

# Analysis of Acupoint Selection and Combinations in Acupuncture Treatment of Migraine: A Protocol for Data Mining

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**Background:** Migraine is a prevalent neurological condition that causes significant disability and has a profound impact on sufferers' ability to work and their overall quality of life. The efficacy of acupuncture in the treatment of migraines has been confirmed via extensive clinical research. However, because each acupoint generates various analgesic processes, and different acupuncture physicians select different acupoints, there is still uncertainty regarding the optimal acupoint selection.

**Objective:** Our purpose is to conduct the initial thorough data mining analysis to determine the optimal acupoint selection and combinations for the treatment of migraines.

**Methods:** We will conduct a search of eight electronic bibliographic databases (PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wanfang Database, Chinese Biomedical Literature Database, and Chongqing VIP Database) from the inception of the databases to July 2024. Clinical trials that evaluate the efficacy of acupuncture therapy in migraine management will be chosen. Literature will be rigorously reviewed in accordance with inclusion and exclusion criteria, and pertinent data will be extracted for analysis. Excel 2021 will be utilized to conduct descriptive statistics. SPSS Modeler 14.1 will be employed to conduct the association rule analysis. SPSS Statistics 26.0 will be employed to conduct exploratory factor analysis, cluster analysis, and decision tree analysis.

**Results:** This study aims to investigate the optimal acupoint selection and combinations for people suffering from migraines.

**Conclusion:** Our research will offer empirical support for the efficacy and possible therapeutic recommendations of acupoint application in treating migraine patients, facilitating collaborative decision-making between physicians and patients.

**Keywords:** acupuncture, migraine, data mining, descriptive statistics, association rule analysis, exploratory factor analysis, cluster analysis, decision tree analysis

## Introduction

Migraine, encompassing migraine without aura, migraine with aura, and chronic migraine, is a widely prevalent neurological illness on a global scale.<sup>1,2</sup> This is a disabling condition marked by repeated episodes that significantly impact the individual's overall well-being.<sup>3</sup> Migraine episodes frequently manifest with symptoms such as nausea, vomiting, and heightened sensitivity to light and sound. These symptoms have a substantial impact on the individual's everyday activities, including their private, social, and professional life, as well as their general quality of life.<sup>4-6</sup> The overall occurrence of migraine in the general population is 12%, with women being three times more likely to have it than males.<sup>7</sup> This illness is more common among those aged 30 to 40 years.<sup>8</sup> According to a study called the American Migraine Prevalence and Prevention Study, the average yearly direct expense per individual for episodic migraines in the United States was \$1757.<sup>9</sup> Migraine has a significant impact on the health and quality of life of patients, often causing severe disability. During migraine episodes, normal activities are limited by up to 78% in those suffering from migraines.<sup>10</sup> Due to its high prevalence and high disease burden globally, migraine becomes an important disease that warrants attention.<sup>1</sup> Currently, the pharmacological preventive treatments for

migraine encompass beta blockers, calcium channel blockers, angiotensin-II receptor antagonists, anti-epileptic drugs, and antidepressants.<sup>11,12</sup> However, the effectiveness of these therapy seems to be moderate, with response rates ranging from around 40% to 50%.<sup>13</sup>

