The Characteristics, Related Factors and Risk Factors of Insomnia among Postoperative Patients with Gastric Cancer: A Cross-sectional Survey

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Abstract

Purpose

This study aims to explore the characteristics, related factors and risk factors of insomnia of patients after operation for gastric cancer.

Methods

A cross-sectional survey was carried out and finally 115 patients with insomnia after operation for gastric cancer were included. The general information, gastric cancer related information, sleep quality and other symptoms were investigated.

Results

The Pittsburgh sleep quality index score of most insomnia patients after gastric cancer surgery was 11–15 points, the sleep quality rating was “Poor”. The sleep quality of patients with insomnia after surgery for gastric cancer is related to the number of chemotherapy cycles, fatigue and depression. The risk of reduced sleep quality with the number of chemotherapy cycles > 6 is 3.640 times that of ≤ 6. The risk of reduced sleep quality during moderate to severe fatigue was 4.390 times that of patients with no or mild fatigue.

Conclusion

Attention to related factors and risk factors may be associated with improvement of sleep quality in patients with gastric cancer after surgery.

1 Introduction

According to the World Health Organization (WHO), there were 896.63 million cancer deaths worldwide in 2016, making it the second leading cause of death. [1] Besed on GLOBOCAN 2018 statistics, the incidence and death of gastric cancer accounted for the 5th and 3rd of all malignant tumors all over the world, respectively. [2] Anti-tumor tends to be comprehensive measures. [3–5] With the continuous improvement of treatment, the survival period of cancer patients has been prolonged. Improving the quality of life of cancer patients has gradually become the focus of attention and urgent problems to be solved for patients, families, society and clinicians. Symptom management of tumor patients has gradually become a hot spot for medical personnel and scientific researchers. [6, 7] The incidence of insomnia in patients with malignant tumors is 52.6%-67.4%, which is twice that of the general population. [8, 9] However, if effective intervention is not given, chronic insomnia often develops. [10, 11] It will increase the psychological burden of cancer patients, reduce the effect of anti-tumor treatment, and seriously affect

the health of patients. [12, 13] Some studies have shown that sleep can significantly affect human immune function. Insufficient sleep can induce the body's innate immune response, inhibit the proliferation of NK cells, and increase the production of IL-1β, IL-17, etc. [14, 15] Researches, in recent years, have found that insomnia became a common clinical symptom in cancer patients, but patients and doctors did not pay enough attention and treatment to insomnia.[11, 16] Surgical resection is the preferred treatment for gastric cancer. [17] Wang X. et al found that the incidence of disturbed sleep was 90.48% and the risk of symptoms was about 4 points through investigation and analysis of the symptoms of patients after gastric cancer. [18]

This study included patients with insomnia after operation for gastric cancer. The characteristics of sleep quality, related factors and risk factors of the patients were summarized through questionnaire survey and statistical analysis.

2 Methods

2.1 Participants

The cross-sectional study included patients who attended the Oncology Clinic of Guang'anmen Hospital, China Academy of Chinese Medical Sciences between April 2019 and January 2020. The diagnosis of gastric cancer refers to “Regulations for Diagnosis and Treatment of Gastric Cancer (2018 Edition)” [3] and “American Joint Committee on Cancer (AJCC) gastric cancer TNM staging (the 8th version)” [19]. Insomnia is diagnosised on the "Chinese Classification and Diagnostic Criteria for Mental Disorders" (the 3rd version) [20]: ①Difficulty falling asleep, ②often awakening and unstable sleep, ③difficulty falling asleep again after waking up, awakening prematurely in the morning, ④sleeping less than 6 hours, lack of energy during the day, and drowsiness, ⑤history of repeated attacks, occurring ≥ 3 times a week and lasting ≥ 1 month.

