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Literature Study

Data mining for points-selection rules in acupuncture treatment of mammary gland hyperplasia

基于数据挖掘探讨针刺治疗乳腺增生病选穴规律分析

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Abstract
Objective: To explore and analyze the points-selection rules in acupuncture treatment of mammary gland hyperplasia (MGH) by data mining and statistical method.
Methods: Clinical literatures about the treatment of MGH with acupuncture published in the recent 16 years were retrieved from Chinese Journal Full-text Database (CJFD) and established into a database by Excel. The SPSS 20 version software and Clementine 12.0 version software were adopted to analyze the frequency and association rules of points-selection in the treatment of MGH with acupuncture.
Results: The top 3 points used most frequently in acupuncture treatment of MGH were Danzhong (CV 17), Taichong (LR 3) and Zusanli (ST 36); points from the Stomach Meridian of Foot Yangming and Liver Meridian of Foot Jueyin were most commonly used; the commonly selected points were predominantly distributed in thoracic and abdominal regions and lower limbs; emphasis on the combination use of local and distal points; of the specific points, the five Shu-Transmitting points were mostly used; association analysis showed that the associations among Taichong (LR 3), Danzhong (CV 17) and Zusanli (ST 36) were the most significant.
Conclusion: The data mining results substantially accord with the general rules of acupuncture-moxibustion theories in traditional Chinese medicine, able to reflect the points-selection principles and features in acupuncture treatment of MGH and provide evidence for the points selection in the treatment of MGH in acupuncture clinic.
Keywords: Acupuncture Therapy; Point, Zusanli (ST 36); Point, Danzhong (CV 17); Point, Taichong (LR 3); Mammary Gland Hyperplasia; Data Mining

【摘要】目的：运用数据挖掘技术及统计学方法，分析并挖掘针刺治疗乳腺增生的选穴规律。**方法：**检索中国期刊全文数据库近16年针刺治疗乳腺增生的临床文献，运用Excel软件建立文献数据库。使用SPSS 20和Clementine 12.0软件对针刺治疗乳腺增生腧穴处方进行频数统计分析和关联规则分析。**结果：**针刺治疗乳腺增生腧穴中使用频次最高的前3位穴位为膻中、太冲和足三里；以足阳明胃经、足厥阴肝经穴位选用最多；常用穴位主要分布在胸腹部和下肢；重视局部选穴和远端取穴相配合；特定穴中五输穴的使用最多；关联规则分析显示穴位间相关性最高的是太冲、膻中和足三里。**结论：**数据挖掘的结果与传统医学中针灸治疗理论的一般规律基本相符，能够反映针刺治疗乳腺增生病的取穴特点及规律，为临床针刺治疗乳腺增生病选穴提供依据。

【关键词】针刺疗法；穴，足三里；穴，膻中；穴，太冲；乳腺增生；数据挖掘
【中图分类号】R246.2　　**【文献标志码】**A

As a common mammary gland disease, mammary gland hyperplasia (MGH) often affects women at 25-45 years old. Its incidence rate is 40% in women at child-bearing age, accounting for 70%-80% of mammary gland diseases. Due to its possibility to turn malignant, MGH has become one of the risk factors for breast cancer[1-2]. Pathologically, lump and pain in breast are the two major symptoms. So far, its pathogenesis hasn't been clarified yet, though it's usually believed that the imbalance between estrogen and progestogen should be blamed. In Western medicine, MGH is often treated with basic intervention in combination with hormone antagonists. However, long-term use of hormonal therapy may induce a series of adverse effects, even serious endocrine disturbance, greatly influencing patient's psychosomatic health and quality of life[3-4]. MGH belongs to the scope of *Ru Pi* (nodules of breast) in traditional Chinese medicine (TCM), usually triggered by depressed mood and imbalanced Thoroughfare and Conception Vessels, etc., and closely related to meridians such as liver, spleen, stomach, and Thoroughfare and Conception Vessels[5-6]. Acupuncture

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has shown its significant advantages in treating MGH: high safety, excellent efficacy, and low cost. But there exist great differences in selecting points in the treatment of MGH with acupuncture and lacks of studies on the standardization of points selection and grouping. Therefore, via data mining method, this research was going to analyze the associations among different points groupings in acupuncture treatment of MGH, revealing the rules in points selection and grouping, and providing scientific evidence for the relevant study.