Acupuncture is globally employed for the treatment of headaches, especially migraines.<sup>14</sup> Prior research findings indicate that acupuncture is an efficacious approach for the treatment and prevention of migraines.<sup>15,16</sup> Its mechanism of action may entail the suppression of meningeal vasodilation and inflammatory factors, as well as the decrease in neurogenic inflammation.<sup>15</sup> Nevertheless, the acupoints that have been chosen for the treatment of migraines through acupuncture have not been consistent across a significant number of clinical trials. The selection of acupoints can vary based on the differing perspectives and experiences of medical practitioners. The selection and combinations of acupoints are regarded as the fundamental elements of the acupuncture treatment system.<sup>17</sup> Acupuncturists often combine many acupoints in clinical settings to enhance the interaction between acupoints and improve the effectiveness of acupuncture treatment. The increasing incidence of successful acupuncture treatments for migraines has mainly relied on the utilization of many acupoint prescriptions. The effectiveness of these prescriptions is inextricably connected to the compatibility of meridians and acupoints, resulting in a complex, conflicting, and unclear relationship. Hence, it is imperative to utilize the available data to scrutinize the principles of acupoint selection and combinations, with the aim of enhancing the therapeutic efficacy of acupuncture. Data mining technology facilitates the discovery of valuable information and expertise within a vast collection of documents.<sup>18</sup> Based on this method, the author and his team have investigated acupoint selection and combinations in acupuncture treatment of various pain-related diseases, including but not limited to carpal tunnel syndrome,<sup>19</sup> piriformis syndrome,<sup>20</sup> benign prostatic hyperplasia,<sup>21</sup> neurogenic bladder,<sup>22</sup> and metabolism-associated fatty liver disease.<sup>23</sup> This study may offer data supporting the notion that there is a distinct relationship between the acupoints of various meridians and the effectiveness of acupuncture is contingent upon the specificity of these acupoints. Hence, it is crucial to ascertain the attributes and principles governing the selection and combinations of acupoints for treating migraines, in order to guide future research and clinical application. The objective of this study is to analyze the correlation patterns of acupoints using data mining techniques and provide a standardized treatment guide for the application of acupoints in treating migraines.

## Methods and Analysis

### Search Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement will be followed.<sup>24</sup> We will conduct a comprehensive search in Chinese and English electronic libraries, covering the period from their establishment to July 2024. The databases to be searched include PubMed, Embase, Cochrane Library, Web of Science (WOS), China National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Biomedical Literature Database (CBM), and Chongqing VIP Database (VIP). The language options will be restricted to Chinese and English. The search phrases utilized in our review will consist of a combination of medical subject heading terms and free-text terms. Table 1 illustrates PubMed as an example of search strategies. This search technique will be modified to accommodate the specific limitations of each database, taking into account their unique qualities.

### Review Process

#### Data Screening

The inclusion criteria included the following: (1) studies that focused on acupuncture therapy as the main intervention, with or without the use of randomized and/or controlled procedures. (2) The minimum requirement for each group/trial is that there must be more than ten patients. (3) The patient received a diagnosis of migraine based on the established diagnostic criteria used in the clinical studies conducted at that particular period. (4) Meridian points, extra nerve points, or ashi points must be utilized for the purpose of needle insertion and/or moxibustion. It was employed either independently or in combination with other treatments such as acupuncture and/or moxibustion (for example, Chinese herbs). (5) The analysis will encompass studies that compare different acupuncture techniques for treating migraines.

**Table I** Search Strategy for PubMed Database

No.	Search Terms
#1	MeSH terms: "paroxysmal hemicrania"
#2	Title/Abstract: "migraine disorders" OR "migraine" OR "cephalagra" OR "hemicrania" OR "Migraine Disorders"
#3	#1 OR #2
#4	MeSH terms: "acupuncture therapy" OR "acupuncture" OR "cupping therapy" OR "bloodletting" OR "electroacupuncture"
#5	Title/Abstract: "needling" OR "needles" OR "needle" OR "pricking blood" OR "blood-letting" OR "bloodletting" OR "cupping" OR "fire acupuncture" OR "warm needling" OR "electro-acupuncture" OR "electroacupuncture" OR "body acupuncture" OR "manual acupuncture" OR "acupuncture"
#6	#4 OR #5
#7	#3 AND #6

The studies that will be excluded based on exclusion criteria include the following: (1) reviews, protocols, animal experiments, case reports, systematic reviews, meta-analyses, and other non-clinical experimental articles. (2) Articles that have not received a thorough and comprehensive evaluation by experts in the field, such as theses, conference papers, and other similar works. (3) Trials using microacupuncture systems, ear needle, head needle, wrist and ankle needle, and other non-body needle techniques will be eliminated due to their lack of relevance to conventional acupoints. (4) Trials that exclusively presented physiological or laboratory data will be omitted. (5) Studies will be eliminated from controlled trials if acupuncture therapy, either alone or in combination, provided fewer benefits for patients compared to the control group. (6) The acupoint prescription in the study will be excluded if it is incomplete or nonexistent.

