

## Original Article

# Effect of psychological counseling plus meticulous care on posttraumatic growth and social support of patients with breast cancer undergoing chemotherapy

Qiong Liu, Shenshen Pan

*Department of Thyroid and Breast Surgery, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang Province, China*

Received June 9, 2020; Accepted September 10, 2020; Epub December 15, 2020; Published December 30, 2020

**Abstract:** Objective: To explore the effect of psychological counseling plus meticulous care on posttraumatic growth (PTG) and social support (SS) of patients with breast cancer (BC) undergoing chemotherapy. Methods: Ninety females with BC who were treated by chemotherapy in our hospital from May 2016 to May 2019 were allocated into the observation group (n=50, psychological counseling plus meticulous care) and the control group (n=40, routine care). This study evaluated surgical indications, levels of serum growth/differentiation factor 3 (GDF3), thymidine kinase (TK1), cancer antigen 15-3 (CA15-3) and carcinoembryonic antigen (CEA), as well as mental health, PTG, SS, nursing quality, adverse events, and patient satisfaction. Results: Patients in the observation group showed better surgical indications, increased GDF3, TK1, CA15-3 and CEA, lower Hamilton anxiety scale (HAMA) and self-rating depression scale (SDS) scores, higher posttraumatic growth inventory (PTGI) and perceived social support scale (PSSS) scores and nursing quality, as well as fewer adverse events and higher patient satisfaction after nursing. Conclusion: Psychological counseling plus meticulous care contributes to the improvement of PTG and SS of chemotherapy-treated BC patients.

**Keywords:** Psychological counseling, meticulous care, breast cancer, PTGI, PSSS

## Introduction

Breast cancer (BC), is one of the most common and fatal cancers among women worldwide [1, 2], it is a highly heterogeneous malignancy with clinical features of genetic and epigenetic diversity [3, 4]. Family cancer history, age at menarche and menopause, and reproductive history are factors affecting BC [5]. Moreover, lifestyle; especially diet, is important for its progression. Red meat and animal fat, as well as milled rice and other carbohydrates are likely to increase the risk [6]. BC spreads easily and often metastasizes to the liver, bones, lungs and brain, making it the second most likely cancer to metastasize to the brain after lung cancer [7]. For this reason, the treatment of BC faces great challenges.

Chemotherapy is generally selected for treatment of BC, for example, using taxane-based chemotherapy for the treatment of triple nega-

tive breast cancer (TNBC) [8]. It can effectively treat a series of symptoms caused by cancers, but has little effect on the overall survival of patients. However, there is evidence that chemotherapy is likely to be counterproductive, for example, taxane-based chemotherapy promotes tumor regeneration by inducing angiogenesis [9-13]. Therefore, nursing care is necessary for chemotherapy-treated patients to improve their survival. Psychological counseling plus meticulous care is an effective nursing mode that takes good care of patients' psychological wellbeing and quality of life. Moreover, clinical nursing based perioperative meticulous care reduces complications and increases satisfaction of patients with lung cancer as well as coronary heart disease [14]. At present, psychological counseling plus meticulous care has been widely used in the nursing process of cardiovascular and cerebrovascular diseases and cancer, but its role in breast cancer and other gynecological diseases has been poorly investi-

gated. Therefore, this study was designed to explore the effect of meticulous care plus psychological counseling on posttraumatic growth (PTG) and social support (SS) of chemotherapy-treated BC patients.

### Materials and methods

#### *General data*

Ninety females with BC who were treated by chemotherapy in our hospital from May 2016 to May 2019 were allocated into the observation group (n=50, psychological counseling plus meticulous care) and control group (n=40, routine care). The present study was approved by the ethics committee of our hospital. All participants consented to be involved and signed relevant agreements.

**Inclusion criteria:** Patients meeting diagnostic criteria for BC and treated with chemotherapy; adult female patients; patients without contraindications to chemotherapy or communication disorders; mentally normal patients. **Exclusion criteria:** Patients with malignant tumors in other organs; patients with serious organ damage and organ dysfunction, communication difficulties, mental illness, severe trauma or medical disorders.

