

Clinical regularities in acupuncture-moxibustion treatment of cancer pain in recent 30 years

近 30 年针灸治疗癌性疼痛临床规律评述

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Abstract

Objective: To explore the clinical regularities in acupuncture-moxibustion treatment of cancer pain by reviewing the relevant studies published between 1985 and 2017.

Methods: Based on the *Chinese Medicine Acupuncture-moxibustion Information Database*, quantitative analysis, correlation analysis and Chi-square test were applied to analyze the commonly used acupoints, meridian affiliations and body region distributions, commonly used methods and acupoint correlations, treatment method correlations, the efficacy of acupuncture-moxibustion plus the three-step analgesic ladder for cancer pain, and indicators.

Results: Zusanli (ST 36), Ashi point and Sanyinjiao (SP 6) ranked the top on the list of frequency; points from Bladder Meridian of Foot Taiyang and Stomach Meridian of Foot Yangming were often used; points from the lower limbs and back had high frequencies. The most commonly used treatment method was acupuncture-moxibustion plus medication. Acupuncture-moxibustion plus the three-step analgesic ladder showed certain advantage compared with the two methods used separately, and among the integrated methods, acupoint application plus the three-step analgesic ladder produced the most significant efficacy. It took (44.77±55.54) min for the analgesic effect to act and the effect lasted for (12.81±14.59) h. Numerical rating scale (NRS), visual analog scale (VAS) and Karnofsky performance status (KPS) scores all showed significant changes after interventions (all $P < 0.01$); there was no significant change in the score of quality of life (QOL) after interventions ($P > 0.05$).

Conclusion: Zusanli (ST 36), Ashi point and Sanyinjiao (SP 6) are commonly selected in acupuncture-moxibustion treatment of cancer pain; acupuncture and acupoint application are often used; acupuncture-moxibustion plus the three-step analgesic ladder can boost the treatment efficacy.

Keywords: Acupuncture Therapy; Moxibustion Therapy; Acupuncture-moxibustion Therapy; Cancer Pain; Databases (Traditional Chinese Medicine); Pain Measurement; Karnofsky Performance Status (KPS); Bibliometrics

【摘要】目的: 回顾 1985 年至 2017 年有关针灸治疗癌性疼痛文献, 探索针灸治疗癌性疼痛的临床规律。**方法:** 根据《中医针灸信息库》, 采用计量分析、关联性分析和卡方检验对针灸治疗癌性疼痛的常用穴位、腧穴归经和部位分布、常用治疗方法及穴位关联性、治疗方法关联性、针灸结合三阶梯治疗癌性疼痛的疗效及效应指标进行分析。**结果:** 足三里、阿是穴和三阴交应用频次最高; 多用足太阳膀胱经和足阳明胃经穴; 下肢穴位和背部穴位使用频次最高。治疗方法以针药并用为主, 针灸结合三阶梯疗法优于单纯三阶梯疗法和单纯针灸疗法, 其中穴位贴敷结合三阶梯疗效更明显。癌性疼痛缓解起效时间为(44.77±55.54) min; 缓解持续时间为(12.81±14.59) h。治疗前后疼痛数字评价量表(NRS)、视觉模拟量表(VAS)和卡氏行为状态量表(KPS)评分比较, 差异均有统计学意义(均 $P < 0.01$); 生活质量(QOL)评分治疗前后比较, 差异无统计学意义($P > 0.05$)。**结论:** 针灸治疗癌性疼痛常取足三里、阿是穴和三阴交; 多用针刺和穴位贴敷法; 针灸结合三阶梯止痛法可提高疗效。

【关键词】 针刺疗法; 灸法; 针灸疗法; 癌性疼痛; 中医药信息数据库; 疼痛测评; 卡氏功能状态; 文献计量学

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In 1985, Lu Xiao-shi, *et al* from Shanghai Prevention and Treatment Center of Tuberculosis once published a paper entitled *Acupoint Block with Pluaine for Late-stage Cancer Pain in Zhongguo Zhen Jiu*, which

had opened the prelude to the study of acupuncture-moxibustion for cancer pain^[1]. The standardized incidence ratio (SIR) of malignant tumors in Chinese population was 190.17/100 000 in 2013, higher than 186.15/100 000 on a global level; the cumulative incidence (0-74 years old) was 21.6%; the incidence was higher in urban areas than in rural areas^[2]. Of all the

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symptoms that may develop in cancer, pain is the most common and difficult one, severely affecting the patients' quality of life (QOL). Through literature analysis of acupuncture treatment of cancer pain in the past 30 years, this paper aimed to summarize its clinical rules and provide evidence for studying cancer pain treated with acupuncture- moxibustion.

