



## Evidence and acupoint combinations in acupuncture for functional dyspepsia: an overview of systematic review and data mining study

ZOU Menglong<sup>a, b</sup>, HU Zhuoyu<sup>b</sup>, LONG Dan<sup>a, b</sup>, SUN Haoxian<sup>a, b</sup>, ZHU Ying<sup>a\*</sup>

*a. Department of Gastroenterology, The First Hospital of Hunan University of Chinese Medicine, Changsha, Hunan 410007, China*

*b. Graduate School, Hunan University of Chinese Medicine, Changsha, Hunan 410208, China*

### ARTICLE INFO

#### Article history

Received 19 June 2023

Accepted 03 September 2023

Available online 25 December 2023

#### Keywords

Functional dyspepsia (FD)

Acupuncture

Data mining

Combined acupoints

Veritas plots

Meta-analysis

Systematic review

### ABSTRACT

**Objective** To evaluate the methodological quality of papers that performed meta-analyzed and systematically reviewed acupoint selections for the treatment of functional dyspepsia (FD) and to identify the ideal acupoint combinations for FD.

**Methods** Chinese databases including China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (VIP), China Biology Medicine (CBM), and Wanfang Database, as well as English databases including PubMed, Embase, and Cochrane Library were searched to retrieve papers about meta-analysis and systematic literature reviews on acupuncture for FD. The time span for the paper retrieval was set from the foundation of the databases to April 30, 2022. The Veritas scores of the papers based on their publication year, study type, Assessment of Multiple Systematic Reviews 2 (AMSTAR2), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), heterogeneity, and publication bias were rated to assess the methodological quality of the included studies. Then, randomized controlled trials (RCTs) were extracted from those meta-analysis papers or systematic literature reviews for analyzing acupoints frequency, meridian frequency, and association rules with the use of R software (V 4.3.1).

**Results** Eight meta-analysis papers were included in the study after screening. The mean Veritas scores of the papers based on publication year, type of study, AMSTAR2, PRISMA, heterogeneity, and publication bias were 4.50, 8.00, 4.63, 4.63, 4.50, and 6.13, respectively. The analysis of the scores revealed insufficiencies in the reviews pertaining to the methodology, comprehension of the research strategy, detailed list of excluded studies, sources of funding, assessment of potential bias risks impact on meta-analysis results in each study, explanation of heterogeneity, and identification of potential conflicts of interest. Furthermore, a total of 85 RCTs were obtained from the eight meta-analysis papers involving 85 acupuncture prescriptions and 67 acupoints for subsequent data mining. The most commonly used meridian was Stomach meridian of Foot-Yangming (ST). Zusanli (ST36), Neiguan (PC6), Zhongwan (CV12), Taichong (LR3), Tianshu (ST25), Gongsun (SP4), Weishu (BL21), Pishu (BL20), Neiting (ST44), and Yinlingquan (SP9) topped the list of frequently selected acupoints. Additionally, a total of 28 association rules were identified, including 10 second-order, 15 third-order, and 3 fourth-order association rules. The top-ranking association rules in each order were “Neiguan (PC6) → Zusanli (ST36)” “Zhongwan (CV12) + Neiguan (PC6) → Zusanli (ST36)” and “Zhongwan (CV12) + Taichong (LR3) + Neiguan (PC6) → Zusanli (ST36)”, respectively.

**Conclusion** Acupuncture could alleviate the clinical symptoms of FD. However, the quality

\*Corresponding author: ZHU Ying, E-mail: [zhuying089@126.com](mailto:zhuying089@126.com).

Peer review under the responsibility of Hunan University of Chinese Medicine.

DOI: [10.1016/j.dcmcd.2024.01.001](https://doi.org/10.1016/j.dcmcd.2024.01.001)

**Citation:** ZOU ML, HU ZY, LONG D, et al. Evidence and acupoint combinations in acupuncture for functional dyspepsia: an overview of systematic review and data mining study. *Digital Chinese Medicine*, 2023, 6(4): 369-380.

of methodology applied in the meta-analysis papers on the subject needs to be improved. Through data mining, a combination of Neiguan (PC6), Zusanli (ST36), Zhongwan (CV12), and Taichong (LR3) was identified as an essential acupoint combination for the treatment of FD.

## 1 Introduction

Around one fifth of the mass population suffers from dyspepsia, which is characterized by burning in the epigastrium, pain, early satiety, postprandial fullness, and bloating [1]. Most dyspeptic patients do not present symptoms such as peptic ulceration [2]. Such patients are defined as patients with functional dyspepsia (FD) [3]. Acupuncture, a simple, convenient, practical, and inexpensive therapeutic modality, has become popular for its complementary role to alleviate certain disease symptoms [4] and to improve FD with limited side effects [5]. Prior studies have found that acupuncture could regulate the abnormal functional connectivity between several areas in the brain and the insula [6], alter the level of ghrelin [7], and improve intestine mucosal barrier [8] in FD rats. Globally, acupuncture is gaining more acceptance for preventing or treating diseases, especially functional diseases [9]. Consequently, multiple papers on meta-analyses related to acupuncture for FD have been published in various journals [10, 11]. But these studies are subject to certain biases, leading to the appearance of an increasing number of non-randomized clinical trials [12]. Regardless, to assess the quality of methodologies adopted in the meta-analysis studies so as to determine whether they are fit to apply the study results to clinical practice, remains a challenge for acupuncturists. Therefore, evaluating the quality of methodologies and reviewing acupuncture strategies for FD have become urgent tasks.

The Veritas plot, an evolving result of the radar plot, is a tool that could display multiple attributes at one time. It was initially used to evaluate the best meta-analysis studies on heart surgery [13]. It is now widely used as a mean to identify and interpret the variability in meta-analysis studies, which enables acupuncturists to have the best evidence for treatment recommendations. However, the use of the Veritas plot in research on acupuncture for FD has not been carried out yet. The association rule mining (ARM) methods have been widely used in traditional Chinese medicine (TCM) study, which assists TCM practitioners in selecting appropriate acupoint or herb combinations for treating specific diseases. But they have not been applied to explore the potential of acupoint combinations for FD treatment yet. Previous studies have provided references on acupoint combinations for the treatment of diabetic gastroparesis [14] and simple obesity [15]

by using these methods, especially the Apriori algorithm-based ARM, which is useful and promising for exploring the optimal acupoint or herb combinations to treat diseases. With metrics such as Confidence, Support, and Lift values in the algorithm, it is able to reveal the frequency of sets of items and determine the significance of association rules.

In light of the uncertainty regarding the quality of meta-analysis studies and the effectiveness of acupuncture for FD treatment, the Veritas plot was adopted to assess the methodological quality, and R software (V 4.3.1) was used to determine the acupoint combinations for FD.