### Data Collection

Yujun He and Yachao Wu will independently assess all the titles and abstracts obtained from the literature search and exclude those that are clearly unrelated, such as studies that concentrate on reviews, animal trials, case reports, and similar topics. The complete texts of the remaining references will be gathered and subjected to another round of scrutiny to eliminate irrelevant publications. They will then assess the eligibility of all remaining papers based on the previously established inclusion criteria. A consistency evaluation will be conducted, and discussions will be employed as a means to resolve conflicts according to a third author (Xiaojun Li).

### Establishing a Database and Processing Data Normalization

The document manager Endnote×9.2 will be used to import the literature obtained from the search. Beforehand, we employ Endnote to eliminate duplicates initially, followed by a manual inspection to further eliminate duplicates. The results are then validated to ensure the accuracy of the included material. Figure 1 will depict the research screening procedure using a flow diagram.

The data that has been extracted will be entered into Excel 2021 in order to create a database for prescribing acupuncture treatments for migraines. The "a group of primary acupoints and a group of secondary acupoints constitute an acupoint prescription" technique will be used to derive valid prescriptions.<sup>25</sup> In addition, when different prescriptions are used for different treatment stages, the prescriptions should be extracted separately, and when different prescriptions are used at the same stage, the acupoints used should be combined and the duplicates removed. In relation to the latest national standards,<sup>26,27</sup> we will standardize the names of the acupoints included in the literature and establish a consistent naming convention for the acupoints mentioned in the literature. Additionally, we will supplement information regarding the corresponding meridians, sites, and specific acupoint attributes associated with each acupoint.

### Managing Missing Data

To evaluate the data using an intention-to-treat approach, we will contact the original authors to obtain any necessary missing information. We will assess solely the data that is presently accessible if comprehensive information is not obtainable in this manner.