1 Materials and Methods

The *Chinese Medicine Acupuncture-moxibustion Information Database* has indexed 78 040 acupuncture literatures, including 237 literatures related to cancer pain treated with acupuncture-moxibustion. In order to improve the quality, the involved complicated acupuncture-moxibustion terms have been unified and standardized in the database. The disease terminologies have referred to the *Medical Subject Headings* (MeSH version 2017)^[3], *Medical Subject Headings Annotated Alphabetic List* (MeSHAAL)^[4] and *Chinese Traditional Medicine and Materia Medica Subject Headings List*^[5]; the treatment methods have referred to the *Chinese Traditional Medicine and Materia Medica Subject Headings List*^[5]; acupoints were all in accordance with the *Nomenclature and Location of Acupuncture Points* (GB/T 12346-2006)^[6]; ear points all conformed to the *Nomenclature and Location of Ear Acupuncture Points* (GB/T13734-2008)^[7]; scalp points were according to the *Standardized Manipulations of Acupuncture and Moxibustion-Part 2: Scalp Acupuncture* (GB/T21709.2-2008)^[8]. This database has provided an ideal platform for retrieving acupoints, acupuncture-moxibustion therapies, efficacies and systematic evaluations.

1.1 Literature source

The literatures published before 2013 were provided by the *Chinese Medicine Acupuncture-moxibustion Information Database* (software registration number: 0980769) developed by Shanghai Research Institute of Acupuncture and Meridian. The acupoints selected and treatments used for a certain disease were analyzed based on the statistics section of the database, by inputting the reference disease name or code, such as 'pain/tumor or 1460'.

The literatures published between January 2014 and December 2017 were searched from China National Knowledge Infrastructure (CNKI), Wanfang Academic Journal Full-text Database (Wanfang) and Chongqing VIP Database (CQVIP). The main retrieval terms were 'acupuncture', 'acupuncture-moxibustion', 'needle', 'moxibustion', 'ear', 'acupoint', 'point', 'application', 'sticking', 'thread embedding', 'electrical stimulation', 'cancerous pain', 'cancer pain', and 'tumor'. The search strategy was developed by subjects, titles or key words linked by AND or OR. The data obtained from the above databases were put into the *Chinese Medicine Acupuncture-moxibustion Information Database*.

All the literatures on acupuncture-moxibustion treatment of cancer pain found in the *Chinese Medicine Acupuncture-moxibustion Information Database* were screened after output.

1.2 Literature screening criteria

1.2.1 Literature inclusion criteria

The general inclusion criteria for literatures on acupuncture-moxibustion treatment of cancer pain: papers studying acupuncture-moxibustion treatment of cancer pain and the type of paper was not limited; the type of research was not limited; the acupuncture-moxibustion method, the type of cancer and the course of treatment were not limited; those with acupoints and treatment methods specifically described.

Inclusion criteria for clinical papers on acupuncture-moxibustion treatment of cancer pain: clinical studies or clinical reports of acupuncture-moxibustion for cancer pain; clinical study designs, including randomized controlled trials (RCTs), controlled clinical trials (CCTs) and simple clinical observations; with definite acupoints, treatment methods, observation indicators, outcome indicators and safety evaluation, while follow-up was not required.

1.2.2 Literature exclusion criteria

Duplicate publications, or published in different languages, such as in both Chinese and English; those with significant errors or mistakes.

1.3 Data processing

The data were generally analyzed by the *Chinese Medicine Acupuncture-moxibustion Information Database*. Frequency analysis was made for the points that occurred in over 15% and treatment methods that appeared in more than 5% of the included studies. The predominantly used points and acupuncture-moxibustion treatment methods were then summarized. Clementine 12.0 data analysis software was used for correlation analysis with the Apriori algorithm.

2 Results

2.1 General analysis of the included studies

A total of 239 articles on acupuncture-moxibustion treatment of cancer pain were retrieved, including 196 clinical studies, accounting for 82.0%, 28 literature research papers, making up for 11.7%, and 15 papers in the form of medical record, famous doctor experience and experimental research, accounting for 6.3%.

It can be seen from Figure 1 that the number of the studies on acupuncture-moxibustion treatment of cancer pain has been increasing, and the first significant growth occurred in 2008 while it went virus since 2013. At the same time, the annual growth tendency in the number of clinical papers was basically consistent with that of the total paper, especially after 2013.

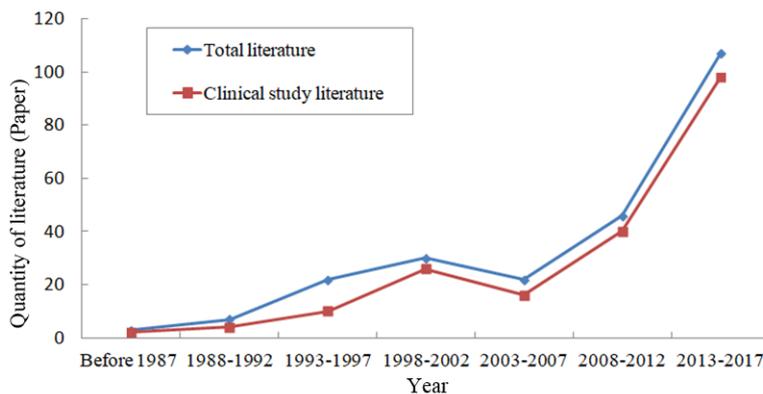


Figure 1. Annual analysis of papers on acupuncture-moxibustion treatment of cancer pain