The cases were screened according to the following: ①The patients diagnosed with gastric cancer, and the staging being $T_{1-4}N_XM_0$; ②after standard surgery for radical treatment of gastric cancer; ③meeting the diagnostic criteria for insomnia, and the Pittsburgh sleep quality index (PSQI) score being > 5 points; ④over 18 years old; ⑤Karnofsky (KPS) score being ≥ 60 points; ⑥having sufficient cognitive ability to complete the survey; ⑦signing the informed consent form voluntarily.

2.2 Procedures

This study was part of a project of Beijing Science and Technology Commission. The proposal was approved by the Ethics Committee of Guang 'anmen Hospital, China Academy of Chinese Medical Sciences (NO. 2016-118-KY-02). Potential participants were approached and invited to the study on the first day they were admitted to the hospital. This was a convenience sample. The method and purpose of the research were explained to them. After the patients signing the informed consent form, the inclusion criteria were determined, and information was collected for patients who met the inclusion criteria.

2.3 Measurements

(1) General information: age, gender, KPS score, etc.; (2) relevant data of gastric cancer: pathological type, differentiation grade, lauren grade, clinical staging, TNM staging, lesion location, surgical method, number of chemotherapy cycles; (3) main observation index: PSQI scale score; (4) other observation indicators: Piper Fatigue Scale -Chinese Version (PFS-CV) score, and Hospital Anxiety and Depression Scale (HADS) score.

- *PSQI*

The PSQI scale is used to evaluate sleep quality. It consists of self-evaluation and other-evaluated items, and only 19 self-evaluation items participated in the scoring, including 7 components. [21] Every component is scored on a scale of 0–3, and the total score ranges from 0 to 21. PSQI score = component (A + B + C + D + E + F + G). Table 1 presents the correlation between total PSQI score and sleep quality. The score is higher, the worse the quality of sleep. The diagnostic sensitivity of this scale is 89.6%, and the specificity is 86.5% (kappa = 0.75, $P \leq 0.001$) [21].

Table 1
The correlation between total PSQI score and sleep quality

the total score of PSQI	sleep quality
0–5	good
6–10	general
11–15	poor
16–21	very poor

- *PFS-CV*

The PFS-CV was translated by scholars from Hong Kong in 2003, including 4 dimensions of behavior, emotion, feeling and cognition, with a total of 22 content. The repeat test reliability is 0.98. [22] Every content contains 11 points (0–10 points). Patients are scored according to the degree of their fatigue. Among them, there are 5 items for evaluating feelings and emotions, and 6 items for evaluating cognition and behaviors. The final score is derived from the average score of 4 dimensions. The score is higher, the heavier the fatigue. 0 means asymptomatic, 1–3 means mild, 4–6 means moderate, and 7–10 means severe.

- *HADS*

In 1983, Zigmond AS. et al designed HADS. [23] After tested, the anxiety subscale (A), depression subscale (D) and HADS total score have good retest consistency. [24] There are a total of 14 questions in the table. Among them, the seven questions of A test are used to evaluate anxiety, and the seven questions of D test are used to evaluate depression. Every question is counted as 0–3 points according to

the degree level. The score is higher, the more severe the degree. 0–7 is asymptomatic, 8–10 is suspicious, and 11–21 is symptomatic. It is divided into 8 boundaries, < 8 is negative, and ≥ 8 is positive.

2.4 Data analysis

Statistical description method: mean ± Standard Deviation ($\bar{x} \pm S$), composition ratio, median and quartile [M(Q25,Q75)], etc.

Statistical inference method: when the data conforms to the normal distribution and the variance is uniform, the independent sample t test is used to compare the samples between groups. When the variance is not uniform, the independent sample approximate t test is used. Non-normally distributed samples between groups use non-parametric test (Mann-Whitney U test). One-way ANOVA test or Kruskal-Wallis test was used for sample comparison among multiple groups. Multivariate binary unconditional logistic regression analysis is used to analyze categorical variables. Pearson correlation coefficient is used for correlation analysis of numerical variables.

SPSS 24.0 software was used for statistical analysis of all data, using a two-sided difference test. $P \leq 0.05$ is considered statistically significant.