#### *Methods*

The control group received routine care: Changes in vital sign parameters were tested and routine dietary guidance was conducted after surgery. Nurses helped patients with mobility difficulties to perform regular exercise, and kept the room clean and tidy. At the time of discharge, patients were asked to have regular reexaminations.

The observation group received meticulous care plus psychological counseling on the basis of routine care services: Nursing staff were trained to improve their comprehensive skills, so that they had a profound understanding of the characteristics, usage and dosage of chemotherapy drugs, as well as the ability to develop emergency plans to deal with toxic and side effects and adverse reactions. Irregular assessments were conducted to correct their mistakes. Psychological counseling was carried out to evaluate the psychological health of patients. For those with mild depression and anxiety, therapeutic communication was per-

formed to understand their real thoughts so as to perform targeted interventions. For those with moderate depression and anxiety, in addition to therapeutic communication, family members were guided to accompany, encourage and comfort patients with appropriate facial expressions and speaking tone. Whereas those with severe depression and anxiety, a psychological nursing team was set up to ease their negative emotions. Before chemotherapy, nursing staff formulated targeted care plans according to patients' conditions. At the same time, health education was performed for family members so that they could master chemotherapy process and recognize relevant adverse reactions in advance. In the process of chemotherapy, nursing staff chose the most suitable catheter type for patients that is, the diameter of the catheter should match the inner diameter of the blood vessel. Tension-free dressing was adopted for catheter fixation, the catheter under the dressing was molded, and the dressing was removed at a zero angle. These measures aimed to prevent infection after skin damage. Maintenance of catheters was carried out afterwards. After chemotherapy, patients were instructed to take reasonable activities and rest, and those with mobility problems were guided for recovery training.

#### *Outcome measures*

(1) **Surgical indications:** Surgical indications, including postoperative in-bed time, intubation time and hospital stay, between the two groups were compared.

(2) **Serum GDF3, TK1, CA15-3, and CEA:** At the time of admission and after 14 days of nursing care, 5 mL of fasting venous blood from the elbow was sampled in the morning and placed in a tube without anticoagulant for a spontaneous agglutination at room temperature for 20-30 min. Serum was isolated at 1500×g and 4°C for 10 min and stored at -20°C. Human growth/differentiation factor 3 (GDF3), thymidine kinase (TK1), cancer antigen 15-3 (CA15-3) and carcinoembryonic antigen (CEA) were determined by enzyme-linked immunosorbent assay (ELISA).

(3) **Mental health:** The mental health of patients at admission and after 30 days of nursing care was evaluated by Hamilton anxiety scale (HAMA) [15] and self-rating depression

**Table 1.** General data

Classification	Observation group (n=50)	Control group (n=40)	t/X <sup>2</sup>	P
Residential area			0.11	0.740
Rural	23 (46.00)	17 (42.50)		
Urban	27 (54.00)	23 (57.50)		
Age (years)	43.73±8.66	44.21±7.85	0.27	0.786
Family type			0.02	0.897
Nuclear family	42 (75.00)	34 (85.00)		
Others	8 (25.00)	6 (15.00)		
Employee			0.45	0.504
Yes	37 (74.00)	32 (80.00)		
No	13 (26.00)	8 (20.00)		
Obesity			0.22	0.640
Yes	34 (68.00)	28 (70.00)		
No	16 (32.00)	12 (30.00)		
History of psychological intervention			0.24	0.627
Yes	30 (60.00)	26 (65.00)		
No	20 (40.00)	14 (35.00)		

scale (SDS) [16]. Higher score indicated worse mental health.

(4) Posttraumatic growth: The PTG between the two groups was compared by posttraumatic growth inventory (PTGI) [17]. Higher score indicated more PTG.

(5) Social support: Perception of SS of patients was evaluated using perceived social support scale (PSSS) [18].

(6) Nursing quality: Nursing quality between the two groups was compared, which comprises disinfection and isolation, primary care, first-aid management, document writing, 'three-basis' assessment (basic theory, basic knowledge, basic skill), head nurse management, and health education awareness.

(7) Adverse reactions: The incidence of adverse reactions was statistically compared, including subcutaneous effusion, gastrointestinal reaction and nosocomial infection.