1 Object and Methods

1.1 Retrieve method

The Chinese Journal Full-text Database (CJFD) was retrieved for literatures published in journals between January 1, 2000 and April 30, 2016, under 'Acupuncture' and 'MGH' as the key words.

1.2 Inclusion criteria

The subjects involved were all diagnosed with MGH; acupuncture was the major treatment method with clear prescription and confirmed therapeutic efficacy; with or without a control group in a clinical trial, the number of subjects enrolled in the treatment group $\geqslant$ 20.

1.3 Exclusion criteria

Animal or cellular experiments; reviews or literatures with low quality or insufficient information; case number $<$ 20; non-acupuncture-related literatures; duplicate publications.

1.4 Data mining method

The collected articles were scanned one by one to record the points prescription, including the fourteen meridians, extraordinary meridians, Ashi points, and specific points. The software of SPSS 20.0 version, Excel 2007 version and Clementine 12.0 version were used to analyze the frequencies of points, meridians, and specific points, as well as the associations in points groupings.

2 Results and Analyses

A total of 138 articles were collected by computer retrieval, and 111 eligible ones were finally recruited for data mining[7-117]. During manual collection, mammary gland lump, tender points in mammary gland and Ashi points were all considered as Ashi points. The analyses of points frequencies, points groupings, associations among points and meridians and specific points are described as follows.

2.1 Rules and analyses of points frequencies

The analyses of the 111 points prescriptions, involving 10 800 cases in total, contained 71 points, including 3 extra points [Zigong (EX-CA 1), Bizhong (Extra), and Jiaji (EX-B 2)] with a total frequency of 902. The points ranked in the top of the frequency list were Danzhong (CV 17), Taichong (LR 3), Zusanli (ST 36), Rugen (ST 18), and Sanyinjiao (SP 6), etc. The top 20 points are shown in Table 1 following a descending order.

Table 1. Top 20 points by the frequency

Ranking	Point	Frequency	Rate of support (%)
1	Danzhong (CV 17)	78	70.3
2	Taichong (LR 3)	72	65.8
3	Zusanli (ST 36)	62	55.9
4	Rugen (ST 18)	61	55.0
5	Sanyinjiao (SP 6)	56	50.5
6	Wuyi (ST 15)	43	38.7
7	Ganshu (BL 18)	39	35.1
8	Qimen (LR 14)	36	32.4
9	Taixi (KI 3)	36	32.4
10	Hegu (LI 4)	33	29.7
11	Shenshu (BL 23)	33	29.7
12	Fenglong (ST 40)	31	27.9
13	Jianjing (GB 21)	30	27.0
14	Pishu (BL 20)	28	25.2
15	Ashi point	26	23.4
16	Tianzong (SI 11)	24	21.6
17	Guanyuan (CV 4)	18	16.2
18	Yanglingquan (GB 34)	17	15.3
19	Xuehai (SP 10)	15	13.5
20	Neiguan (PC 6)	14	12.6

2.2 Association rules and analyses

The association rule describes the regulation and pattern of the concurrency of certain features of a subject, aiming to discover the associations and rules. The support and confidence rates are most commonly used to prove the effectiveness of an association rule. The rate of support stands for the prevalence of the rule; the rate of confidence reflects the predicted intensity[118]. Clementine 12.0 was used to analyze the association rules of the 71 points, and those with rate of support $\geqslant$30% and rate of confidence $\geqslant$80% were ranked in a descending order by the rate of support. The rate of confidence represents the probability of the occurrence of the latter item following the former item; the rate of support stands for the probability of the concurrency of the two items. For example, when Zusanli (ST 36) occurred, the probability of the occurrence of Danzhong (CV 17) was 83.9%, and the rate of support of this association rule was 55.9% (Table 2).