3 Results

141 cases of postoperative patients with gastric cancer were initially screened, and 115 cases were finally included. Figure 1 presents the process of recruiting study participants. General data, gastric cancer data and other symptom data of the included cases were presented in the Table 2.

Table 2 Basic information of included cases (n=115)

Group	Number	Percent	Group	Number	Percent
Gender group			**N stage**		
Male	73	63.48%	N0	24	20.87%
Female	42	36.52%	N1	34	29.57%
Age group			N2	25	21.74%
≤60	63	53.78%	N3	32	27.83%
60	52	46.22%	**Surgical methods**		
KPS group			proximal gastrectomy	19	16.52%
90	35	30.43%	distal gastrectomy	38	33.04%
≥90	80	69.57%	total gastrectomy	58	50.43%
Lesion site			**The number of chemotherapy cycle**		
gastric cardia	22	21.36%	≤6	55	52.88%
The body of stomach	38	36.89%	6	49	47.12%
the antrum of stomach	43	41.75%	**PSQI score**		
Degree of differentiation			7-10	37	32.17%
High differentiation	4	3.81%	11-15	60	52.17%
Poor differentiation	60	57.14%	16-21	18	15.65%
Moderate differentiation	28	26.67%	**PFS-CV score**		
Moderate to poor differentiation	13	12.38%	≤4	43	37.39%
Lauren type			4	72	62.61%
Intestinal type	26	28.89%	**HADS score**		
Diffuse type (stomach type)	44	48.89%	**Anxiety subtable**		
Hybrid	20	22.22%	8	17	14.78%
Clinical stage			≥8	98	85.22%
	6	5.22%	**Depression subtable**		
	41	35.65%	8	28	24.35%
	68	59.13%	≥8	87	75.65%

T stage		
T1	7	6.09%
T2	26	22.61%
T3	48	41.74%
T4	34	29.56%

3.1 The characteristics

There were 60 cases (52.17%) with a PSQI score of 11-15, 37 cases (32.17%) with a score of 7-10, and 18 cases (15.65%) with a score of 16-21. The average score of the PSQI score was 12.05±3.25. Among them, the “daytime dysfunction” component had the highest score, and the hypnotic drug component had the lowest score. (see Table 3)

Table 3 PSQI scale components and scores

	score（$\bar{x}$±S）
A. Sleep quality	2.09±0.78
B．Time to fall asleep	2.04±0.73
C．Sleep time	1.90±0.82
D．Sleep efficiency	1.68±1.01
E．Sleep disorders	1.45±0.63
F．Hypnotic drugs	0.63±1.12
G．Daytime dysfunction	2.17±0.85
Total score	11.96±3.31

3.2 Related factors

3.2.1 General information

The independent-sample t test was used to compare the PSQI scores of gender and age groups, t=-0.010 and -1.092, *P* all >0.05. The PSQI score of KPS group was subjected to non-parametric test (Mann-Whitney U test), Z= -0.010, *P* >0.05; Table 4.

Table 4 Correlation analysis of general data and PSQI score					
		n	PSQI score (x̄±S)	t	*P*
Gender	Male	73	11.96±3.08	-0.010	0.992▲
	Female	42	11.95±3.71		
Age	≤60	63	11.65±3.66	-1.092	0.277▲
	＞60	52	12.33±2.81		
			M（Q25,Q75）	Z	*P*
KPS	＜90	18	12.00（12.00，14.00）	-1.706	0.088▲
	≥90	40	11.00（8.25，14.00）		
▲*P*＜0.05					

3.2.2 Relevant data of gastric cancer

Kruskal-Wallis tests were respectively performed on the PSQI scores among the groups of the lesion site, differentiation grade, lauren type, clinical stage, N stage and surgical method, χ^2=3.111, 4.664, 2.350, 1.576, 0.715 and 5.292, *P* all >0.05. One-way ANOVA test was used in the PSQI scores among the group of the T stage, F=0.793, *P* >0.05; Table 5.