## 2 Data and methods

### 2.1 Evidence analysis

**2.1.1 Literature search** A systematic search in Chinese databases including China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (VIP), China Biology Medicine (CBM), and Wanfang Database, and English databases including PubMed, Embase, and Cochrane Library was conducted to retrieve papers about meta-analysis and systematic reviews on acupuncture for FD treatment. The time span for the paper retrieval was set from the foundations of the databases to April 30, 2022. The terms such as “acupuncture” OR “electroacupuncture” OR “needle warming therapy” AND “functional dyspepsia” OR “dyspepsia” AND “meta-analysis” OR “systematic review” were searched in databases, without restrictions on subheadings.

**2.1.2 Inclusion criteria** Studies were included if: (i) they were about meta-analysis and systematic reviews; (ii) they were subject to FD patients who had undergone standardized diagnostic criteria (e.g., Rome criteria); (iii) they included two study groups, with the treatment group using either simple acupuncture, electroacupuncture, warm acupuncture, or a mix, and drugs, and the control group adopting gastrointestinal prokinetic medication or placebo; (iv) there were no limitations on the age, gender, or ethnicity of the patients, but were published only in Chinese or English.

**2.1.3 Exclusion criteria** Studies were excluded if: (i) they were published in more than one place; (ii) their data were incomplete or unobtainable; (iii) they only presented a program or an abstract.

**2.1.4 Data selection and extraction** The literature from the databases was imported into EndNote X9 (<https://endnote.com>) to remove duplicate studies. Each eligible study was reviewed independently by two researchers for information, including name of the first author, data sources, year of publication, time frame in which the study was conducted, detailed research protocols, number of patients, methods for reporting publication bias, and outcomes. The obtained data were checked by a third researcher.

**2.1.5 The Veritas scores** The Veritas scores of the studies were calculated based on their publication year, study type, Assessment of Multiple Systematic Reviews 2 (AMSTAR2), Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), heterogeneity, and publication bias to determine the quality of the included meta-analysis studies or systematic literature reviews. The heterogeneity of a study was impacted by its publication year only because the acupuncture techniques and disease information have been updated over time. It is essential to note that the AMSTAR2 scores are associated with the quality of the methodologies applied in the studies, while the PRISMA scores are associated with the quality of the journals in which the studies are reported. The heterogeneity in study design has a significant impact on the results of the meta-analysis studies, and is often a factor contributing to the acupuncturists' decisions. Another issue of meta-analysis studies is publication bias, since some of the papers are not published in indexed journals and some whose negative results are unknown to the public.

**2.1.6 The Veritas score ranking** Six factors were taken into consideration while ranking the meta-analysis studies, which were the year of publication, study type, publication bias, heterogeneity, AMSTAR2 score, and PRISMA score [16]. If two studies were published in the same year, then the month in which they were published was taken into consideration for the score ranking. Studies that met all of the criteria of the AMSTAR2 scored 1 point; those that met some but not all of the criteria gained 0.5 points; and those that did not meet any of the criteria got 0 points. In PRISMA, studies would get 2 points if they met all of the criteria, 1 point if they partially met the criteria, and 0 points if they met none. If no heterogeneity derived from  $0\% \leq I^2 \leq 50\%$ , the score would be 3 points; if there was a slight heterogeneity derived from  $50\% < I^2 \leq 75\%$ , 2 points would be obtained; if significant heterogeneity derived from  $I^2 > 75\%$ , the score would be 1 point. The score for each category was determined by the following guidelines: the best study got the highest score ( $n$ ), where  $n$  represents the number of studies. The second best study would be awarded with  $n - 1$  points, and so on. In the case of equal performance presented by two studies,

the second best study would receive  $n - 2$  points. A statistical analysis was carried out based on the Veritas scores obtained.

## 2.2 Data mining of acupoint combinations

**2.2.1 Data sources** Data in this study were primarily retrieved from the included systematic review or meta-analysis on acupuncture for FD treatment.

**2.2.2 Inclusion criteria** Studies were eligible if: (i) they were randomized controlled trials (RCTs); (ii) they had a complete acupuncture prescription; (iii) the treatment group reported clear efficacy supported by standardized clinical measures.

**2.2.3 Exclusion criteria** Studies were ineligible if: (i) their acupoint prescriptions were unclear; (ii) their evaluation criteria were not standardized; (iii) they were published in more than one journal.

**2.2.4 Data extraction** Similarly, each eligible study was reviewed independently by two researchers for information including title of the article, name of the first author, diagnostic criteria, therapeutic measures, acupoints, and outcome measures. The acupoints were named collectively following the World Health Organization (WHO) rules for acupuncture points naming [17]. In the end, a dataset of acupoints for FD treatment was constructed using Microsoft Excel 2021.

**2.2.5 Data mining analysis** Association rule learning algorithms are the most common method for identifying trends or relationships in transactional data, so is the case in the medical field, for investigating hidden relations [18,19]. Generally, ARM is divided into two parts based on the Apriori algorithm: an antecedent and a consequent, both of which are lists of items. What is emphasized here is co-occurrence instead of causality. Apriori algorithm-based ARM was performed using R software (V 4.1.3) in this study. By using the R package "arules", the procedure was fitted, while the association rules for visualization were also fitted using the R package "arulesViz" function.

Three kernel values called Confidence, Support, and Lift in the Apriori algorithm were applied to calculate associations across items. The frequency of a particular acupoint in all the acupuncture prescriptions was represented by Support. Confidence refers to the likelihood of acupoint A occurring in a prescription, given that acupoint B has occurred. Lift quantifies the ratio of joint antecedent and consequent probabilities and the product of each marginal probability.

The frequency of meridians and acupoints through mining data from the retrieved papers was identified. Then the ARM was conducted to determine the Support value of the acupoints and the core acupoints association network for FD treatment. The study of LU et al. [15] was

referred to for setting the Support and Confidence values. The degree for Support was set to 0.2, indicating that acupoints A and B appear together with a frequency of 20%. The Confidence value was set at 0.8.