2.2 Analysis of acupoints selected in clinical studies

2.2.1 Analysis of acupoints commonly used for acupuncture-moxibustion treatment of cancer pain

The 196 clinical papers on acupuncture-moxibustion treatment of cancer pain involved a total of 8 606 patients, of which 7 771 showed effective, and the effective rate was 90.3%. A total of 154 points were involved, including 103 from the fourteen ordinary

meridians, 29 auricular points, 19 extra points, and 3 scalp points. It can be seen from Table 1 that Zusanli (ST 36) had the highest frequency of use, which was 93, followed by Ashi point whose frequency was 72; the acupoints with comparatively higher total efficiency were Ashi point, Sanyinjiao (SP 6) and Ganshu (BL 18), which all reached over 91.7%.

Table 1. Major acupoints used in acupuncture-moxibustion treatment of cancer pain

Acupoint	Frequency	Total number of patients (case)	Effective cases (case)	Invalid cases (case)	Total effective rate (%)
Zusanli (ST 36)	93	4 033	3 629	404	90.0
Ashi point	72	2 978	2 737	241	91.9
Sanyinjiao (SP 6)	50	2 255	2 070	185	91.8
Neiguan (PC 6)	47	2 067	1 853	214	89.6
Hegu (LI 4)	40	1 716	1 560	156	90.9
Feishu (BL 13)	28	1 215	1 095	120	90.1
Ganshu (BL 18)	27	1 199	1 100	99	91.7

2.2.2 Meridian and body region distribution of the acupoints used for acupuncture-moxibustion treatment of cancer pain

The Bladder Meridian of Foot Taiyang had the highest frequency, which was 150, and then it was the Stomach Meridian of Foot Yangming, whose frequency was 131 (Table 2). The lower-limb and back points had higher frequencies, which were 278 and 178, respectively (Table 3). The acupoint regularity analysis showed that in acupuncture-moxibustion treatment of cancer pain, topical points and distant points were used together. The topical points were represented by Ashi point, and points in the chest and abdomen regions such as Zhongwan (CV 12), Qimen (LR 14), Guanyuan (CV 4) and Danzhong (CV 17). The distant points showed the concept of holism in acupuncture-moxibustion therapy and thus had certain advantage in regulating the whole. The mostly selected distant points included the lower-limb points Zusanli (ST 36), Sanyinjiao (SP 6),

Yanglingquan (GB 34) and Taichong (LR 3), and Back-Shu points such as Feishu (BL 13), Ganshu (BL 18), Shenshu (BL 23) and Weishu (BL 21).

2.2.3 Acupoints correlation analysis in acupuncture-moxibustion treatment of cancer pain

Correlation analysis was made for the most commonly-selected points (Table 4).

Support indicates the rate of the number of the former item to the total amount. In this article, it meant the rate of the number of articles containing the former acupoint to the total amount of literatures. The acupoints with a confidence level >95% were sequenced, and the one with the highest support was Zusanli (ST 36).

Regulatory support indicates the rate of the number of studies containing both the former and latter items to the total number of studies. In this article, the acupoint pair that owned the highest regulatory support was Zusanli (ST 36) and Sanyinjiao (SP 6).

Confidence stands for the ratio between the regulatory support and the support. It's found that seven pairs of acupoints owned a confidence of 100%, indicating that the ratio of the studies containing both the former and latter items to the studies containing the former item was 100%, such as Zusanli (ST 36) versus Feishu (BL 13) plus Neiguan (PC 6).

2.3 Analysis of treatment methods in the clinical studies

2.3.1 Analysis of the commonly used acupuncture-moxibustion treatments for cancer pain

As can be seen from Table 5, acupuncture-moxibustion treatment of cancer pain involved a total of 16 treatment methods. The use of acupuncture-moxibustion plus medication had the highest frequency, and the total effective rate of acupoint application was

93.4%.

2.3.2 Correlation analysis of the treatment methods in acupuncture-moxibustion treatment of cancer pain

The treatment methods with a confidence level of 50% or higher were sequenced (Table 6). Acupuncture-moxibustion plus medication was found having the highest support, and the integrated treatment method with the highest regulatory support was acupuncture-moxibustion plus medication and acupoint application. In this paper, the treatment combination that had the highest confidence was acupuncture-moxibustion plus medication and acupoint application, which meant that 68% of the studies using acupoint application to treat cancer pain also used acupuncture-moxibustion plus medication. Acupuncture-moxibustion plus medication and electroacupuncture (EA) ranked the second.