The PSQI scores of the number of chemotherapy cycles grouped (≤6 cycles, >6 cycles) were subjected to non-parametric test (Mann-Whitney U test), Z= -4.447, *P*=0.000; Supplementary Table 1.

Table 5 Correlation analysis between gastric cancer data and PSQI score

		n	PSQI score M（Q25,Q75）	χ^2	*P*
Lesion site	Gastric cardia	22	11 (8, 12)	3.111	0.211▲
	Body of stomach	38	12.5 (8, 16)		
	Antrum of stomach	43	12 (11, 14)		
Differentiation grade	High differentiation	4	12 (12, 12)	4.664	0.198▲
	Poor differentiation	60	11 (9, 13.75)		
	Moderate differentiation	28	13.5 (8, 16)		
	Moderate to poor differentiation	13	11 (8, 12.5)		
Lauren type	Intestinal type	26	12 (9.75, 16.25)	2.350	0.309▲
	Diffuse type (stomach type)	44	12 (10,14)		
	Hybrid	20	11 (8,13)		
Clinical stage	□	6	13 (11, 16)	1.576	0.455▲
	□	41	12 (9, 13.5)		
	□	68	12 (10, 14)		
N stage	N_0	24	12 (10.25, 15.25)	0.715	0.870▲
	N_1	34	12 (9, 14)		
	N_2	25	12 (9.5, 14)		
	N_3	32	12 (10, 14.75)		
Surgical methods	proximal gastrectomy	19	11 (7, 12)	5.292	0.071▲
	distal gastrectomy	38	12 (11, 14)		
	total gastrectomy	58	12 (8.75, 14.25)		
		n	$\bar{x}\pm S$	F	*P*
T stage	T_1	4	12.25±0.96	0.793	0.503▲
	T_2	13	12.92±3.82		

	T_3	24	12.21±3.40
	T_4	17	11.12±2.89

▲*P*0.05

3.3.3 Fatigue, depression and anxiety

The Pearson correlation coefficients between the total PSQI score and the final score of the PFS-CV scale, between the total PSQI score and the HADS scale (depression subscale) score, and between the total PSQI score and the HADS scale (anxiety subscale) score were respectively 0.428, 0.261 and 0.060. *P*=0.000, 0.005 and 0.527; Supplementary Figure 1, Supplementary Figure 2 and Supplementary Figure 3.

3.4 Risk factors

The PSQI score was used as the dependent variable and assigned a value: 0= “PSQI score<11 points (sleep quality is general)”; 1= “PSQI score ≥11 points” (sleep quality is poor or very poor). The above related factors with *P*<0.05 [the number of cycles of chemotherapy, the PFS-CV scale, the HADS scale (depression subscale)] were used as independent variables and assigned values: 0="The number of chemotherapy cycles≤6", 1="The number of chemotherapy cycles>6"; 0="PFS-CV scale ≤4 points", 1="PFS-CV scale >4 points"; 0 = "HADS Scale (depression subscale) <8 points", 1 = "HADS Scale (depression subscale) ≥ 8 points". A multivariate binary unconditional logistic regression model was established, and the forward method was used to select and eliminate independent variables. The regression analysis showed that the number of chemotherapy cycles and fatigue were significant risk factors for the reduction of sleep quality in patients with insomnia (*P*<0.05).

Compared with the number of chemotherapy cycles ≤ 6, when the number of previous chemotherapy cycles after gastric cancer surgery is greater than 6, the risk of reduced sleep quality is increased (OR=3.640,95% CI: 1.416-9.357, *P*=0.007). Compared with patients with no or mild fatigue, patients with moderate or severe fatigue after gastric cancer surgery have an increased risk of sleep quality (OR=4.390,95% CI:1.843-10.460, *P*=0.001; Supplementary Table 2).