### 3 Results

#### 3.1 Study screening

A total of 153 papers were retrieved from the databases initially, with 124 remaining after removing duplicates. Then, 112 of the 124 papers were excluded judging by their titles and abstracts. Finally, eight meta-analysis studies were included after reviewing their full texts. In addition, as many as 85 RCTs were extracted from the eight meta-analysis studies to further explore the association rules of acupoints (Figure 1). The Veritas score was used to rank the quality of the methodologies that were applied in the eight meta-analysis studies. The baseline characteristics of the eight meta-analysis studies were summarized as well (Table 1). The studies were published between 2015 and 2021. The original data were gathered from 19 databases, including PubMed, Embase, Cochrane Library, Korea Citation Index (KCI), Oriental Medicine Advanced Searching Integrated System (OASIS), Korean studies Information Service System (KISS), Revised International Staging System (RISS), Korean Medical Database (KMedbase), CNKI, Wanfang, Allied and Complementary Medicine Database (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Korean database, Cochrane Central

Register of Controlled Trials (CENTRAL), Medline, CBM, VIP, Web of Science, and SinoMed. In total, 132 clinical trials involving 12 491 patients were included in the eight meta-analysis studies. The time spans for the papers were specified only in seven meta-analysis studies [20-27]. Detailed research strategies were presented in all the meta-analysis studies. Two researchers here reviewed the papers independently to collect useful information. The Cochrane Collaboration's risk of bias tool was used in five meta-analysis studies [22, 24-27], while the Jadad scale was used in the other three [20, 21, 23]. There was no publication bias reported in three meta-analysis studies [22, 23, 25].

#### 3.2 The Veritas score

The Veritas scores of the eight meta-analysis studies based on the six factors were summarized in Table 2. Also, detailed scores of heterogeneity, AMSTAR2 scores, and PRISMA scores of the included studies were exhibited (Supplementary Table S1 – S3). The average Veritas scores of the eight meta-analysis studies based on their publication year, study type, AMSTAR2 score, PRISMA score, heterogeneity, and publication bias were 4.50, 8.00, 4.63, 4.63, 4.50, and 6.13, respectively. There were four meta-analysis studies whose Veritas score based on the publication year, no study on the study type, four studies on the AMSTAR2, four studies on the PRISMA, four studies on the heterogeneity, and five studies on the publication bias exceeded the mean value. A study conducted by KWON et al. [26] had the highest Veritas score of 7.00, while a study by KIM et al. [25] had the lowest of 3.50.

#### 3.3 Frequency statistics of acupoints

The eight meta-analysis papers were reviewed to extract acupuncture prescriptions for FD treatment. A total of 85 acupuncture prescriptions involving 67 acupoints were included. Figure 2 shows the top 20 acupoints for FD treatment. More than half of the acupuncture prescriptions applied acupoints including Zusanli (ST36), Neiguan (PC6), and Zhongwan (CV12). There were six acupoints with frequency  $\geq 20$ , which were Zusanli (ST36, 75), Neiguan (PC6, 63), Zhongwan (CV12, 56), Taichong (LR3, 39), Tianshu (ST25, 24), and Gongsun (SP4, 22).

#### 3.4 Frequency statistics of meridians

Table 3 lists the meridians and acupoints used in acupuncture for FD treatment. In acupuncture for FD, 14 meridians and one extra meridian were worked on. Six meridians were applied more than 50 times, including Stomach meridian of Foot-Yangming (ST), conception vessel (CV), Pericardium meridian of Hand-Jueyin (PC), Bladder meridian of Foot-Taiyang (BL), Liver meridian of Foot-Jueyin (LR), and Spleen meridian of Foot-Taiyin

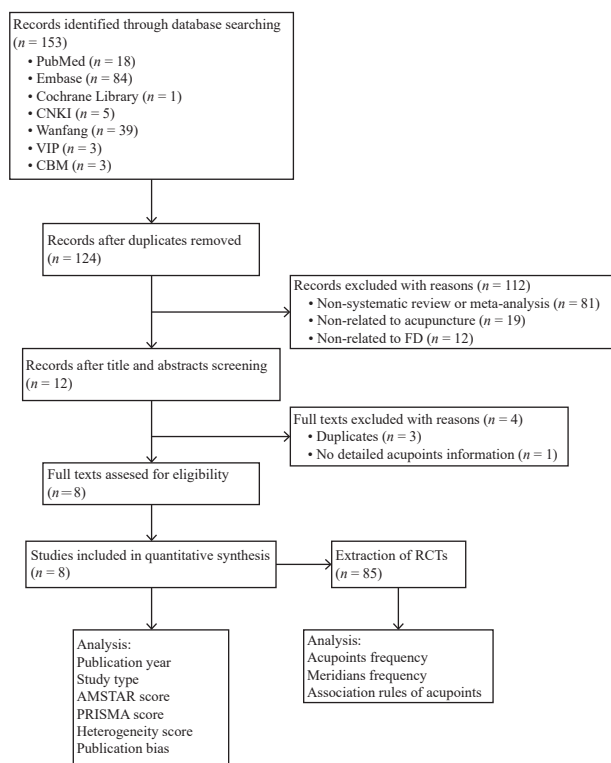


Figure 1 Flow chart of the research process

**Table 1** Baseline characteristics of the eight meta-analysis studies

Study	Data source	Time	Detailed research strategy	Search process	Number of articles	Number of patients	Bias assessment tool	Outcome	Reported publication bias
KWON CY, 2021 [26]	Medline, Embase, CENTRAL, AMED, CINAHL, OASIS, KISS, RISS, KMBase, KCI, CNKI, and Wanfang	Before December 2020	Yes	Reviewed independently by two researchers	22	2 240	Cochrane Collaboration's risk of bias tool	Symptom score, NDI score, TER, short-form health survey, biomarkers related to FD, and safety data	Funnel plot
MAO X, 2020 [27]	Embase, the Cochrane library, and PubMed	Before February 2020	Yes	Reviewed independently by two researchers	7	853	Cochrane Collaboration's risk of bias tool	Symptom score, TER, electrogastrogram, gastric empty, and motilin level	Funnel plot
JIN X, 2018 [21]	CNKI, CBM, Wanfang, VIP, and PubMed	Not mentioned	Yes	Reviewed independently by two researchers	20	1 310	Jadad Scale	Symptom score, NDI score, and adverse effect	Funnel plot
PENG JR, 2018 [22]	CBM, CNKI, VIP, Medline, PubMed, and Embase	Before October 2016	Yes	Reviewed independently by two researchers	7	1 044	Cochrane Collaboration's risk of bias tool	TER, symptom score, and adverse effect	None
PANG B, 2016 [23]	CENTRAL, PubMed, Embase, CBM, CNKI, VIP, and Wanfang	Before December 2015	Yes	Reviewed independently by two researchers	16	1 436	Jadad Scale	Symptom score, NDI score, SF-36, ineffective rate, and adverse effect	None
ZHOU W, 2016 [24]	PubMed, Medline, Web of Science, SinoMed, CNKI, VIP, and Google Scholar	Before April 2014	Yes	Reviewed independently by two researchers	24	3 097	Cochrane Collaboration's risk of bias tool	Symptoms, FD-related quality of life, and plasma motilin	Funnel plot
KIM KN, 2015 [25]	PubMed, Cochrane Library, AMED, CINAHL, and the Korean database	Before November 2012	Yes	Reviewed independently by two researchers	20	1 423	Cochrane Collaboration's risk of bias tool	VAS, NDI, TER, and adverse effect	None
WU X, 2015 [20]	CNKI, CBM, PubMed, Embase, and Cochrane Library	Not mentioned	Yes	Reviewed independently by two researchers	16	1 088	Jadad Scale	TER and adverse effect	Funnel plot

AMED, Allied and Complementary Medicine Database. CENTRAL, Cochrane Central Register of Controlled Trials. CINAHL, Cumulative Index to Nursing and Allied Health Literature. CNKI, China National Knowledge Infrastructure. KCI, Korea Citation Index. KISS, Korean studies Information Service System. RISS, Revised International Staging System. KMBase, Korean Medical Database. OASIS, Oriental Medicine Advanced Searching Integrated System. CBM, Chinese Biology Medicine. VIP, Chinese Science and Technique Journal Database. SF-36, the MOS item short from health survey. NDI, Nepean dyspepsia index. TER, total effective rate. FD, functional dyspepsia. VAS, visual analogue scale.