Table 2. Meridian distribution of acupoints used for acupuncture-moxibustion treatment of cancer pain

Meridian	Frequency	Point and frequency (time)
Bladder Meridian	150	Feishu (BL 13) (28), Ganshu (BL 18) (27), Shenshu (BL 23) (18), Weishu (BL 21) (14), Xinshu (BL 15) (11), Pishu (BL 20) (11), Dachangshu (BL 25) (9), Geshu (BL 17) (8), Fengmen (BL 12) (5), Danshu (BL 19) (5), Dazhu (BL 11) (2), Weizhong (BL 40) (2), Tianzhu (BL 10) (1), Sanjiaoshu (BL 22) (1), Qihai (BL 24) (1), Guanyuanshu (BL 26) (1), Xiaochangshu (BL 27) (1), Ciliao (BL 32) (1), Gaohuang (BL 43) (1), Zhibian (BL 54) (1), Kunlun (BL 60) (1), Shenmai (BL 62) (1)
Stomach Meridian	131	Zusanli (ST 36) (93), Liangqiu (ST 34) (9), Tianshu (ST 25) (8), Fenglong (ST 40) (5), Shangjuxu (ST 37) (4), Xiajuxu (ST 39) (3), Rugen (ST 18) (2), Liangmen (ST 21) (2), Ruzhong (ST 17) (1), Huaroumen (ST 24) (1), Wailing (ST 26) (1), Guilai (ST 29) (1), Xiaguan (ST 7) (1)
Conception Vessel	78	Zhongwan (CV 12) (24), Guanyuan (CV 4) (12), Danzhong (CV 17) (10), Shenque (CV 8) (8), Shangwan (CV 13) (7), Tiantu (CV 22) (6), Qihai (CV 6) (5), Zhongting (CV 16) (3), Xiawan (CV 10) (1), Qugu (CV 2) (1), Chengjiang (CV 24) (1)
Liver Meridian	76	Qimen (LR 14) (22), Taichong (LR 3) (21), Ququan (LR 8) (10), Zhangmen (LR 13) (9), Zhongdu (LR 6) (8), Xingjian (LR 2) (6)
Spleen Meridian	70	Sanyinjiao (SP 6) (50), Yinlingquan (SP 9) (10), Xuehai (SP 10) (7), Daheng (SP 15) (1), Gongsun (SP 4) (1), Dijie (SP 8) (1)
Large Intestine Meridian	59	Hegu (LI 4) (40), Quchi (LI 11) (11), Shousanli (LI 10) (5), Jugu (LI 16) (1), Yingxiang (LI 20) (1), Wenliu (LI 7) (1)
Pericardium Meridian	48	Neiguan (PC 6) (47), Laogong (PC 8) (1)
Gallbladder Meridian	45	Yanglingquan (GB 34) (23), Xuanzhong (GB 39) (5), Fengchi (GB 20) (4), Qiuxu (GB 40) (4), Huantiao (GB 30) (3), Toulinqi (GB 15) (1), Jianjing (GB 21) (1), Riyue (GB 24) (1), Wushu (GB 27) (1), Xiashi (GB 43) (1), Shuaigu (GB 8) (1)
Lung Meridian	27	Kongzui (LU 6) (11), Chize (LU 5) (7), Zhongfu (LU 1) (3), Lieque (LU 7) (3), Taiyuan (LU 9) (2), Shaoshang (LU 11) (1)
Governor Vessel	25	Dazhui (GV 14) (12), Baihui (GV 20) (5), Shuigou (GV 26) (2), Yintang (GV 29) (2), Yaoyangguan (GV 3) (2), Mingmen (GV 4) (2)
Triple Energizer Meridian	11	Zhigou (TE 6) (5), Waiguan (TE 5) (3), Sanyangluo (TE 8) (3)
Kidney Meridian	9	Zhubin (KI 9) (3), Yongquan (KI 1) (2), Taixi (KI 3) (2), Henggu (KI 11) (1), Zhaohai (KI 6) (1)
Heart Meridian	7	Shaofu (HT 8) (4), Shenmen (HT 7) (3)
Small Intestine Meridian	7	Tianzong (SI 11) (3), Yanglao (SI 6) (2), Quyuan (SI 13) (1), Jianwaishu (SI 14) (1)

Table 3. Body region distribution of acupoints used for acupuncture-moxibustion treatment of cancer pain