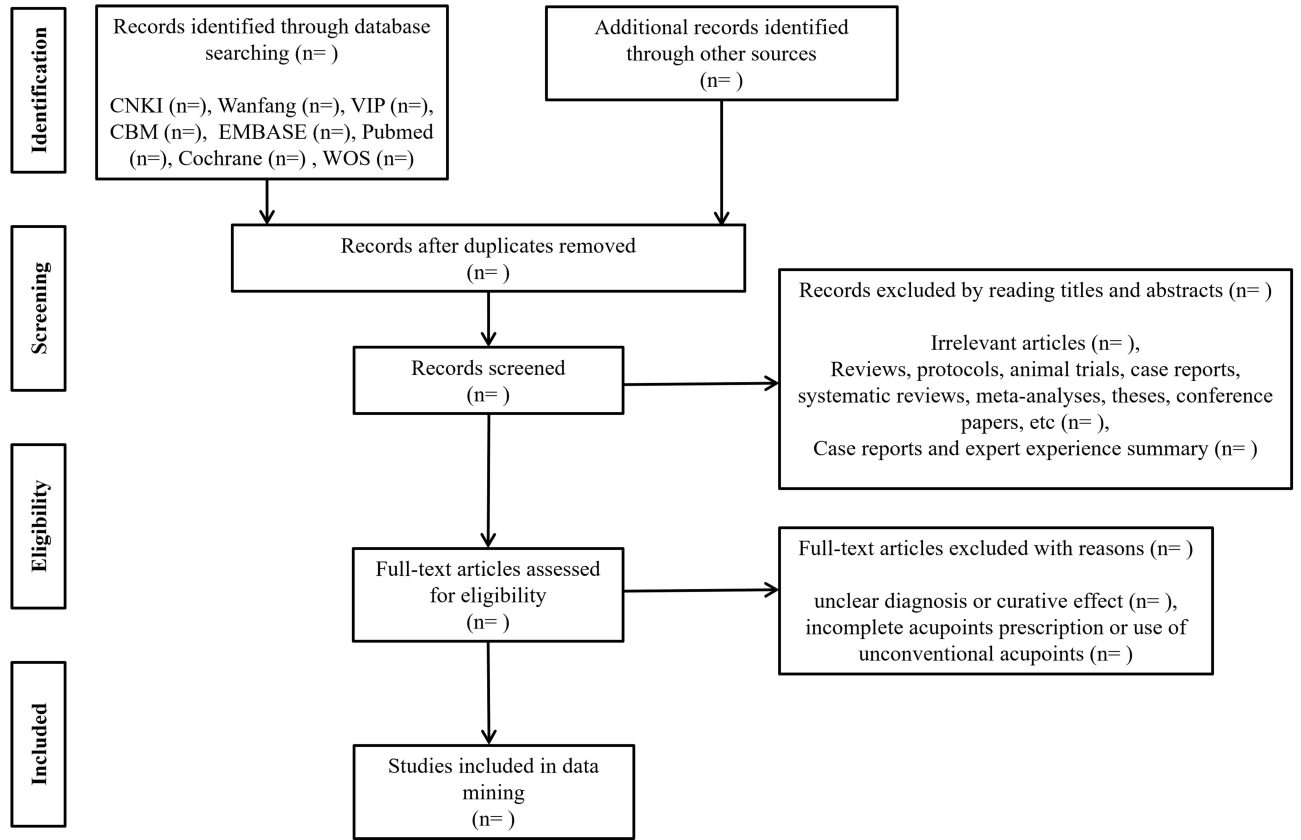


Figure 1 Flow diagram of the study selection process.

## Data Analysis

### Literature Quality Evaluation

Two reviewers (Yujun He and Yachao Wu) will independently use the STRICTA scale to evaluate reports on specialized acupuncture interventions.<sup>28</sup> Then, a consistency evaluation will be conducted. Disagreements will be resolved through discussion or negotiation with a third researcher (Xiaojun Li).

### Descriptive Statistics

Refer to the method of previous study,<sup>19–23</sup> the acupoint prescriptions from the literature will be imported into an Excel 2021 table. This table will be used to generate a PivotTable, which will enable us to conduct descriptive statistical analysis on various aspects such as the frequency of acupoint usage, the meridians to which they belong, the sites of the points, and the specific acupoint attributes of each acupoint. (Table 2–5).

### High-Frequency Acupoints Analysis

According to Price’s law, we determine the high-frequency acupoints with  $M = 0.749 (P_{max})^{1/2}$ , where  $P_{max}$  represents the highest frequency of the acupoint.<sup>29</sup> If the number of high-frequency acupoints analysed by this method exceeds

**Table 2** Frequency of Acupoint Application for Migraine Treatment

No.	Acupoint	Frequency (%)

**Table 3** Frequency of Meridian Application for Migraine Treatment

Meridian	Frequency (%)	Amount (%)	Acupoints

**Table 4** Frequency of Site of Points Application for Migraine Treatment

Site of points	Frequency (%)	Amount (%)	Acupoints

**Table 5** Frequency of Specific Acupoints for Migraine Treatment

Specific acupoint	Frequency (%)	Amount (%)	Acupoints

a threshold of 50 ( $n \geq 50$ ), an alternative method will be employed. Determine the mean frequency of acupoints ( $X$ ), where  $X$  is equal to the total frequency divided by the total number of acupoints. Acupoints with a frequency greater than or equal to  $X$  are classified as high-frequency acupoints.<sup>30</sup> GraphPad 8.0 will be used to depict high-frequency acupoints using bar charts.