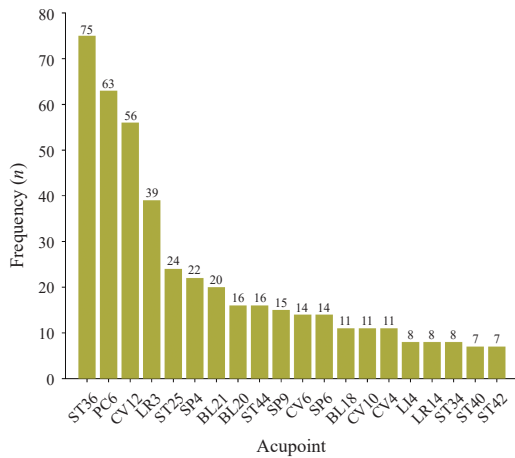
**Table 2** Scores of the included studies

Study	Study characteristics						Veritas score
	Year of publication (score)	Type of study (score)	Publication bias (score)	Heterogeneity (score)	AMSTAR2 (score)	PRISMA (score)	
KWON CY, 2021 [26]	2021 (8)	RCTs (8)	Partially assessed (8)	2.08 (2)	12.0 (8)	51 (8)	7.00
MAO X, 2020 [27]	2020 (7)	RCTs (8)	Partially assessed (8)	2.33 (4)	10.5 (7)	49 (7)	6.83
JIN X, 2018 [21]	2018 (6)	RCTs (8)	Partially assessed (8)	2.83 (7)	9.0 (3)	38 (2)	5.67
PENG JR, 2018 [22]	2018 (5)	RCTs (8)	None (3)	2.60 (6)	8.0 (1)	41 (4)	4.50
PANG B, 2016 [23]	2016 (4)	RCTs (8)	None (3)	2.20 (3)	10.0 (6)	49 (7)	5.50
ZHOU W, 2016 [24]	2016 (3)	RCTs (8)	Partially assessed (8)	1.75 (1)	9.5 (4)	46 (5)	4.83
KIM KN, 2015 [25]	2015 (2)	RCTs (8)	None (3)	2.50 (5)	8.5 (2)	35 (1)	3.50
WU X, 2015 [20]	2015 (1)	RCTs (8)	Partially assessed (8)	3.00 (8)	10.0 (6)	40 (3)	5.67
Mean Veritas score	4.50	8.00	6.13	4.50	4.63	4.63	5.40

RCTs, randomized control trials. AMSTAR, Assessment of Multiple Systematic Reviews tool. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

**Table 3** Meridians and acupoints used in acupuncture therapy for FD

Meridian	Frequency (n)	Number of acupoints (n)	Frequency (acupoint, n)
Stomach meridian of Foot-Yangming (ST)	162	20	Zusanli (ST36, 75), Tianshu (ST25, 24), Neiting (ST44, 16), Liangqiu (ST34, 8), Chongyang (ST42, 7), Fenglong (ST40, 7), Liangmen (ST21, 4), Shangjuxu (ST37, 3), Dubei (ST35, 3), Tiaokou (ST38, 2), Yinshi (ST33, 2), Futu (ST32, 2), Taiyi (ST23, 2), Xiangu (ST43, 1), Xiajuxu (ST39, 1), Shuidao (ST28, 1), Daju (ST27, 1), Chengman (ST20, 1), Chengqi (ST2, 1), Burong (ST19, 1)
Conception vessel (CV)	106	9	Zhongwan (CV12, 56), Qihai (CV6, 14), Guanyuan (CV4, 11), Xiawan (CV10, 11), Danzhong (CV17, 5), Shangwan (CV13, 4), Shenque (CV8, 2), Jianli (CV11, 2), Zhongji (CV3, 1)
Pericardium meridian of Hand-Jueyin (PC)	64	2	Neiguan (PC6, 63), Jianshi (PC5, 1)
Bladder meridian of Foot-Taiyang (BL)	59	9	Weishu (BL21, 20), Pishu (BL20, 16), Ganshu (BL18, 11), Xinshu (BL15, 4), Geshu (BL17, 3), Shenshu (BL23, 2), Feishu (BL13, 1), Dachangshu (BL25, 1), Shenmai (BL62, 1)
Liver meridian of Foot-Jueyin (LR)	56	4	Taichong (LR3, 39), Qimen (LR14, 8), Zhangmen (LR13, 6), Xingjian (LR2, 3)
Spleen meridian of Foot-Taiyin (SP)	51	3	Gongsun (SP4, 22), Yinlingquan (SP9, 15), Sanyinjiao (SP6, 14)
Large intestine meridian of Hand-Yangming (LI)	11	3	Hegu (LI4, 8), Shousanli (LI10, 2), Sanjian (LI3, 1)
Gallbladder meridian of Foot-Shaoyang (GB)	7	5	Yanglingquan (GB34, 3), Zulinqi (GB41, 1), Qiuxu (GB40, 1), Guangming (GB37, 1), Waiqiu (GB36, 1)
Governor vessel (GV)	7	2	Baihui (GV20, 4), Shenting (GV24, 3)
Points of head and neck (EX-HN)	5	2	Yintang (EX-HN3, 3), Sishencong (EX-HN1, 2)
Heart meridian of Hand-Shaoyin (HT)	3	2	Shenmen (HT7, 2), Tongli (HT5, 1)
Sanjiao meridian of Hand-Shaoyang (SJ)	2	2	Zhigou (SJ6, 1), Waiguan (SJ5, 1)
Kidney meridian of Foot-Shaoyin (KI)	2	2	Zhaohai (KI6, 1), Youmen (KI21, 1)
Small intestine meridian of Hand-Taiyang (SI)	1	1	Houxi (SI3, 1)
Lung meridian of Hand-Taiyin (LU)	1	1	Lieque (LU7, 1)



**Figure 2** The top 20 acupoints for FD treatment

Zusanli (ST36), Neiguan (PC6), Zhongwan (CV12), Taichong (LR3), Tianshu (ST25), Gongsun (SP4), Weishu (BL21), Pishu (BL20), Neiting (ST44), Yinlingquan (SP9), Qihai (CV6), Sanyinjiao (SP6), Ganshu (BL18), Xiawan (CV10), Guanyuan (CV4), Hegu (LI4), Qimen (LR14), Liangqiu (ST34), Fenglong (ST40), and Chongyang (ST42).