Body region	Frequency	Point and frequency (time)
Lower limbs	276	Zusanli (ST 36) (93), Sanyinjiao (SP 6) (50), Yanglingquan (GB 34) (23), Taichong (LR 3) (21), Ququan (LR 8) (10), Yinlingquan (SP 9) (10), Liangqiu (ST 34) (9), Zhongdu (LR 6) (8), Xuehai (SP 10) (7), Xingjian (LR 2) (6), Xuanzhong (GB 39) (5), Fenglong (ST 40) (5), Shangjuxu (ST 37) (4), Qiuxu (GB 40) (4), Huantiao (GB 30) (3), Xiajuxu (ST 39) (3), Zhubin (KI 9) (3), Weizhong (BL 40) (2), Yongquan (KI 1) (2), Taixi (KI 3) (2), Kunlun (BL 60) (1), Shenmai (BL 62) (1), Xiashi (GB 43) (1), Zhaohai (KI 6) (1), Gongsun (SP 4) (1), Dijii (SP 8) (1)
Back	168	Feishu (BL 13) (28), Ganshu (BL 18) (27), Shenshu (BL 23) (18), Weishu (BL 21) (14), Dazhui (GV 14) (12), Xinshu (BL 15) (11), Pishu (BL 20) (11), Dachangshu (BL 25) (9), Geshu (BL 17) (8), Fengmen (BL 12) (5), Danshu (BL 19) (5), Tianzong (SI 11) (3), Dazhu (BL 11) (2), Yaoyangguan (GV 3) (2), Mingmen (GV 4) (2), Sanjiaoshu (BL 22) (1), Gao Huang (BL 43) (1), Jianjing (GB 21) (1), Jugu (LI 16) (1), Quyuan (SI 13) (1), Jianwaishu (SI 14) (1), Qihai (BL 24) (1), Guanyuanshu (BL 26) (1), Xiaochangshu (BL 27) (1), Ciliao (BL 32) (1), Zhibian (BL 54) (1)
Upper limbs	149	Neiguan (PC 6) (47), Hegu (LI 4) (40), Kongzui (LU 6) (11), Quchi (LI 11) (11), Chize (LU 5) (7), Lieque (LU 7) (3), Shousanli (LI 10) (5), Zhigou (TE 6) (5), Shaofu (HT 8) (4), Shenmen (HT 7) (3), Waiguan (TE 5) (3), Sanyangluo (TE 8) (3), Yanglao (SI 6) (2), Taiyuan (LU 9) (2), Shaoshang (LU 11) (1), Laogong (PC 8) (1), Wenliu (LI 7) (1)
Chest and abdomen	131	Zhongwan (CV 12) (24), Qimen (LR 14) (22), Guanyuan (CV 4) (12), Danzhong (CV 17) (10), Zhangmen (LR 13) (9), Shenque (CV 8) (8), Tianshu (ST 25) (8), Shangwan (CV 13) (7), Tiantu (CV 22) (6), Qihai (CV 6) (5), Zhongting (CV 16) (3), Zhongfu (LU 1) (3), Rugen (ST 18) (2), Liangmen (ST 21) (2), Xiawan (CV 10) (1), Riyue (GB 24) (1), Ruzhong (ST 17) (1), Huaroumen (ST 24) (1), Qugu (CV 2) (1), Wushu (GB 27) (1), Henggu (KI 11) (1), Daheng (SP 15) (1), Wailing (ST 26) (1), Guilai (ST 29) (1)
Head	19	Baihui (GV 20) (5), Fengchi (GB 20) (4), Yintang (GV 29) (2), Shuigou (GV 26) (2), Chengjiang (CV 24) (1), Yingxiang (LI 20) (1), Xiaguan (ST 7) (1), Taiyang (EX-HN 5) (1), Toulinqi (GB 15) (1), Shuaigu (GB 8) (1)

Table 4. Correlation analysis of acupoints used for acupuncture-moxibustion treatment of cancer pain

Sequence	Former item	Latter item	Regulatory support (%)	Support (%)	Confidence (%)
1	Feishu (BL 13) and Neiguan (PC 6)	Zusanli (ST 36)	6.3	6.3	100.0
2	Feishu (BL 13), Neiguan (PC 6) and Sanyinjiao (SP 6)	Zusanli (ST 36)	5.2	5.2	100.0
3	Hegu (LI 4), Neiguan (PC 6) and Sanyinjiao (SP 6)	Zusanli (ST 36)	10.4	10.4	100.0
4	Hegu (LI 4) and Zusanli (ST 36)	Sanyinjiao (SP 6)	10.4	10.4	100.0
5	Neiguan (PC 6) and Sanyinjiao (SP 6)	Zusanli (ST 36)	6.9	6.9	100.0
6	Hegu (LI 4), Neiguan (PC 6) and Sanyinjiao (SP 6)	Zusanli (ST 36)	6.3	6.3	100.0
7	Hegu (LI 4), Neiguan (PC 6) and Zusanli (ST 36)	Sanyinjiao (SP 6)	6.3	6.3	100.0
8	Ashi point and Sanyinjiao (SP 6)	Zusanli (ST 36)	14.9	15.5	96.3
9	Hegu (LI 4) and Neiguan (PC 6)	Zusanli (ST 36)	12.6	13.2	95.7

Table 5. Commonly used acupuncture-moxibustion treatments for cancer pain

Treatment method	Frequency	Total patients (case)	Total effective cases (case)	Invalid cases (case)	Total effective rate (%)
Acupuncture plus medication	82	3 298	3 045	253	92.3
Acupuncture	54	2 426	2 175	251	89.7
Hydroacupuncture	31	1 392	1 251	141	89.9
Acupoint application	31	1 391	1 299	92	93.4
Auricular acupuncture	24	1 307	1 193	114	91.3
Moxibustion	23	880	809	71	91.9
EA	17	701	641	60	91.4
Wrist-ankle acupuncture	10	360	327	33	90.8