### Association Rule Analysis

Referred to the method of previous study,<sup>19–23</sup> the analysis of the association rules between high-frequency acupoints will be conducted using SPSS Modeler 14.1 software, employing the Apriori algorithm. The probability of both the anterior and posterior items occurring will be denoted by the degree of support, while the degree of confidence will represent the probability of the subsequent item occurring given that the anterior item has already appeared. After conducting many tests, the optimal and minimum level of support and the minimum level of confidence will be established, with the highest value for the former being set at 2 (Table 6). Next, an intricate network diagram will be created to examine the association between the acupoints.

### Exploratory Factor Analysis

Referred to the method of previous study,<sup>19,21,22</sup> the high-frequency acupoints will undergo exploratory factor analysis using SPSS Statistics 26.0. Additionally, the prescription data will be subjected to Kaiser–Meyer–Olkin ( $KMO$ ) and Bartlett sphericity tests. Factor analysis will be conducted if the  $KMO$  measure is greater than 0.5 and the  $p$ -value ( $P$ ) is

**Table 6** Association Rules of Acupoints for Migraine Treatment

No.	Latter item	Former item	Frequency	Support (%)	Confidence (%)	Lift

less than 0.05. The major factor components will be extracted using maximum variance rotation. Factor analysis is not appropriate if the *KMO* measure is less than 0.5 or if the *p*-value is greater than 0.05.

### Cluster Analysis

Referred to the method of previous study,<sup>19–23</sup> the high-frequency acupoints will undergo cluster analysis using SPSS Statistics 26.0. Using between-groups link method for clustering analysis. The interval of measure will be set as Pearson correlation. Minimum number of clusters will be set as 5 and maximum number of clusters will be set as 10. The resulting cluster analysis tree created by SPSS will be utilized to investigate the clustering relationship among the acupoints.

### Decision Tree Analysis

Referred to the method of previous study,<sup>29</sup> a decision tree model analysis will be performed on acupoints using the CHAID algorithm in SPSS Statistics 26.0 software. The objective is to identify the most efficient treatment strategy for migraine by minimizing the number of acupoints required. The CHAID growth approach is suitable for binary variables, namely acupoint data types that can only be categorized as either “1” or “0”, representing with or without use, respectively. Set the sample size folds for cross validation to 10, then set the parent node to 100 and the child node to 50. Finally, the decision tree model is generated.

## Discussion

Migraine is a common type of chronic pain that affects a billion people worldwide, causing disability for hours or even days.<sup>31</sup> Over the years, there have been improvements in migraine treatments, including non-pharmacologic therapies. These therapies can be used alone, in combination with medication, or in conjunction with other non-pharmacologic treatments, providing more options for individuals who cannot tolerate or respond to medication, or who prefer to avoid it.<sup>32</sup> Despite the recent development of calcitonin gene-related peptide-targeted therapies, many migraine sufferers still do not experience satisfactory relief from their headaches with currently available treatments. Therefore, there is a need for effective and well-tolerated treatments specifically designed for migraines. It is crucial to explore treatments that are more efficient and safer and have strong evidence supporting their role in regulating migraine pathways.<sup>33</sup>