4 Discussion

This study investigated the characteristics of sleep quality included in patients. It was found that poor sleep quality accounted for 52.17%; patients with very poor sleep quality accounted for 15.65%. In the analysis of related factors, the total PSQI score was not statistically different among the groups of gender, age, KPS score, gastric cancer lesion location, differentiation grade, lauren classification, clinical stage, T stage and N stage (*P*0.05). That showed that the severity of insomnia in patients after gastric cancer surgery was not significantly related to the above factors. At present, some studies have concluded that gender, age, cancer stage and other factors have nothing to do with the degree of insomnia in the included cases, which was the same as the results of this study. [16, 25, 26] However,

there were still studies that differ from the results of this study. Ohayon MM et al. believed that gender and age were factors that induce insomnia in cancer patients. [27] We will need to design a prospective study including a larger sample size to verify the conclusions.

By analyzing the influence of the number of chemotherapy cycles on the degree of insomnia, it was found that the total PSQI score of patients with chemotherapy cycles > 6 [13 (12, 16)] was significantly higher than that of patients with chemotherapy cycles ≤ 6 [10 (8, 12)] (P = 0.000). The multivariate binary unconditional logistic regression analysis showed that the number of chemotherapy cycles > 6 was a significant risk factor for reduced sleep quality in patients with insomnia after operation for gastric cancer ($P < 0.05$). The risk of reduced sleep quality with the number of chemotherapy cycles > 6 is 3.640 times that of ≤ 6. Chemotherapy, as one of the main anti-tumor treatments, has a certain cytotoxic effect, causing patients to have side effects such as anorexia, nausea, vomiting, fatigue, pain, bone marrow suppression and so on. As a result, the patient loses confidence in the treatment effect, and insomnia also occurs or worsens. [28,29]

The sleep quality of insomnia patients after gastric cancer surgery was positively correlated with fatigue and depression (Pearson = 0.428 and 0.261, $P = 0.000$ and 0.005), but not correlated with anxiety ($P = 0.527$). Hoang HTX et al. also found that the incidence and severity of insomnia in cancer patients had nothing to do with the characteristics of the participants, cancer information or treatment factors, but were related to the emotional score of the participants. [6] The results of a systematic review also pointed out that patients with insomnia and mood have a two-way effect. [30] The hypothalamus, hippocampus and other brain tissues regulate emotion and sleep at the same time by secreting neuropeptides and neurotransmitters, so that the two are connected. [31, 32] A Chinese study also found that when a patient suffered from depression and insomnia, the level of neuropeptide Y in the body was lower than that of healthy people, and the level of substance P was higher than that of healthy people. [33] In addition, insomnia and fatigue often occur simultaneously in cancer patients. Xu JN 's study included 60 patients with cancer-related fatigue and found that 70% of them suffered from insomnia. [34] Moreover, this study established a multivariate binary unconditional logistic regression analysis to show that the risk of reduced sleep quality in patients with moderate or severe fatigue after gastric cancer surgery was 4.390 times that of patients with no or mild fatigue ($P = 0.001$).

The advantage of this study was to specifically select patients with insomnia after operation for gastric cancer to explore their sleep quality characteristics, related factors and risk factors.

4.1 Study limitations

However, this study was a cross-sectional study. There is no control group to give the findings perspective or relevance for the findings of prevalence and severity. Due to its inherent limitations, this study cannot point out how insomnia and its related symptoms affect each other before they appear and how they change throughout the course of the disease. In addition, this study was only a single-center study with a small sample size.

4.2 Clinical implications

This study confirmed that the sleep quality of insomnia patients after operation for gastric cancer was mainly "poor". That was correlated with the number of chemotherapy cycles, depression and fatigue. The number of chemotherapy cycles > 6 and moderate to severe fatigue were the risk factors for reducing sleep quality in insomnia patients after operation for gastric cancer. Conclusions indicated that the quality of sleep in cancer patients might be related to previous treatments. Early assessment of insomnia and immediate intervention will be needed to improve the quality of life of cancer patients and their treatment compliance. Cancer patients may have symptom clusters including insomnia, depression and fatigue, and they may affect each other. Therefore, further research can be carried out to explore the incidence and characteristics of insomnia in cancer patients at different treatment stages.

