinjiao (SP6)	10.502	81.522	8.562	1.002
Yinlingquan (SP9)	Sanyinjiao (SP6)	10.502	71.739	7.534	1.726
Yanglingquan (GB34)	Weizhong (BL40)	10.616	69.892	7.42	1.14
Xuehai (SP10)	Sanyinjiao (SP6)	10.502	67.391	7.078	1.133
Xuehai (SP10)	Xiyangguan (GB33)	11.644	59.804	6.963	1.006
Zusanli (ST36)	Weizhong (BL40)	10.616	64.516	6.849	1.21
Zusanli (ST36)	Xiyangguan (GB33)	11.644	53.922	6.279	1.011

which is supplementary to selection along meridians and syndrome differentiation. Ashi point can work directly to patients and achieve the purpose of relieving rigidity of muscles and activating collaterals. The above-mentioned acupoints focus on locally affected areas following the principle of selecting points in nearby location that reflects the proximal curative effect of features of acupoints.

Regarding the meridian distribution of acupoints, it was dominated by six foot meridians, and acupoints of yang meridian were the most frequent. The most frequently used meridians were Stomach Meridian and Spleen Meridian. In "Miraculous Pivot-On Channels", it reads, "The Stomach Meridian, the diseases of blood dominated by this channel … swelling and pain of knee joint". Yangming meridian has large amounts of qi and blood. Spleen and Stomach are the acquired foundation and source of qi and blood. Cold and dampness can be removed if the Spleen and the Stomach are healthy. Therefore, points of Spleen and Stomach Meridians can promote the generation of qi and blood and transportation and transformation of dampness. The Stomach Meridian, Spleen Meridian, Bladder Meridian, Gallbladder Meridian and Liver Meridian all converge to the knee joint, showing the distal curative effect of the acupoints on the fourteen meridians. This follows the principle of selecting points at distant location that represents the distal curative effect of the acupoints on the fourteen meridians, and explains the saying that "the indication extends to where the meridian reaches."

Regarding the division of acupoints, acupoints were concentrated mainly in the lower limbs. The lesion site of KOA is mainly concentrated in the knee. Choosing acupoints around of knee denotes the proximal curative effect of each acupoint.

Regarding the compatibility of acupoints, the results of AR pointed out some new messages, which made up for gaps in modern clinical literature reports on acupoint compatibility. The results of this study showed that the most frequent methods of acupoint compatibility were local acupoint combinations, distal-proximal acupoint combinations, anterior-posterior point combinations, superficies-interior points combinations, and combinations of affected meridian. Dubi (ST35) and Neixiyan (EX-LE4) was the most commonly used and the best combination, which is the embodiment of selecting points in combination with adjacent acupoints, as well as Neixiyan (EX-LE4) and Yanglingquan (GB34), Heding (EX-LE2) and Yinglingquan (SP9) and so on. Sanyinjiao (SP6) and Zusanli (ST36), Weizhong (BL40) and Neixiyan (EX-LE4) reflected these methods of distal-proximal acupoint combinations and anterior-posterior point combinations. The Spleen is internally and externally related to the Stomach, this combination of Dubi (ST35) and Xuehai (SP10) respect the combination of acupoints from interiorly–exteriorly related meridian. Dubi (ST35) and Zusanli (ST36) of Stomach Meridian, Yanglingquan (GB34) and Xiyangguan (GB33) of Gallbladder Meridian showing the combination of acupoints from same meridian. In short, the method of compatibility points in acupuncture and moxibustion in the clinical treatment of KOA mainly followed the rule of selecting acupoints in nearby location and acupoint selection along the meridians.

Conclusions

In conclusion, acupoints selection and formulation of the prescriptions of acupuncture and moxibustion in the clinical treatment of KOA were specific and consistent. Reasonable selection of acupoints for the treatment of KOA showed good outcomes. In this study, data mining was applied to identify the most frequently used acupoints, meridians, and the distribution of acupoints, as well as the correlating rules for selecting acupoints in practice for treating KOA. Therefore, acupoint selection in patients with KOA must follow the theory of meridians, and focus on locally affected areas under the premise of syndrome differentiation and treatment to achieve efficacy of invigorating liver and kidney, benefiting qi and nourishing blood, promoting blood circulation for removing obstruction in collaterals, dispelling pathogenic wind and cold, removing dampness, and dredging channel blockade. Our findings indicate that Neixiyan (EX-LE4), Dubi (ST35), Xuehai (SP10), Yanglingquan (GB34), Zusanli (ST36), Yinlingquan (SP9), Ashi point, Heding (EX-LE2), Xiyangguan (GB33), Weizhong (BL40), and Sanyinjiao (SP6) should be investigated further in forthcoming trials or used in acupuncture and moxibustion for the clinical treatment of KOA.

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