(SP). The most frequently used meridian was ST, which appeared 162 times and involved 20 acupoints. The second most commonly used meridian was CV, which appeared 106 times and involved nine acupoints. PC was the third mostly used meridian, with 64 times in frequency and two points.

**3.5 Association rules of acupoints**

A total of 28 association rules were identified based on the acupoints data, comprising 10 second-order association rules (Table 4), 15 third-order association rules (Table 5), and 3 fourth-order association rules (Table 6). The association rules were visualized as a scatter plot (Figure 3) and a network plot (Figure 4). Through the analysis of association rules, it was found that Neiguan (PC6), Zusanli (ST36), Zhongwan (CV12), and Taichong (LR3) were the kernel acupoint combination for the treatment of FD. The location of the kernel acupoints in regard to the treatment of FD is depicted in Figure 5, created by Figdraw ([www.figdraw.com](http://www.figdraw.com)).

**Table 4** Second-order association rules of acupoints for FD treatment

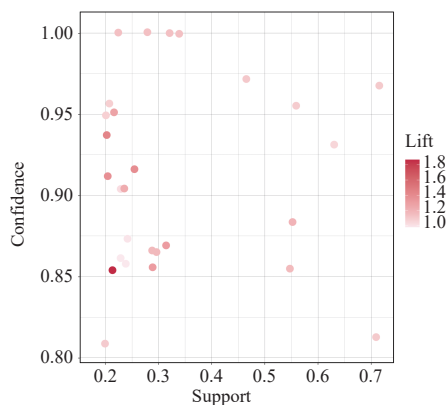
Antecedent	Succedent	Support	Confidence	Lift
Neiguan (PC6)	Zusanli (ST36)	0.72	0.97	1.10
Zusanli (ST36)	Neiguan (PC6)	0.72	0.81	1.10
Zhongwan (CV12)	Zusanli (ST36)	0.61	0.93	1.05
Zhongwan (CV12)	Neiguan (PC6)	0.56	0.86	1.16
Taichong (LR3)	Zusanli (ST36)	0.45	0.97	1.10
Tianshu (ST25)	Zhongwan (CV12)	0.26	0.92	1.39
Tianshu (ST25)	Zusanli (ST36)	0.25	0.88	0.99
Gongsun (SP4)	Neiguan (PC6)	0.24	0.91	1.23
Weishu (BL21)	Zusanli (ST36)	0.22	0.95	1.08
Gongsun (SP4)	Zusanli (ST36)	0.22	0.86	0.98

**Table 5** Third-order association rules of acupoints for FD treatment

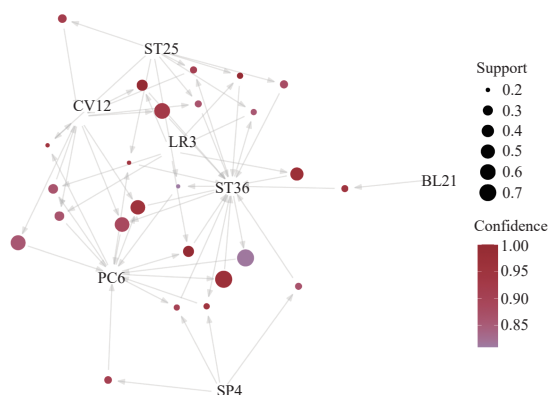
Antecedent	Succedent	Support	Confidence	Lift
Zhongwan (CV12) + Neiguan (PC6)	Zusanli (ST36)	0.54	0.96	1.09
Zhongwan (CV12) + Zusanli (ST36)	Neiguan (PC6)	0.54	0.88	1.19
Zhongwan (CV12) + Taichong (LR3)	Zusanli (ST36)	0.34	1.00	1.13
Taichong (LR3) + Neiguan (PC6)	Zusanli (ST36)	0.34	1.00	1.13
Zhongwan (CV12) + Taichong (LR3)	Neiguan (PC6)	0.29	0.86	1.16
Taichong (LR3) + Neiguan (PC6)	Zhongwan (CV12)	0.29	0.86	1.31
Zhongwan (CV12) + Tianshu (ST25)	Zusanli (ST36)	0.22	0.86	0.98
Tianshu (ST25) + Zusanli (ST36)	Zhongwan (CV12)	0.22	0.90	1.37
Neiguan (PC6) + Gongsun (SP4)	Zusanli (ST36)	0.21	0.90	1.02
Gongsun (SP4) + Zusanli (ST36)	Neiguan (PC6)	0.21	0.95	1.28
Taichong (LR3) + Tianshu (ST25)	Zusanli (ST36)	0.21	1.00	1.13
Tianshu (ST25) + Zusanli (ST36)	Taichong (LR3)	0.21	0.86	1.87
Neiguan (PC6) + Tianshu (ST25)	Zhongwan (CV12)	0.20	0.94	1.43
Neiguan (PC6) + Tianshu (ST25)	Zusanli (ST36)	0.20	0.94	1.07
Tianshu (ST25) + Zusanli (ST36)	Neiguan (PC6)	0.20	0.81	1.09

**Table 6** Fourth-order association rules of acupoints for FD treatment

Antecedent	Succedent	Support	Confidence	Lift
Zhongwan (CV12) + Taichong (LR3) + Neiguan (PC6)	Zusanli (ST36)	0.29	1.00	1.13
Zhongwan (CV12) + Taichong (LR3) + Zusanli (ST36)	Neiguan (PC6)	0.29	0.86	1.16
Taichong (LR3) + Neiguan (PC6) + Zusanli (ST36)	Zhongwan (CV12)	0.29	0.86	1.31

**Figure 3** Scatter plot of the 28 association rules of acupoints for FD treatment

Each circle represents one association rule. The color represents the Lift value, the redder the color, the higher the Lift value.