Table 2. Common points groupings in acupuncture treatment of MGH

Ranking	Grouping		Rate of support (%)	Rate of confidence (%)
	Latter	Former		
1	Taichong (LR 3)	Zusanli (ST 36)	55.9	82.3
2	Danzhong (CV 17)	Zusanli (ST 36)	55.9	83.9
3	Danzhong (CV 17)	Rugen (ST 18)	55.0	83.6
4	Danzhong (CV 17)	Sanyinjiao (SP 6)	50.5	82.1
5	Taichong (LR 3)	Sanyinjiao (SP 6)	50.5	89.3
6	Zusanli (ST 36)	Taichong (LR 3), Danzhong (CV 17)	47.7	81.1
7	Taichong (LR 3)	Zusanli (ST 36), Danzhong (CV 17)	46.8	82.7
8	Danzhong (CV 17)	Zusanli (ST 36), Taichong (LR 3)	45.9	84.3
9	Danzhong (CV 17)	Sanyinjiao (SP 6), Taichong (LR 3)	45.0	80.0
10	Zusanli (ST 36)	Sanyinjiao (SP 6), Danzhong (CV 17)	41.4	84.8
11	Taichong (LR 3)	Sanyinjiao (SP 6), Danzhong (CV 17)	41.4	87.0
12	Zusanli (ST 36)	Rugen (ST 18), Taichong (LR 3)	40.5	82.2
13	Rugen (ST 18)	Wuyi (ST 15)	38.7	81.4
14	Sanyinjiao (SP 6)	Zusanli (ST 36), Taichong (LR 3), Danzhong (CV 17)	38.7	81.4
15	Zusanli (ST 36)	Wuyi (ST 15)	38.7	83.7
16	Danzhong (CV 17)	Wuyi (ST 15)	38.7	88.4
17	Danzhong (CV 17)	Rugen (ST 18), Zusanli (ST 36)	37.8	83.3
18	Taichong (LR 3)	Rugen (ST 18), Zusanli (ST 36)	37.8	88.1
19	Taichong (LR 3)	Sanyinjiao (SP 6), Zusanli (ST 36)	36.9	90.2
20	Danzhong (CV 17)	Sanyinjiao (SP 6), Zusanli (ST 36)	36.9	95.1
21	Zusanli (ST 36)	Sanyinjiao (SP 6), Taichong (LR 3), Danzhong (CV 17)	36.0	87.5
22	Taichong (LR 3)	Sanyinjiao (SP 6), Zusanli (ST 36), Danzhong (CV 17)	35.1	89.7
23	Rugen (ST 18)	Wuyi (ST 15), Danzhong (CV 17)	34.2	81.6
24	Zusanli (ST 36)	Wuyi (ST 15), Danzhong (CV 17)	34.2	84.2
25	Danzhong (CV 17)	Rugen (ST 18), Zusanli (ST 36), Taichong (LR 3)	33.3	81.1
26	Danzhong (CV 17)	Sanyinjiao (SP 6), Zusanli (ST 36), Taichong (LR 3)	33.3	94.6
27	Danzhong (CV 17)	Qimen (LR 14)	32.4	80.6
28	Sanyinjiao (SP 6)	Taixi (KI 3)	32.4	83.3
29	Rugen (ST 18)	Wuyi (ST 15), Zusanli (ST 36)	32.4	83.3
30	Taichong (LR 3)	Wuyi (ST 15), Zusanli (ST 36)	32.4	83.3
31	Danzhong (CV 17)	Wuyi (ST 15), Zusanli (ST 36)	32.4	88.9
32	Taichong (LR 3)	Taixi (KI 3)	32.4	91.7
33	Taichong (LR 3)	Wuyi (ST 15), Rugen (ST 18)	31.5	80.0
34	Sanyinjiao (SP 6)	Rugen (ST 18), Zusanli (ST 36), Danzhong (CV 17)	31.5	80.0
35	Sanyinjiao (SP 6)	Rugen (ST 18), Taichong (LR 3), Danzhong (CV 17)	31.5	80.0
36	Zusanli (ST 36)	Wuyi (ST 15), Rugen (ST 18)	31.5	85.7
37	Zusanli (ST 36)	Rugen (ST 18), Sanyinjiao (SP 6)	31.5	85.7
38	Taichong (LR 3)	Rugen (ST 18), Zusanli (ST 36), Danzhong (CV 17)	31.5	85.7
39	Zusanli (ST 36)	Rugen (ST 18), Taichong (LR 3), Danzhong (CV 17)	31.5	85.7
40	Danzhong (CV 17)	Wuyi (ST 15), Rugen (ST 18)	31.5	88.6
41	Danzhong (CV 17)	Rugen (ST 18), Sanyinjiao (SP 6)	31.5	88.6
42	Taichong (LR 3)	Rugen (ST 18), Sanyinjiao (SP 6)	31.5	91.4