5 Conclusion

Attention to related factors and risk factors may be associated with improvement of sleep quality in patients with gastric cancer after surgery.

Declarations

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Conflict of interest The authors declare that they have no conflict of interests.

Ethical approval The study obtained ethical approval from the Ethics Committee of Guang 'anmen Hospital, China Academy of Chinese Medical Sciences.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication Written informed consent for publication was obtained from all participants.

Availability of data and material Not applicable.

Code availability Not applicable.

Author contributions

GZ and Juan L contributed equally to this work. Jie L was involved in study concept and design. GZ and Juan L wrote the first draft. Jie L, BX, MD, HW, XW and JH contributed to the revision of the final report. All authors read and approved the final manuscript.

References

1. The World Health Organization (2018) Global Health Estimates 2016:Deaths by Cause,Age,Sex,by Country and by Region,2000-2016[DB/OL]. Geneva:World Health Organization (2018-04-15)[2020-06-05]. http://www. who.int/healthinfo/global_burden_disease/estimates/en/
2. Bray F, Ferlay J, Soerjomataram I et al (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68(6):394-424.
3. National Health Commission (2019) Standards for Diagnosis and Treatment of Gastric Cancer (2018 Edition). Chinese Journal of Digestion and Medical Imageology(Electronic Edition) 9(03):118-144. (in China)
4. Wu J, Zhang D, Ni M, Xue J et al (2020) Effectiveness of Huachansu injection combined with chemotherapy for treatment of gastric cancer in China: a systematic review and Meta-analysis. J Tradit Chin Med 40(5):749-757.
5. Peng W, Zhang F, Wang Z et al (2020) Large Scale, Multicenter, Prospective Study of Apatinib in Advanced Gastric Cancer: A Real-World Study from China. Cancer Manag Res 12:6977-6985.
6. Hoang HTX, Molassiotis A, Chan CW et al (2020) New-onset insomnia among cancer patients undergoing chemotherapy: prevalence, risk factors, and its correlation with other symptoms. Sleep Breath 24(1):241-251.
7. Li D, Li H, Liu H et al (2020) Impact of Electroacupuncture Stimulation on Postoperative Constipation for Patients Undergoing Brain Tumor Surgery. J Neurosci Nurs 52(5):257-262. (in China)
8. Mo YL, Li L, Qin L et al (2014) Cognitive function, mood, and sleep quality in patients treated with intensity-modulated radiation therapy for nasopharyngeal cancer: a prospective study. Psycho-oncology 23(10):1185-91.
9. Tian J , Chen GL , Zhang HR (2011) Sleep status of cervical cancer patients and predictors of poor sleep quality during adjuvant therapy. Supportive Care in Cancer 23(5):1401-1408.
10. Savard J, Ivers H, Villa J, Caplette-Gingras A, Morin CM (2011) Natural Course of Insomnia Comorbid With Cancer: An 18-Month Longitudinal Study. Journal of Clinical Oncology 29(26):3580-3586.
11. Morin CM, Bélanger L, LeBlanc M et al (2009) The natural history of insomnia: a population-based 3-year longitudinal study. Archives of Internal Medicine 169(5):447-453.
12. Palesh O, Aldridge-Gerry A, Zeitzer JM et al (2014) Actigraphy-measured sleep disruption as a predictor of survival among women with advanced breast cancer. Sleep 37(5):837-842.
13. Lockefeer JP, De VJ (2013) What is the relationship between trait anxiety and depressive symptoms, fatigue, and low sleep quality following breast cancer surgery?[J]. Psycho-oncology 22(5):1127-1133.
14. Ingiosi AM, Opp MR, Krueger JM (2013) Sleep and immune function:glial contributions and consequences of aging. Curr Opin Neurobiol 23 (5) :806-811.
15. van Leeuwen WM, Lehto M, Karisola P et al (2009) Sleep restriction increases the risk of developing cardiovascular diseases by augmenting proinflammatory responses through IL-17 and CRP. PLo S One 4 (2) :e4589.