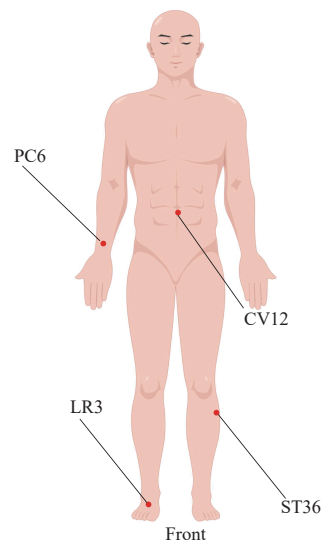
**Figure 4** Network plot of the 28 association rules of acupoints for FD treatment

Each circle represents one association rule. The arrows indicate linkages between the acupoints. The color represents the Confidence value, the redder the color, the higher the Confidence value. The circle size represents the Support value, the higher the Support value, the larger the circle. Zusanli (ST36), Neiguan (PC6), Zhongwan (CV12), Tianshu (ST25), Gongsun (SP4), Weishu (BL21), and Taichong (LR3).

## 4 Discussion

### 4.1 Literature quality

In the study, the Veritas plot was demonstrated as a tool that acupuncturists could use to evaluate the quality of meta-analysis studies before clinical application. A total of eight meta-analysis studies were included. The mean Veritas scores of the studies based on publication year, type of study, AMSTAR2, PRISMA, heterogeneity, and

**Figure 5** Location of core acupoints for the treatment of FD patients

Zusanli (ST36), Neiguan (PC6), Zhongwan (CV12), and Taichong (LR3).

publication bias were 4.50, 8.00, 4.63, 4.63, 4.50, and 6.13, respectively, indicating that the included meta-analysis studies performed well in the following areas: update results on time, high degree of consistency in study design, compliance with PRISMA statements, and low heterogeneity. However, the statement of the review method, the comprehension of the research strategy, the detailed list of the excluded studies, the sources of funding, the assessment of the potential impact of bias risks on the results of the meta-analysis in each study, the explanation of heterogeneity, and the potential sources of conflict of interest in AMSTAR2 were insufficient. In some meta-analysis studies, publication bias was not assessed, suggesting that more attention should be paid to the methodological guarantee of bias, and more consideration should be taken into evaluating the clinical value of the study results.

### 4.2 Acupoint combinations

In TCM, FD is essentially synonymous with the term “stuffiness and fullness”. According to the TCM theory, drink or food injury, congenital defects, and emotional injury are the major pathogenic factors of FD. All these factors have contributed to abnormal function in the spleen and stomach. The spleen is regarded as the source of Qi and blood production and transformation. So spleen deficiency is a huge factor contributing to the



pathogenesis of FD. A study conducted by CHEN et al. [28] showed that acupuncture improved the clinical symptoms of FD patients by strengthening the spleen. In our study, we identified 28 association rules, including 10 second-order, 15 third-order, and 3 fourth-order association rules. The top-ranking association rules of each order were “Neiguan (PC6) → Zusanli (ST36)” “Zhongwan (CV12) + Neiguan (PC6) → Zusanli (ST36)” and “Zhongwan (CV12) + Taichong (LR3) + Neiguan (PC6) → Zusanli (ST36)”, respectively. The location of Zusanli (ST36), a confluent acupoint of the ST, is in the anterolateral leg, 3 cun under the acupoint Dubi (ST35), one transverse finger away from tibia anterior margin.

As a result of data mining, we found that Neiguan (PC6), Zusanli (ST36), Zhongwan (CV12), and Taichong (LR3) were the kernel acupoint combination for the treatment of FD. Electroacupuncture at Zusanli (ST36) has been shown to improve gastric motility by enhancing vagal efferent activity and suppressing anorexigenic hormones [29]. Interstitial cells of Cajal (ICC) function as pacemakers, generating electrical slow waves that cause segmental contractions [30]. An increasing body of evidence suggests a positive correlation between improvements in ICC structure and gastrointestinal motility [31, 32]. Electroacupuncture at Zusanli (ST36) was demonstrated to improve gastrointestinal motility disorders in FD rat models by alleviating the pathological changes of ICC [33]. Furthermore, there seems to be a significant link between the central nervous system and the stomach as evidence accumulates [34, 35]. In recent studies of acupuncture's ability to treat gastrointestinal disorders, focus has also been placed on aspects of the nervous system [36, 37]. For example, electroacupuncture enhances the intestinal propulsive rate in rats with FD by activating the hippocampus [6]. Zhongwan (CV12) is located 4 cun above the anterior median umbilicus. Acupuncture at Zusanli (ST36) and Zhongwan (CV12) could adjust spleen and stomach, which makes the ascending and descending of spleen and stomach in a good order [38]. WANG et al. [39] reported that decreased gastric motility of FD rats was associated with the over-expression of the hippocampal glutamatergic system, and electroacupuncture at Zhongwan (CV12) could reduce glutamate in FD rats' hippocampi by regulating the N-methyl-D-aspartate receptors (NMDAR)-nitric oxide (NO)-cyclic guanosine monophosphate (cGMP) pathways. The pathophysiology of FD includes visceral hypersensitivity, decreased gastric accommodation, and impaired gastric motility [40]. The vagal nerve mediates the process of gastric accommodation. Upon ingesting food, the vagal nerve is activated and NO is released, causing the stomach to relax [41]. A weakening of the vagal nerve may be responsible for the loss of gastric accommodation, resulting in early satiety and postprandial fullness. The acupoint Neiguan (PC6) is located on the palmar side of the

forearm, 2 cun across the wrist, between the palmar longus tendon and the radial flexor carpi tendon. XU et al. [42] found that transcutaneous electroacupuncture at acupoints Neiguan (PC6) and Zusanli (ST36) significantly improved postprandial slow waves, gastric accommodation, as well as dyspeptic symptoms by regulating the vagus nerve. Taichong (LR3) acupoint is located between the first and second metatarsals of the back of the foot. Electroacupuncture at Zusanli (ST36) and Taichong (LR3) could decrease mRNA expressions of vasoactive intestinal peptide, thus playing an intervention role for FD treatment [43].

### 4.3 Strengths and limitations

The present study possesses several strengths. First, we comprehensively assessed the methodological quality of the meta-analysis studies related to the treatment of FD with acupuncture from six dimensions. Second, we included only RCTs in the data mining analysis, which allowed the conclusions to be more objective. But, there are also some limitations to this study. First, how the population factor affected the results was not examined. Second, a number of factors might influencing the effects of acupuncture were not investigated, such as time of retaining the needle and depth of needling. Third, large-scale trials or animal experiments that confirmed the acupoint combinations and core acupoints for FD treatment were rarely conducted.

## 5 Conclusion

Acupuncture could improve the clinical symptoms of FD, but the methodological quality of the literature needs to be improved. Additionally, based on 85 RCTs, Neiguan (PC6), Zusanli (ST36), Zhongwan (CV12), and Taichong (LR3) are considered as kernel acupoint combinations for treating FD, with Zusanli (ST36) being the most frequently selected acupoint for FD treatment.