(8) Patient satisfaction: Patient satisfaction with nursing care was evaluated and compared with a self-made questionnaire. With a total score of 100: 100-85 indicated satisfied, more than 60 indicated moderately satisfied, and less than 60 indicated dissatisfied.

#### Statistical methods

Data processing was performed with SPSS 19.0 (Asia Analytics Formerly SPSS China).

Counting data were analyzed with chi-squared test, and measurement data expressed by mean ± standard deviation ( $\bar{x} \pm sd$ ) were analyzed by t test. Values of  $P < 0.05$  were assumed to be statistically significant.

## Results

### General data

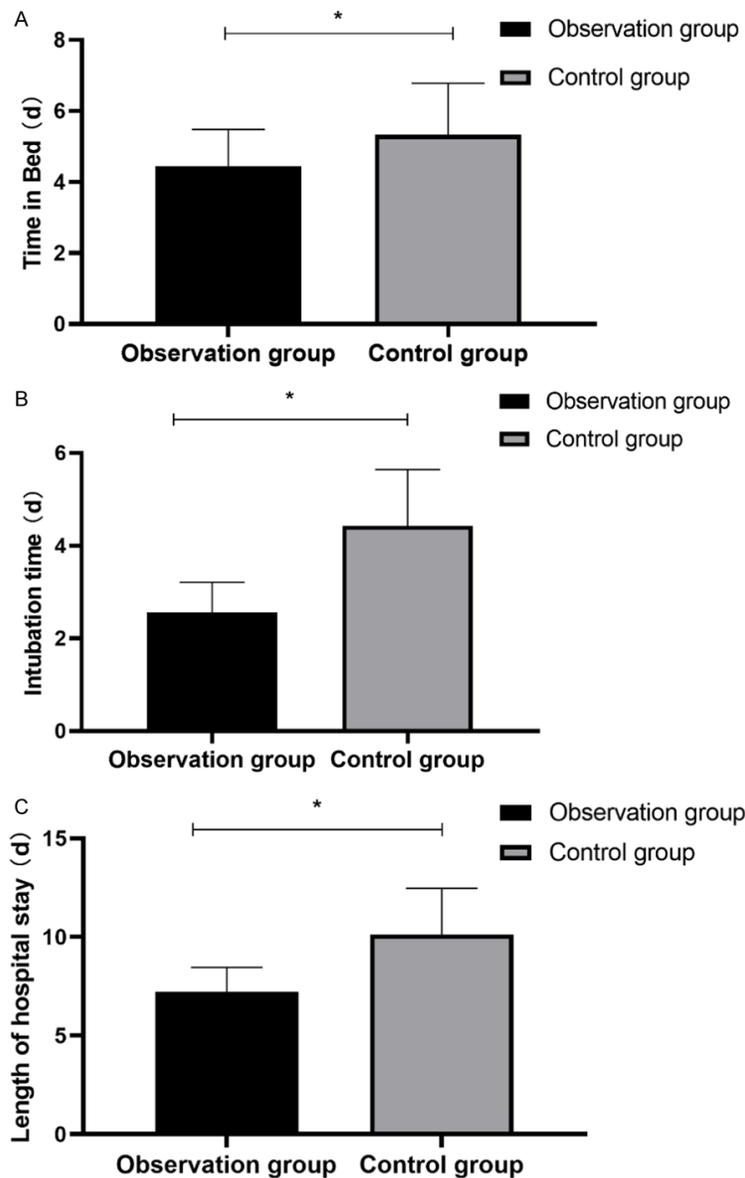
There was no significant difference between the two groups in the general data of residential area, age, body mass index (BMI), smoking history, drinking history and obesity ( $P > 0.05$ ) (Table 1).

### Better surgical indications in the observation group

After comparing the surgical indications, it was found that the in-bed time, intubation time and hospital stay in the observation group were shorter than those in the control group ( $P < 0.05$ ) (Figure 1).

### Decreased levels of serum GDF3, TK1, CA15-3 and CEA in the observation group

The levels of serum GDF3, TK1, CA15-3 and CEA in the two groups were not significantly different at the time of admission. However, they decreased after 14 days of nursing, and those in the observation group were lower than in the control group ( $P < 0.05$ ) (Figure 2).