Acupuncture has been proven effective in clinical trials for treating migraines.<sup>34–36</sup> It has been included in multiple guidelines for migraine treatment.<sup>37,38</sup> The field of acupuncture for migraines has advanced since 2008.<sup>39</sup> Acupuncture has consistently shown significant benefits for migraines, including reducing headache severity, duration, frequency, and the need for acute medication. Randomized controlled trials have also provided evidence for both the long-term and immediate effects of acupuncture.<sup>32</sup> According to traditional Chinese medical philosophy, acupoints located near a specific area of concern are believed to address that particular uncomfortable symptom. Scalp acupoints are commonly used in clinical practice to treat migraines.<sup>40</sup> Scalp acupoints are believed to directly activate and modify the corresponding areas of the brain's cortex and their blood flow.<sup>41</sup> They may also affect the trigeminal nerve, which is involved in migraines.<sup>42</sup> However, not only scalp acupoints but also acupoints located elsewhere on the body, can have an effect on migraines, possibly through different mechanisms.<sup>34</sup> For example, acupuncture near ST36 can increase the concentration of extracellular adenosine, a substance that has neuroprotective, anti-inflammatory, and pain-relieving properties.<sup>43</sup> A meta-analysis was conducted on the analgesic effect and potential mechanisms of acupuncture for migraine rats, and the results showed that the mechanism of acupuncture on migraine is related to prohibited serum inflammatory factors, downregulation of 5-HT expression, etc. This study also found a underlying correlation between acupoint selection and the mechanism of action.<sup>44</sup> Therefore, different acupoints can alleviate migraines through different pathways. It is crucial to use scientific methods to determine the most effective choice and combinations of acupoints.

To examine the underlying rules, the data mining technique will be utilized, since it is a promising and pragmatic method. Data mining technology uses algorithms to establish correlations between individual data points, quantifies the frequency of each item in the database, and identifies associations with other entities. This technology effectively determines the most significant relationships between various elements.<sup>45</sup> Through the implementation of descriptive statistical analysis, we may discern the acupoints, meridians, sites of acupoint, and specific acupoints that are frequently

utilized in the treatment of migraines. Association rule mining is a data mining technique that uses rule-based machine learning to discover relationships within a dataset and formulate conditional implication rules.<sup>46–48</sup> The Apriori algorithm is a specific type of association rule mining algorithm that identifies frequent individual item sets in a database.<sup>49</sup> Exploratory factor analysis is a statistical method within factor analysis that is used to uncover the underlying structure of sets of variables and explain the correlation between observed variables.<sup>50</sup> The goal of exploratory factor analysis is to determine the potential structure of a scale and reduce the number of items. It discerns and categorizes the variables that offer repetitive information regarding the fluctuation in the data; these sets of variables are referred to as factors.<sup>51</sup> Clustering analysis is a pattern recognition technique that involves the aggregation of similar objects from diversified data.<sup>52</sup> It can assist the user in separating the structure of data and simplifying the complexity of data from mass information.<sup>53</sup> The decision tree analysis method aids users in discerning data structure and simplifying the complexity of information from a large amount of data. It is particularly useful for making informed decisions based on knowledge. The model is based on the recursive classification of the tree structure. The algorithm utilizes index factors to represent the data and uses a tree structure to categorize the spatial qualities for decision-making purposes. The root node is determined by the criteria of index factor categorization. Each subnode represents a classification challenge involving index factors. The classification is based on the degree of index factors and is divided into two or more blocks. Each block can be classed iteratively till the creation of leaf nodes. A leaf node is a classification at the lowest level when there are several indication properties. Every route from the main node to the end node signifies a classification rule.<sup>54,55</sup> Due to the characteristics of different data mining methods, each has its own advantages and disadvantages. We will use the results analyzed by these different data mining methods to provide multidimensional references. The proposed methodology will identify the most effective acupoint selection and combinations for migraine, thereby providing evidence-based medicine for clinical evidence.

## Conclusion

The results of our research will offer proof on the efficacy and possible treatment recommendations of acupoint application for those suffering from migraine. This will assist healthcare professionals and patients in making a more knowledgeable decision collaboratively.

## Abbreviations

CNKI, Knowledge Infrastructure; CBM, Chinese Biomedical Literature Database; VIP, Chongqing VIP Database; WOS, Web of Science.

## Patient and Public Involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

## Ethical Statement

Since the study was based on published clinical studies, no ethical approval was required.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors have no conflicts of interest to declare.

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