2.3 Frequencies and analyses of the affiliated meridians

In acupuncture treatment of MGH, points were majorly selected from the Stomach Meridian of Foot Yangming, the Liver Meridian of Foot Jueyin and the Bladder Meridian of Foot Taiyang. The affiliations of the top 20 points and the rank of the involved meridians are shown in Table 3.

2.4 Frequencies and analyses of the specific points

A total of 44 specific points occurred in acupuncture treatment of MGH with a total frequency of 878. Specific points ranked in the top five of the frequency list were the five Shu-Transmitting points, Front-Mu points, Yuan-Primary points, Eight Influential points, and Back-Shu points, of which, the five Shu-Transmitting points, Back-Shu points and Front-Mu points were more commonly used. Danzhong (CV 17), Taichong (LR 3) and Zusanli (ST 36) ranked the top three in the list of specific points (Table 4).

2.5 Rules and analyses of the distribution areas of the points

In the treatment of MGH with acupuncture, it's found that the points were predominantly distributed in thoracic and abdominal regions and lower limbs, and the frequencies were 36.0% and 35.1% respectively (Table 5).

Table 3. Frequency of the affiliated meridians in the treatment of MGH with acupuncture

Ranking	Meridian	Frequency	Number of point	Point and frequency
1	Stomach	197	4	Zusanli (ST 36) 62, Rugen (ST 18) 61, Wuyi (ST 15) 43, Fenglong (ST 40) 31
2	Liver	108	2	Taichong (LR 3) 72, Qimen (LR 14) 36
3	Bladder	100	3	Ganshu (BL 18) 39, Shenshu (BL 23) 33, Pishu (BL 20) 28
4	Conception	96	2	Danzhong (CV 17) 78, Guanyuan (CV 4) 18
5	Spleen	71	2	Sanyinjiao (SP 6) 56, Xuehai (SP 10) 15
6	Gall Bladder	47	2	Jianjing (GB 21) 30, Yanglingquan (GB 34) 17
7	Kidney	36	1	Taixi (KI 3) 36
8	Large Intestine	33	1	Hegu (LI 4) 33
9	Small Intestine	24	1	Tianzong (SI 11) 24
10	Pericardium	14	1	Neiguan (PC 6) 14

Table 4. Frequency of the specific acupoints in the treatment of MGH with acupuncture