## Fundings

National Natural Science Foundation of China (81874466), and Natural Science Foundation of Hunan Province (2021JJ30531).

## Competing interests

The authors declare no conflict of interest.

## References

- [1] FORD AC, MAHADEVA S, CARBONE MF, et al. Functional dyspepsia. *Lancet*, 2020, 396(10263): 1689-1702.
- [2] PUTHANMADHOM NARAYANAN S, O'BRIEN DR, SHARMA

- M, et al. Duodenal mucosal barrier in functional dyspepsia. *Clinical Gastroenterology and Hepatology*, 2022, 20(5): 1019–1028.
- [3] LACY BE, CHASE RC, CANGEMI DJ. The treatment of functional dyspepsia: present and future. *Expert Review of Gastroenterology & Hepatology*, 2023, 17(1): 9–20.
- [4] BROCK SYMONS T, PARK J, KIM JH, et al. Attenuation of skeletal muscle atrophy via acupuncture, electro-acupuncture, and electrical stimulation. *Integrative Medicine Research*, 2023, 12(2): 100949.
- [5] YANG JW, WANG LQ, ZOU X, et al. Effect of acupuncture for postprandial distress syndrome: a randomized clinical trial. *Annals of Internal Medicine*, 2020, 172(12): 777–785.
- [6] CHEN Y, ZHAO Y, TAN RY, et al. The influence of stomach back-shu and front-mu points on insular functional connectivity in functional dyspepsia rat models. *Evidence-Based Complementary and Alternative Medicine*, 2021, 2021: 2771094.
- [7] TANG L, ZENG Y, LI L, et al. Electroacupuncture upregulated ghrelin in rats with functional dyspepsia via AMPK/TSC2/rheb-mediated mTOR inhibition. *Digestive Diseases and Sciences*, 2020, 65(6): 1689–1699.
- [8] WANG D, ZHANG JL, YANG DY, et al. Electroacupuncture restores intestinal mucosal barrier through TLR4/NF- $\kappa$ B p65 pathway in functional dyspepsia-like rats. *Anatomical Record*, 2023, 306(12): 2927–2938.
- [9] CEULEMANS M, WAUTERS L, VANUYTSEL T. Targeting the altered duodenal microenvironment in functional dyspepsia. *Current Opinion in Pharmacology*, 2023, 70: 102363.
- [10] YU B, LI MY, HUANG HP, et al. Acupuncture treatment of diabetic peripheral neuropathy: an overview of systematic reviews. *Journal of Clinical Pharmacy and Therapeutics*, 2021, 46(3): 585–598.
- [11] WEN JY, CHEN X, YANG Y, et al. Acupuncture medical therapy and its underlying mechanisms: a systematic review. *The American Journal of Chinese Medicine*, 2021, 49(1): 1–23.
- [12] GUO Y, WEI W, CHEN JD. Effects and mechanisms of acupuncture and electroacupuncture for functional dyspepsia: a systematic review. *World Journal of Gastroenterology*, 2020, 26(19): 2440–2457.
- [13] HUANG F, QIU MW, ZHAO SY, et al. Evaluating the characteristics, reporting and methodological quality of systematic reviews of acupuncture for low back pain by using the veritas plot. *Journal of Pain Research*, 2020, 13: 2633–2652.
- [14] LU PH, KENG JL, TSAI FM, et al. An apriori algorithm-based association rule analysis to identify acupoint combinations for treating diabetic gastroparesis. *Evidence-Based Complementary and Alternative Medicine*, 2021, 2021: 6649331.
- [15] LU PH, CHEN YY, TSAI FM, et al. Combined acupoints for the treatment of patients with obesity: an association rule analysis. *Evidence-Based Complementary and Alternative Medicine*, 2022, 2022: 7252213.
- [16] LIN HX, WANG XT, MO YJ, et al. Acupuncture for primary osteoporosis: evidence, potential treatment prescriptions, and mechanisms. *Evidence-Based Complementary and Alternative Medicine*, 2019, 2019: 2705263.
- [17] World Health Organization Western Pacific Region. WHO standard acupuncture point locations in the Western Pacific Region. *Beijing: People's Medical Publishing House*, 2010.
- [18] QI XJ, GUO ZH, CHEN QY, et al. A data mining-based analysis of core herbs on different patterns (Zheng) of non-small cell lung cancer. *Evidence-Based Complementary and Alternative Medicine*, 2021, 2021: 3621677.
- [19] YOU X, XU YK, HUANG J, et al. A data mining-based analysis of medication rules in treating bone marrow suppression by kidney-tonifying method. *Evidence-Based Complementary and Alternative Medicine*, 2019, 2019: 1907848.
- [20] WU XW, JI HZ, XU LE, et al. The effect of acupuncture and moxibustion on functional dyspepsia compared with prokinetic agents: a meta-analysis. *Chinese Journal of Integrated Traditional and Western Medicine on Digestion*, 2015, 23(2): 100–104.
- [21] JIN X, CAI WR, XU PD. The effect of acupuncture and moxibustion on functional dyspepsia compared with prokinetic agents: a meta-analysis. *World Latest Medicine Information*, 2018, 18(68): 9–12.
- [22] PENG JR, TAO SY, YANG CX, et al. Efficacy of acupuncture on dyspepsia subtypes: a systematic review. *Liaoning Journal of Traditional Chinese Medicine*, 2018, 45(8): 1594–1598.
- [23] PANG B, JIANG T, DU YH, et al. Acupuncture for functional dyspepsia: what strength does it have? A systematic review and meta-analysis of randomized controlled trials. *Evidence-Based Complementary and Alternative Medicine*, 2016, 2016: 3862916.
- [24] ZHOU WM, SU JW, ZHANG HJ. Efficacy and safety of acupuncture for the treatment of functional dyspepsia: meta-analysis. *Journal of Alternative and Complementary Medicine*, 2016, 22(5): 380–389.
- [25] KIM KN, CHUNG SY, CHO SH. Efficacy of acupuncture treatment for functional dyspepsia: a systematic review and meta-analysis. *Complementary Therapies in Medicine*, 2015, 23(6): 759–766.
- [26] KWON CY, KO SJ, LEE B, et al. Acupuncture as an add-on treatment for functional dyspepsia: a systematic review and meta-analysis. *Frontiers in Medicine*, 2021, 8: 682783.
- [27] MAO XY, GUO S, NI WC, et al. Electroacupuncture for the treatment of functional dyspepsia: a systematic review and meta-analysis. *Medicine*, 2020, 99(45): e23014.
- [28] CHEN P, CHEN AP. Clinical observation of “experienced ten acupoints” for functional dyspepsia of liver stagnation and spleen deficiency. *Chinese Acupuncture & Moxibustion*, 2020, 40(11): 1169–1171.
- [29] LIU Y, ZHANG SJ, YE F, et al. Ameliorating effects and mechanisms of chronic electroacupuncture at ST36 in a rodent model of dyspepsia induced by cisplatin. *Neurogastroenterology and Motility*, 2019, 31(1): e13474.
- [30] AFFO S, NAIR A, BRUNDU F, et al. Promotion of cholangiocarcinoma growth by diverse cancer-associated fibroblast subpopulations. *Cancer Cell*, 2021, 39(6): 866–882.e11.
- [31] FU SL, ZHU LN, YIN HH, et al. Da-Cheng-Qi decoction combined with lactobacillus acidophilus improves gastrointestinal