**Figure 1.** Surgical indications in the two groups: A. In-bed time: In-bed time in the observation group is shorter than that in the control group ( $P<0.05$ ). B. Intubation time: Intubation time in the observation group is shorter than that in the control group ( $P<0.05$ ). C. Hospital stay: Hospital stay in the observation group is shorter than that in the control group ( $P<0.05$ ). Note: \* $P<0.05$  vs. control group.

*Enhanced mental health in the observation group*

There was no significant difference in HAMA and SDS scores between the two groups at the time of admission. The scores decreased after 14 days of nursing, and the observation group score was lower than the control group ( $P<0.05$ ) (Figure 3).

*More PTG in the observation group*

PTGI scores showed no significant changes in the two groups before nursing, and the observation group was higher than the control group after nursing ( $P<0.05$ ) (Table 2).

*More SS in the observation group*

There was no significant differences in PSSS score between the two groups before nursing, but the score in the observation group was higher than that in control group after nursing ( $P<0.05$ ) (Table 3).

*Higher nursing quality in the observation group*

After comparing the nursing quality, it was found that scores of disinfection and isolation, primary care, first-aid management, document writing, 'three-basis' assessment, head nurse management and health education awareness in the observation group were higher than those in the control group ( $P<0.05$ ) (Table 4).

*Fewer adverse reactions in the observation group*

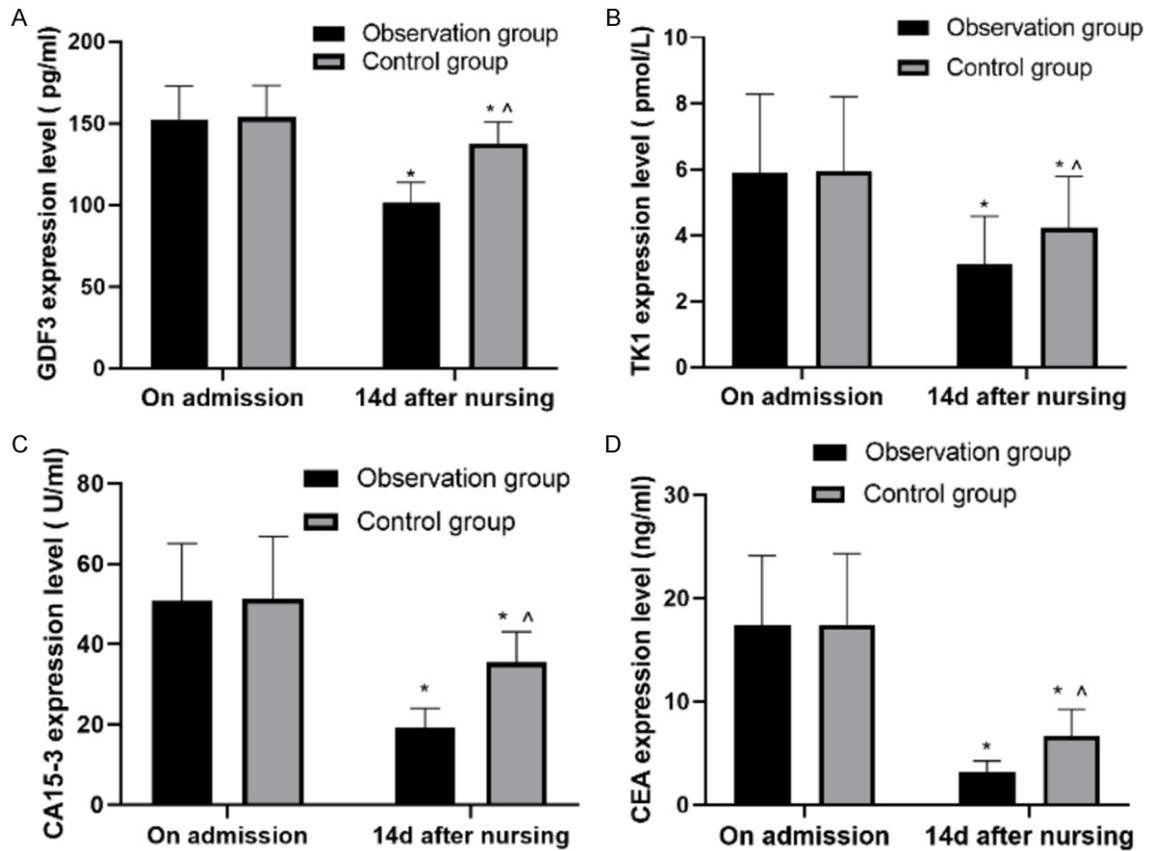
The incidence of adverse reactions in the observation group was lower than that in control group ( $P<0.05$ ) (Table 5).