Table 6. Correlation analysis of acupuncture-moxibustion methods for cancer pain

Sequence	Former item	Latter item	Regulatory support (%)	Support (%)	Confidence (%)
1	Acupoint application	Acupuncture plus medication	13.3	19.7	67.7
2	EA	Acupuncture plus medication	5.8	9.9	58.8
3	Hydroacupuncture and acupuncture	Moxibustion	2.9	5.3	55.6
4	-	Acupuncture plus medication	50.9	100.0	50.9
5	Wrist-ankle acupuncture	Acupuncture plus medication	2.9	5.8	50.0
6	Moxibustion	Acupuncture plus medication	6.4	12.7	50.0

2.3.3 Comparison of the treatment efficacy of three different treatment methods for cancer pain

The randomized controlled studies were sorted by Western medication, acupuncture-moxibustion therapy (including acupuncture, acupoint application, auricular acupuncture, wrist-ankle acupuncture, moxibustion and EA) and Western medication plus acupuncture-moxibustion therapy to compare the clinical efficacy. According to Table 7, there were 71 articles using Western medication, 28 articles using acupuncture-moxibustion therapy, and 73 articles using Western

medication plus acupuncture-moxibustion therapy, indicating that the acupuncture-moxibustion therapy had a low reliability in clinical treatment of cancer pain and novel effective treatment is required; the total effective rate of Western medication plus acupuncture-moxibustion therapy was 91.6%, which was higher than that of either using Western medication or acupuncture-moxibustion therapy alone, with statistical significance ($P<0.01$), indicating that Western medication plus acupuncture-moxibustion therapy can boost the clinical efficacy.

Table 7. Therapeutic comparison of three different treatment methods

Treatment method	Frequency	Total patients (case)	Total effective cases (case)	Total invalid cases (case)	Effective rate (%)
Western medication	71	3 296	2 819	477	85.5
Western medication plus acupuncture-moxibustion	73	3 013	2 759	254	91.6 ¹⁾
Acupuncture-moxibustion	28	938	825	113	88.0

Note: Compared with Western medication or acupuncture-moxibustion, 1) $P<0.01$

2.3.4 Three-step analgesic ladder for cancer pain

The three-step analgesic ladder recommended by the World Health Organization (WHO) in 1986 for cancer pain can alleviate more than 90% of cancer pain. It helps improve the QOL and prolong the life span, since some patients have become more confident due to the disappearance of pain. This article classified and analyzed the analgesic drugs involved in the literatures. The main drugs included the first-step drug indomethacin, the second-step drug tramadol hydrochloride sustained-release tablets and oxycodone hydrochloride sustained-release tablets, and the third-step drug fentanyl transdermal plaster and morphine modified-release tablets. Other treatments used together with the three-step ladder analgesics were also sorted. The studies that used the second-step drug when the first-step drug was not effective were classified into the use of the second-step drug. The studies that used the second- and third-step drugs simultaneously were classified into the use of the third-step drug. It can be seen from Table 8 that acupuncture-moxibustion plus the third-step drug accounted for the largest proportion in the relevant

studies, followed by acupuncture-moxibustion therapy plus the second-step drug, indicating that it was the moderate-to-severe cancer pain that this type of treatment mainly focused. Moreover, acupuncture-moxibustion plus the three-step analgesic ladder showed a better treatment result than the three-step analgesic ladder alone. The integrated treatment produced a total effective rate of 92.0% for the moderate-to-severe cancer pain and 100% for the mild ones.

2.4 Analysis of effect indicators in clinical studies

In the studies of acupuncture-moxibustion treatment of cancer pain, the effect indicators mainly included pain relief time, referring to both the onset time and lasting duration of pain relief. The QOL was commonly evaluated by Karnofsky performance status scale (KPS), QOL scale, the European Organization for the Research and Treatment of Cancer (EORTC) QOL questionnaire core 30 (EORTC QLQ-C30), Zubrud-the Eastern Cooperative Oncology Group (ECOG)-WHO (ZPS) score and functional assessment of cancer therapy-general (FACT-G). The scales for pain included numerical rating scale (NRS), visual analog scale (VAS), and the brief pain

questionnaire (BPQ). We summarized and analyzed the most commonly used indicators including the onset time of pain relief, duration of pain relief, VAS, NRS, KPS, and QOL. The results showed that the onset time of cancer pain relief by acupuncture-moxibustion

treatment was (44.77±55.54) min, and the pain relief lasted for (12.81±14.59) h; the NRS, VAS and KPS scores changed significantly after the treatment (all $P<0.01$); there was no significant change in the QOL score after the intervention ($P>0.05$), (Table 9).