16. Akman T, Yavuzsen T, Sevgen Z et al (2015) Evaluation of sleep disorders in cancer patients based on Pittsburgh Sleep Quality Index. European Journal of Cancer Care 24(4):553-559.
17. Liu K, Chen XZ, Zhang YC et al (2020) The value of spleen-preserving lymphadenectomy in total gastrectomy for gastric and esophagogastric junctional adenocarcinomas: A long-term retrospective propensity score match study from a high-volume institution in China. Surgery S0039-6060(20)30526-2.
18. Wang X, Zhang WH, Chen CX et al (2018) Investigation and analysis of symptom group in postoperative patients with gastric cancer. Nursing Practice and Research 15(14):8-10.
19. Amin MB, Edge SB, Greene FL, et al (2016) AJCC Cancer Staging Manual. 8th ed. New York: Springer 203-220.
20. Psychiatric Branch of Chinese Medical Association (2001) The Chinese Classification and the Diagnose Criterion of Mental Disorder (CCMD-3). Jinan: Shandong Technology Press 9-168. (in China)
21. Buysse DJ, Reynolds CF 3rd, Monk TH et al (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 28(2):193-213.
22. So WKW , Dodgson J , Tai JWM (2003) Fatigue and Quality of Life Among Chinese Patients With Hematologic Malignancy After Bone Marrow Transplantation. Cancer Nursing 26(3):211-219.
23. Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. Acta Psychiatr Scand 67 (6) :361-370.
24. Sun ZX, Liu HX, Jiao LY et al (2017) Reliability and validity of hospital anxiety and depression scale. Chinese Journal of Clinicians(Electronic Edition) 11(02):198-201. (in China)
25. Phillips KM, Jim HS, Donovan KA et al (2012) Characteristics and correlates of sleep disturbances in cancer patients. Support Care Cancer 20(2):357-365.
26. Morris BA, Thorndike FP, Ritterband LM et al (2015) Sleep disturbance in cancer patients and caregivers who contact telephone-based help services. Support Care Cancer 23(4):1113-1120.
27. Ohayon MM, Roth T (2001) What are the contributing factors for insomnia in the general population? J Psychosom Res 51(6):745–755.
28. Pai A, Sivanandh B, Udupa K (2020) Quality of Sleep in Patients with Cancer: A Cross-sectional Observational Study. Indian J Palliat Care 26(1):9-12.
29. Lewandowska A, Rudzki G, Lewandowski T et al (2020) Quality of Life of Cancer Patients Treated with Chemotherapy. Int J Environ Res Public Health 17(19):E6938.
30. Alvaro PK, Roberts RM, Harris JK (2013) A systematic review assessing bidirectionality between sleep disturbances, anxiety, and depression. Sleep 36(7):1059–1068.
31. Li P, Wang CM, Li F (2018) A relevant research between spontaneous activity of resting state of brain area and severity of illness of patients with EOD under functional magnetic resonance imaging. China Medical Equipment 15(6):61-66.

32. Wang EF, Liu LY, Zhang HJ et al (2015) Evaluation of the resting state MRI brain default network in patients with primary insomnia accompanied by depressive symptoms. Chinese Journal of Neurology 48(11):1000-1006.
33. Yang Y, Hu M, Ge HM (2016) Serum level of neuropeptide Y and substance P among depressive patients accompanied by insomnia. Journal of International Psychiatry 43(5):781-783. (in China)
34. Xu JN (2016) Analysis of the clinical characteristics of gastrointestinal tumor cancer-induced fatigue and observation of the interventional effect of Yiqi Jianpi Bushen Fang. Beijing University of Chinese Medicine. (in China)