Ranking	Specific point	Frequency	Number of point	Point and frequency
1	Five Shu-Transmitting points	216	13	Taichong (LR 3) 73, Taixi (KI 3) 36, Yanglingquan (GB 34) 17, Xingjian (LR 2) 6, Zulinqi (GB 41) 5, Zusanli (ST 36) 5, Shaoze (SI 1) 4, Xiaxi (GB 43) 4, Quchi (LI 11) 3, Shaochong (HT 9) 1, Yinlingquan (SP 9) 3, Xiangu (ST 43) 1, Yuji (LU 10) 1
2	Front-Mu points	144	6	Danzhong (CV 17) 78, Qimen (LR 14) 36, Guanyuan (CV 4) 18, Zhongwan (CV 12) 8, Tianshu (ST 25) 3, Zhongfu (LU 1) 1
3	Yuan-Primary points	144	4	Taichong (LR 3) 73, Taixi (KI 3) 36, Hegu (LI 4) 33, Daling (PC 7) 2
4	Eight Influential points	110	4	Danzhong (CV 17) 78, Yanglingquan (GB 34) 17, Zhongwan (CV 12) 8, Geshu (BL 17) 7
5	Back-Shu points	107	7	Ganshu (BL 18) 39, Shenshu (BL 23) 33, Pishu (BL 20) 28, Weishu (BL 21) 4, Xinshu (BL 15) 1, Danshu (BL 19) 1, Sanjiaoshu (BL 22) 1
6	Lower He-Sea points	79	2	Zusanli (ST 36) 62, Yanglingquan (GB 34) 17
7	Luo-Connecting points	46	3	Fenglong (ST 40) 31, Neiguan (PC 6) 14, Guangming (GB 37) 1
8	Confluent Points of the Eight Extraordinary Meridians	31	4	Neiguan (PC 6) 14, Waiguan (TE 5) 9, Zulinqi (GB 41) 5, Zhaohai (KI 6) 3
9	Xi-Cleft points	1	1	Shuiquan (KI 5) 1

Table 5. Distribution areas of points used in the treatment of MGH with acupuncture

Ranking	Region	Frequency	Number of point	Point and frequency
1	Face and neck	8	4	Fengfu (GV 16) 3, Baihui (GV 20) 2, Renying (ST 9) 2, Dazhui (GV 14) 1
2	Upper limbs	71	11	Hegu (LI 4) 33, Neiguan (PC 6) 14, Waiguan (TE 5) 9, Shaoze (SI 1) 4, Quchi (LI 11) 3, Daling (PC 7) 2, Ruxian (Extra) 2, Xiongtong (Extra) 1, Bizhong (Extra) 1, Yuji (LU 10) 1, Shaochong (HT 9) 1
3	Thoracic and abdominal regions	331	25	Danzhong (CV 17) 78, Rugen (ST 18) 61, Wuyi (ST 15) 43, Qimen (LR 4) 36, Ashi 26, Guanyuan (CV 4) 18, Yingchuang (ST 16) 12, Qihai (CV 6) 11, Zhongwan (CV 12) 8, Zigong (EX-CA 1) 6, (KI 23) 5, Lingxu (KI 24) 4, Jiuwei(CV 15) 4, Bulang (KI 22) 3, Tianshu (ST 25) 3, Tianxi (SP 18) 3, Guilai (ST 29) 2, Huangshu (KI 16) 1, Wailing (ST 26) 1, Zhongfu (LU 1) 1, Xiawan (CV 10) 1, Daimai (GB 26) 1, Huaroumen (ST 24) 1, Yinjiao (CV 7) 1, Shuifen (CV 9) 1
4	Dorsal region	175	13	Ganshu (BL 18) 39, Shenshu (BL 23) 33, Jianjing (GB 21) 30, Pishu (BL 20) 28, Tianzong (SI 11) 24, Geshu (BL 17) 7, Weishu (BL 21) 4, Mingmen (GV 4) 3, Jiaji (EX-B 2) 3, Xinshu (BL 15) 1, Danshu (BL 19) 1, Sanjiaoshu (BL 22) 1, Gaohuang (BL 43) 1
5	Lower limbs	317	18	Taichong (LR 3) 73, Zusanli (ST 36) 62, Sanyinjiao (SP 6) 56, Fenglong (ST 40) 31, Taixi (KI 3) 36, Yanglingquan (GB 34) 17, Xuehai (SP 10) 15, Xingjian (LR 2) 6, Zulinqi (GB 41) 5, Xiaxi (GB 43) 4, Zhaohai (KI 6) 3, Yinlingquan (SP 9) 3, Futong (Extra) 1, Shenbing (Extra) 1, Ququan (LR 8) 1, Shuiquan (KI 5) 1, Guangming (GB 37) 1, Xiangu (ST 43) 1