Table 8. Therapeutic analysis of the three-step analgesic ladder for cancer pain

Category	Group	Frequency	Patients (case)	Effective cases (case)	Invalid cases (case)	Effective rate (%)
First-step drug	Western medication	1	34	26	8	76.5
	Western medication plus acupuncture-moxibustion	1	60	60	0	100.0
Second-step drug	Western medication	34	1 369	1 155	214	84.4
	Western medication plus acupuncture-moxibustion	31	1 274	1 178	96	92.5
Third-step drug	Western medication	31	1 211	999	212	82.5
	Western medication plus acupuncture-moxibustion	37	1 530	1 400	130	91.5

Table 9. Analysis of effect indicators in the studies of acupuncture-moxibustion treatment of cancer pain

Item	VAS (n=43)	NRS (n=23)	KPS (n=41)	QOL (n=14)
Pre-treatment	13.03±13.77	6.76±1.60	54.66±15.56	35.97±22.54
Post-treatment	5.53±4.67	3.11±1.16	63.51±18.84	32.17±19.91
t-value	4.921	9.238	-5.716	0.769
P-value	0.000	0.000	0.000	0.456

3 Discussion

3.1 Cancer pain

According to the latest data released by the National Cancer Center in 2017, the incidence of malignant tumors nationwide was 270.59/100 000, and the mortality rate was 163.83/100 000. Lung cancer was the leading cause of death and had the highest incidence amongst all types of cancers. About 591 000 people died of lung cancer every year. Cancer has become a significant threat to human health. Over 70% of the cancer patients experience pain, which is considered as the most common and difficult symptom of cancer. 30% of the patients reported mild pain, 40% had moderate pain and those suffered from severe pain also accounted for 40%. However, cancer pain is not well controlled in nearly 50% of the cases, seriously affecting patients' QOL. Eliminating pain in cancer and the nursing care are equally important throughout the treatment^[9].

3.2 Acupoints

Our study showed that in acupuncture-moxibustion treatment of cancer pain, Zusanli (ST 36) had the highest frequency, followed by Ashi point, Sanyinjiao (SP 6), Neiguan (PC 6) and Hegu (LI 4). They were used in over 20% of all the studies, and each of them was used at least 40 times. Zusanli (ST 36) is an acupoint of the Stomach Meridian of Foot Yangming. It works to regulate the function of the spleen and stomach,

replenish qi and blood, and strengthen the healthy qi. Modern researches hold that EA at Zusanli (ST 36) may alleviate the visceral pain in rats through inhibiting the membrane translocation of spinal PKC, and it may reduce the paclitaxel-induced peripheral neuropathy by down-regulating the level of interleukin (IL)-1 α in blood^[10-11]. Meanwhile, EA at Zusanli (ST 36) can activate the sciatic nerve to exert anti-inflammatory effect^[12], that is to say, the analgesic mechanism of Zusanli (ST 36) may be achieved by activating the body's anti-inflammatory effect^[13]. Ashi points are extra points located where the pain occurs. They work directly on the affected areas and produce an analgesic effect. Sanyinjiao (SP 6) is the intersection of the three foot yin meridians. It can regulate qi and blood of the three meridians. The analgesic mechanism of Sanyinjiao (SP 6) may relate to the up-regulation of the serum dynorphin (Dyn) level, and down-regulation of serum 5-hydroxytryptamine (5-HT), dopamine (DA) and noradrenaline (NE) expressions. As a point of the Pericardium Meridian of Hand Jueyin and one of the Eight Confluent Points, Neiguan (PC 6) is mainly used for stomach and cardiac diseases. It can also produce an analgesic effect and is often used in acupuncture anesthesia. EA at Neiguan (PC 6) may release pain by activating the expression of P2X₂ and P2X₃ receptor proteins in the dorsal horn of the spinal cord^[14], and activating the autonomic nerves to exert an anti-inflammatory effect^[15]. Hegu (LI 4) is a point from

the Large Intestine Meridian of Hand Yangming. Yangming meridians are rich in qi and blood. Therefore, this point can boost qi-blood circulation to relieve pain. It is also commonly used for acupuncture anesthesia. Acupuncture at this point can increase the pain threshold^[16], which may be associated with suppressing the increased mRNA levels of P2X₂ and P2X₃ receptors^[17].

The correlation analysis showed that the probability of simultaneous use of Zusanli (ST 36), Hegu (LI 4), Neiguan (PC 6) and Sanyinjiao (SP 6) was 100%, while the probability of simultaneous use of Sanyinjiao (SP 6), Hegu (LI 4), Ashi point, and Zusanli (ST 36) was also 100%. It's indicated that the above two groups of acupoints were usually used together in acupuncture-moxibustion treatment of cancer pain, i.e., Zusanli (ST 36) would definitely appear in the studies that used Hegu (LI 4), Neiguan (PC 6), or Sanyinjiao (SP 6), and Sanyinjiao (SP 6) was inevitably used when Hegu (LI 4), Ashi point, or Zusanli (ST 36) was used.

At the same time, auricular points were also commonly used to treat cancer pain. A total of 29 auricular points were involved, mainly including auricular Shenmen (TF₄, 23 times), Subcortex (AT₄, 20 times), and Sympathetic (AH_{6a}, 18 times). Amongst the studies using Sympathetic (AH_{6a}) and Subcortex (AT₄), auricular Shenmen (TF₄) was inevitably used. Clinical studies have shown that the auricular Shenmen (TF₄) can curb the dosage of analgesics^[18].