Figures

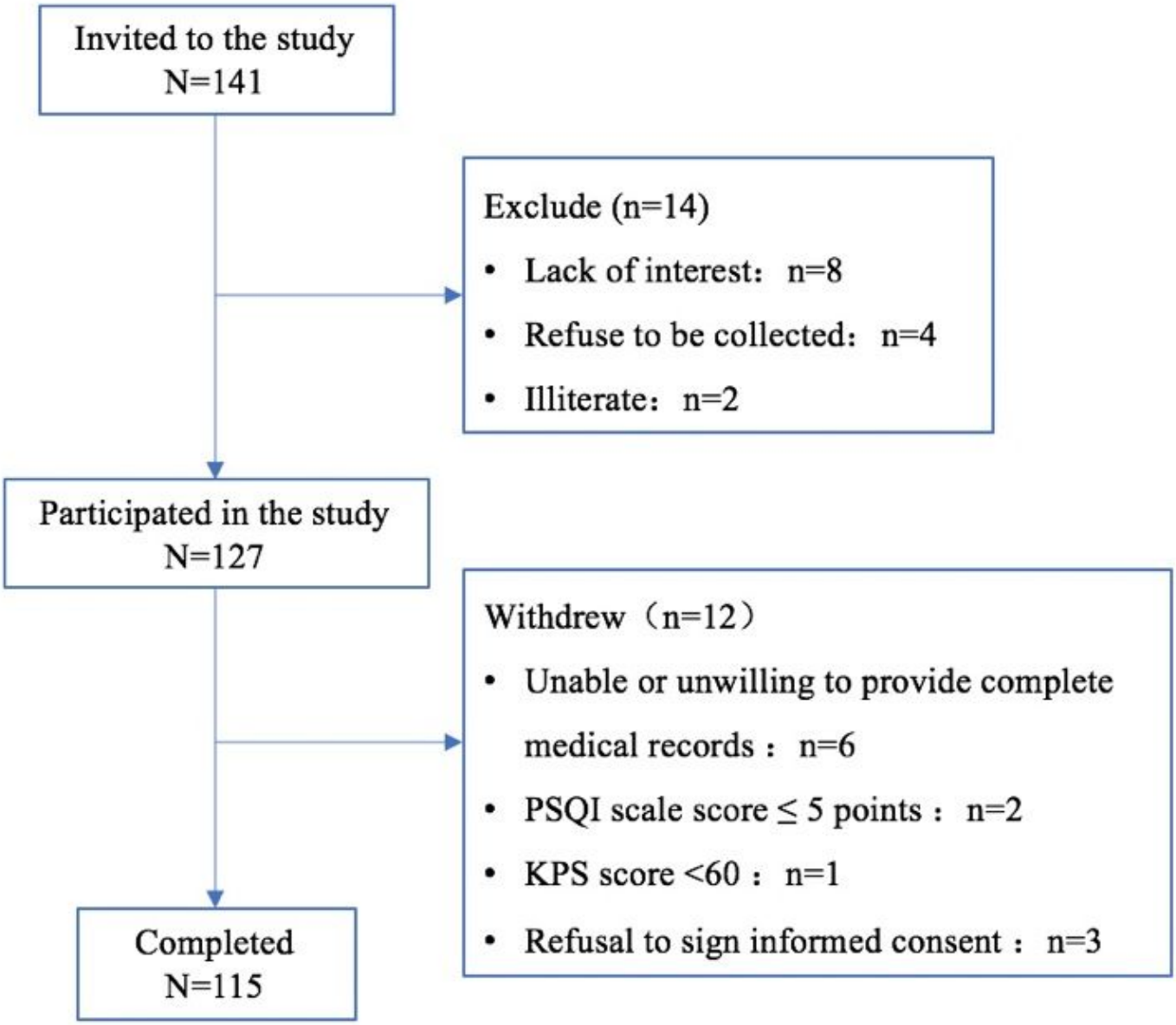

Figure 1

Flowchart of study recruitment

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