*Higher satisfaction of patients in the observation group*

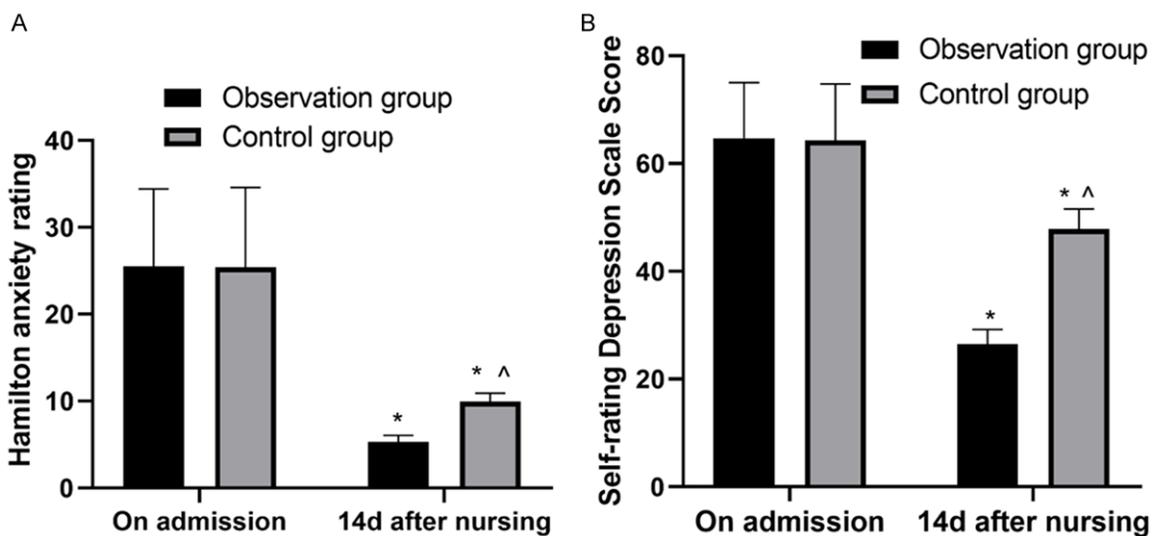
Patients in the observation group were more satisfied with the nursing care than those in the control group ( $P<0.05$ ) (Table 6).

**Discussion**

Chemotherapy is a preferred treatment option for aggressive and easily metastatic BC, it can help alleviate pathological changes in patients.



**Figure 2.** Levels of GDF3, TK1, CA15-3 and CEA in two groups: A. Level of GDF3: The level of GDF3 in the observation group is remarkably lower than that in the control group after 14 days of nursing. B. Level of TK1: The level of TK1 in the observation group is remarkably lower than that in the control group after 14 days of nursing. C. Level of CA15-3: The level of CA15-3 in the observation group is remarkably lower than that in the control group after 14 days of nursing. D. Level of CEA: The level of CEA in the observation group is remarkably lower than that in the control group after 14 days of nursing. Note: \* $P < 0.05$  vs. before nursing, ^ $P < 0.05$  vs. control group.



**Figure 3.** Mental health in the two groups: A. HAMA score: HAMA score decreases in both groups one month after nursing, and the observation group is lower than the control group after 14 days of nursing ( $P < 0.05$ ). B. SDS score: SDS score decreases in both groups one month after nursing, and the observation group is lower than the control group after 14 days of nursing ( $P < 0.05$ ). Note: \* $P < 0.05$  vs. before nursing, ^ $P < 0.05$  vs. control group.