3.3 Treatment methods

The systematic evaluation of treatment methods showed that acupuncture plus medication produced was superior to using medication alone in reducing cancer pain^[19]. It was also found that most of the studies used acupuncture-moxibustion and medication together because of the intensity of cancer pain. Here, medication usually means Western medication, especially the three-step analgesic ladder. Most studies that majorly used acupuncture-moxibustion treatment claimed that analgesics were still needed for emergency^[20]. Correlation analysis of therapies unveiled that 68% of all the studies that used acupoint application for cancer pain used the three-step analgesic ladder at the same time. When the relevant studies were sorted based on grouping, the Western medication group and acupuncture plus medication group were equal to each other in the frequency, while the acupuncture group had a lower frequency.

3.4 Comparison of scales

The current principle in tumor treatment is to relieve pain, enhance the QOL and live with the existence of tumor. Therefore, the majority of the studies about cancer pain observed the QOL using multiple scales, including KPS, QOL for tumor patients, EORTC QLQ-C30, ZPS and FACT-G. KPS is a scale for evaluating functional impairment, with a full score of 100. The lower the

score, the worse the QOL. ZPS estimates the physical status at a 5-level (score) basis. The higher the level (score), the worse the functional status. It is usually used to analyze the healthy outcome^[21]. The EORTC QLQ-C30 scale has a wider range of application than KPS, including not only physical functions, but also social functions^[22]. It consists of 30 items in total, covering 15 domains. EORTC QLQ-C30 has been used for determining the QOL of cancer patients. The higher the score in the function and overall health domains, the better the function, while it means the opposite for the symptom domains^[23]. The QOL for cancer patients is a draft formulated by China in 1990 in reference to foreign indicators, with a full score of 60. The higher the score, the better the QOL. FACT-G is a common module for determining the QOL of cancer patients in cancer treatment and function evaluation. It contains 27 items which cover four domains, with a full score of 108. The higher the score, the better the QOL^[24]. The statistical analysis showed that the NRS, VAS and KPS scores all changed significantly after the treatment ($P < 0.01$), while the QOL score didn't show significant change ($P > 0.05$). However, since the data collected in this paper were rather limited, the results obtained here can only be taken for reference.

3.5 Future application and development of acupuncture-moxibustion treatment of cancer pain

3.5.1 Treatment principle

To regulate the spleen-stomach function, replenish qi and blood, and regulate qi to stop pain. To combine topical and integral treatment.

3.5.2 Acupoint selection

Basic prescription: Zusanli (ST 36), Ashi, Sanyinjiao (SP 6), Neiguan (PC 6), and Hegu (LI 4).

Symptoms-based adjustment: For pain in lung cancers, Feishu (BL 13), Danzhong (CV 17) and Kongzui (LU 6) are added; for pain in liver cancers, Ganshu (BL 18), Qimen (LR 14), Taichong (LR 3) and Yanglingquan (GB 34) are added; for pain in stomach cancers, Weishu (BL 21), Zhongwan (CV 12) and Guanyuan (CV 4) are added.

3.5.3 Method

Acupuncture: According to the primary disease and the site of the pain, corresponding adjunct points and Back-Shu points are selected. For excess syndrome, reducing manipulations are used; for deficient syndrome, supplementing manipulations are adopted. Points are selected either from one side or from both sides, and punctured by stainless filiform needles of 0.30 mm in diameter and 25-40 mm in length after standard sterilization. Needling manipulations are performed accordingly upon qi arrival. The needles are retained for 0.5-1.0 h, during which, the needles are manipulated once every 5 minutes. The treatment is conducted once per day.

Acupoint application: According to the theory of 'taking where affected by pain as the point' in traditional Chinese medicine, the ointment is directly applied to the most painful area, which enables the medicine to be absorbed transdermally and reach deep tissues. The treatment is conducted once a day.

The three-step analgesic ladder plus acupuncture-moxibustion should be applied based on the disease condition to enhance the efficacy in the treatment of moderate-to-severe cancer pain. The addition of acupoint application will make this treatment more effective.

3.5.4 Recommendations for clinical research

According to the literature analysis, acupuncture-moxibustion plus the three-step analgesic ladder has certain advantage in clinical efficacy. It is suggested that clinical observations should adopt a large sample size in the future and fortify the use of indicators, such as the onset and length of pain relief, QOL scales including KPS, QOL, EORTC QLQ-C30, ZPS and FACT-G, and pain scales including NRS, VAS and BPQ.

Through classifying and summarizing the literatures studying acupuncture-moxibustion treatment of cancer pain, this paper concluded the commonly used acupoints and methods, the Bladder Meridian of Foot Taiyang as the meridian to be treated for cancer pain, conducted correlation analysis for acupoints and treatment methods, and compared the therapeutic efficacy of acupuncture-moxibustion and/or Western medication. This article also analyzed using acupuncture-moxibustion together with the three-step analgesic ladder in the treatment of cancer pain, finding that this integrated method was often used for moderate-to-severe cancer pain and the treatment result was satisfactory. This study is expected to provide reliable evidence for acupuncture-moxibustion treatment of cancer pain.

Conflict of Interest

The authors declared that there was no potential conflict of interest in this article.

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