- function of traumatic brain-injured model mice. *Chinese Journal of Integrative Medicine*, 2020, 26(10): 762-768.
- [32] JOUNG JY, CHOI SH, SON CG. Interstitial cells of Cajal: potential targets for functional dyspepsia treatment using medicinal natural products. *Evidence-Based Complementary and Alternative Medicine*, 2021, 2021: 9952691.
- [33] ZHANG GS, XIE S, HU W, et al. Effects of electroacupuncture on interstitial cells of Cajal (ICC) ultrastructure and connexin 43 protein expression in the gastrointestinal tract of functional dyspepsia (FD) rats. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*, 2016, 22: 2021-2027.
- [34] TAO J, CAMPBELL JN, TSAI LT, et al. Highly selective brain-to-gut communication via genetically defined vagus neurons. *Neuron*, 2021, 109(13): 2106-2115.
- [35] NIESLER B, KUERTEN S, DEMIR IE, et al. Disorders of the enteric nervous system - a holistic view. *Nature Reviews Gastroenterology & Hepatology*, 2021, 18(6): 393-410.
- [36] ZHOU W, LIU G, HUNG RJ, et al. Causal relationships between body mass index, smoking and lung cancer: univariable and multivariable Mendelian randomization. *International Journal of Cancer*, 2021, 148(5): 1077-1086.
- [37] LEE IS, CHAE Y. Exploring acupuncture actions in the body and brain. *Journal of Acupuncture and Meridian Studies*, 2022, 15(3): 157-162.
- [38] QIN WM, ZHAO K, YANG HY. Effect of acupoint catgut embedding therapy combined with Chinese medicine for nourishing the kidneys and promoting blood circulation and improving blood glucose and lipid levels as well as the pregnancy rate in obese PCOS patients with infertility. *Experimental and Therapeutic Medicine*, 2016, 12(5): 2909-2914.
- [39] WANG H, LIU WJ, HU MJ, et al. Acupuncture at gastric back-shu and front-mu acupoints enhances gastric motility via the inhibition of the glutamatergic system in the hippocampus. *Evidence-Based Complementary and Alternative Medicine*, 2020, 2020: 3524641.
- [40] SINGH R, ZOGG H, GHOSHAL UC, et al. Current treatment options and therapeutic insights for gastrointestinal dysmotility and functional gastrointestinal disorders. *Frontiers in Pharmacology*, 2022, 13: 808195.
- [41] VERBEURE W, VAN GOOR H, MORI H, et al. The role of gasotransmitters in gut peptide actions. *Frontiers in Pharmacology*, 2021, 12: 720703.
- [42] XU F, TAN Y, HUANG ZH, et al. Ameliorating effect of transcutaneous electroacupuncture on impaired gastric accommodation in patients with postprandial distress syndrome-predominant functional dyspepsia: a pilot study. *Evidence-Based Complementary and Alternative Medicine*, 2015, 2015: 168252.
- [43] XU PD, ZHANG HX, YANG Y, et al. Effects of electroacupuncture on gastrointestinal motility and expressions of VIP and CGRP in functional dyspepsia model rats. *Chinese Journal of Integrated Traditional and Western Medicine*, 2017, 37(3): 360-364.

## 针灸治疗功能性消化不良的证据及穴位组合：一项系统评价再评价 联合数据挖掘研究

邹孟龙<sup>a,b</sup>, 胡卓瑜<sup>b</sup>, 龙丹<sup>a,b</sup>, 孙豪娴<sup>a,b</sup>, 朱莹<sup>a\*</sup>

a. 湖南中医药大学第一附属医院消化科, 湖南长沙 410007, 中国

b. 湖南中医药大学研究生院, 湖南长沙 410208, 中国

**【摘要】目的** 本研究旨在对针灸治疗功能性消化不良 (FD) 的 meta 分析和系统评价文献进行方法学质量评估, 并分析其穴位组合规律。**方法** 分别在中国知网 (CNKI)、维普数据库 (VIP)、中国生物医学数据库 (CBM) 和万方数据库等中文数据库, 以及 PubMed、Embase 和 Cochrane Library 等英文数据库中检索针灸治疗 FD 的 meta 分析和系统评价, 时间均从各个数据库建库至 2022 年 4 月 30 日。根据文献发表年份、研究类型、多系统评价评估问卷 2 (AMSTAR2)、系统评价和 meta 分析的首选报告条目 (PRISMA)、异质性和发表偏倚 6 个维度计算 Veritas 总分评估 meta 分析和系统评价的方法学质量。进一步从 meta 分析和系统评价中提取随机对照试验 (RCTs) 并使用 R 软件 (V 4.3.1) 进行穴位频次、经络频次及关联规则分析。**结果** 经筛选后, 纳入 8 项 meta 分析进行研究, 其出版年份、设计类型、AMSTAR2、PRISMA、异质性及发表偏倚风险的 Veritas 平均分分别为 4.50、8.00、4.63、4.63、4.50 和 6.13 分。根据各个维度评分发现在审查方法的陈述、研究策略的理解、排除标准的详细列表、资金来源、个体研究的偏倚风险、异质性的解释及潜在利益冲突说明等方面尚存在不足之处。从 8 项 meta 分析中对提取的 85 个 RCTs 进行数据挖掘, 共包含 85 个针灸处方和 67 个穴位。其中, 频次最高的经络是足阳明胃经; 频次排列前 10 位的穴位分别足三里、内关、中脘、太冲、天枢、公孙、胃俞、脾俞、内庭和阴陵泉。此外, 关联规则分析鉴定出 28 条, 包括二阶关联规则 10 条、三阶关联规则 15 条和四阶关联规则 3 条, 各阶关联规则排名第一的分别是: 内关→足三里、中脘+内关→足三里和中脘+太冲+内关→足三里。**结论** 针灸可以显著改善 FD 患者的临床症状, 但目前该领域 meta 分析文献的方法学质量有待提高。此外, 通过数据挖掘发现内关、足三里、中脘和太冲是治疗 FD 核心穴位组合。

**【关键词】** 功能性消化不良; 针灸; 数据挖掘; 联合穴位; Veritas 图; meta 分析; 系统评价