3 Discussion

Modern medicine holds that endocrine disturbance is the underlying cause of MGH. Besides, Huang XM[119] found that the imbalanced $CD4^+$ and $CD8^+$ and impaired immunity level make it difficult for the immune system to distinguish, inhibit and kill the abnormal cells, and subsequently cause MGH. Studies showed that acupuncture can modulate the level of estradiol and inhibit it from binding with its receptors[120-121]; moreover, acupuncture can regulate the immune function via enhancing the levels of $CD4^+$ and interleukin (IL)-2 and down-regulating the levels of $CD8^+$ and tumor necrosis factor (TNF)-α, and finally inhibit the development of MGH[122-123].

As a novel technique, data mining is to extract and discover the rules of things from mass data[124-125]. This study was to analyze the points prescriptions and explore the points-selection features and rules in acupuncture treatment of MGH. The results revealed the following characteristics: Danzhong (CV 17), Taichong (LR 3), Zusanli (ST 36) and Sanyinjiao (SP 6) were most commonly used, and the grouping of Taichong (LR 3), Zusanli (ST 36) and Danzhong (CV 17) was the most predominant points grouping; the points were basically selected along the meridian, majorly including the Stomach Meridian of Foot Yangming, Liver Meridian of Foot Jueyin and Bladder Meridian of Foot Taiyang; regarding the use of specific points, the five Shu-Transmitting points, Front-Mu points and Yuan-Primary points were most frequently selected, and the five Shu-Transmitting points ranked the top; the selected points were substantially distributed in thoracic and abdominal regions and lower limbs, focused on the areas around mammary gland and the Conception Vessel: Guanyuan (CV 4) and Qihai (CV 6) were predominant among the abdominal points, Taichong (LR 3) and Zusanli (ST 36) ranked the top among the lower-limb points; the combination of thoracic and lower-limb points showed the emphasis on both local and distant points in acupuncture for MGH.

The results showed that acupuncture treatment of MGH involved 10 meridians, of which, the associations among the Stomach Meridian, Liver Meridian, Bladder Meridian and Conception Vessel were most distinctive. The high frequencies of the use of these meridians reflect that the clinical practice is in accordance with the acupuncture theories. Modern research showed that acupuncture at Danzhong (CV 17) and Sanyinjiao (SP 6) can down-regulate the high level of estrogen in serum caused by external estradiol[126]; acupuncture at Zusanli (ST 36) and Taichong (LR 3) can regulate the endocrine function and produce analgesic effect[127-128]; acupuncture at lower-abdominal points such as Guanyuan (CV 4) and Zigong (EX-CA 1) can enhance the discharge rate of the neurons related to gonadotropin-releasing hormone (GnRH) and effectively modulate the activity of hypothalamic-pituitary-ovarian axis[129]. The involved local points are in the same or similar segmental innervations with mammary glands, and the rich lymphatic vessels inside mammary tissues can adjust the immune function. Therefore, acupuncture at

the local points benefits the inhibition of MGH.

In a summary, in acupuncture treatment of MGH, local point Danzhong (CV 17) was predominantly selected in combination with distant points including Taichong (LR 3), Zusanli (ST 36) and Sanyinjiao (SP 6); the data mining results are in accordance with the theories of traditional acupuncture therapy, providing evidences for both clinical and experimental research on acupuncture treatment of MGH.

Conflict of Interest

There was no potential conflict of interest in this article.

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