## Psychological counseling and meticulous care in chemotherapy-treated BC patients

**Table 2.** PTGI score in the two groups

Classification	Observation group (n=50)	Control group (n=40)	t	P
Before nursing	41.78±6.23	42.21±4.54	0.37	0.716
After nursing	64.21±13.57	52.45±5.79	5.12	<0.001
t	10.62	8.80		
P	<0.001	<0.001		

**Table 3.** PSSS score in the two groups

Classification	Observation group (n=50)	Control group (n=40)	t	P
Before nursing	45.31±7.43	45.02±5.12	0.21	0.834
After nursing	61.32±13.57	51.31±6.98	4.36	<0.001
t	7.32	5.15		
P	<0.001	<0.001		

**Table 4.** Nursing quality in the two groups

Classification	Observation group (n=50)	Control group (n=40)	t	P
Disinfection and isolation	89.23±9.57	71.05±6.22	10.38	<0.001
Primary care	92.41±3.34	72.43±1.45	35.24	<0.001
First-aid management	90.67±5.21	71.67±4.34	18.49	<0.001
Document writing	98.22±1.23	75.26±3.62	41.97	<0.001
Social functioning	96.17±2.83	74.32±5.34	24.91	<0.001
Physical functioning	92.32±4.34	69.54±6.43	20.01	<0.001
Psychological functioning	92.83±5.23	71.33±5.87	18.35	<0.001

**Table 5.** Incidence of adverse reactions

Classification	Observation group (n=50)	Control group (n=40)	X <sup>2</sup>	P
Subcutaneous effusion	1 (1.25)	4 (10.00)		
Gastrointestinal reaction	0 (0.00)	2 (5.00)		
Nosocomial infection	0 (0.00)	2 (5.25)		
Incidence of adverse reactions (%)	1 (1.25)	8 (20.00)	8.00	0.005

**Table 6.** Patient satisfaction in the two groups

Classification	Observation group (n=50)	Control group (n=40)	X <sup>2</sup>	P
Satisfied	32 (64.00)	16 (40.00)	-	-
Moderately satisfied	15 (30.00)	14 (35.00)	-	-
Dissatisfied	3 (6.00)	10 (25.00)	-	-
Satisfaction rate (%)	47 (94.00)	30 (75.00)	6.49	0.011

However, it tends to induce sequelae, adverse reactions, and even recurrence and death [19-21]. In this study, adverse reactions in the observation group with psychological counseling plus meticulous care were fewer than those in the control group with routine care. So psychological counseling plus meticulous care is able to reduce adverse reactions of patients with BC. TK1, an enzyme associated with DNA

synthesis and cell proliferation, is highly expressed and serves as a prognostic factor in BC, and it can be suppressed by chemotherapeutic agents [22]. GDF3 belongs to transforming growth factor- $\beta$  (TGF- $\beta$ ) superfamily and has been revealed to be highly expressed in multiple cancers including BC [23]. Overexpressed CEA and CA15.3 in BC are biomarkers for therapeutic responses of patients [24, 25]. In this

study, the observation group presented decreased levels of serum GDF3, TK1, CA15-3 and CEA, which indicates that psychological counseling plus meticulous care alleviates the pathological reactions and adverse reactions, and contributes to the recovery of patients with BC. From the methods section, it can be seen that medical staff who carried out meticulous care were well-trained. They communicated with patients frequently and tried to eliminate depression and anxiety of patients. Besides, the selection and removal of catheters during intraoperative chemotherapy were very detailed to rule out surgical errors. All these are of great help to the recovery of patients. The lower score of mental health in the observation group indicates that psychological counseling plays a pivotal role in relieving anxiety and depression of chemotherapy-treated BC patients. More than that it has been reported to improve sleep quality and relieve postoperative pain and fatigue of patients with BC [26]. Owing to the alleviating effect of psychological counseling and meticulous care, psychological burdens of patients were reduced, and postoperative adverse reactions were decreased, resulting in shortened in-bed time, intubation time, and hospital stay.

In this study, we also made a detailed analysis of the PTG and SS of patients. It turned out that the PTGI and PSSS scores in the observation group increased after nursing. In patients with BC, higher PSSS score means higher SS, and higher SS means better health, higher quality of life, fewer psychosocial problems, less recurrence and longer survival [27]. Communication is the key to improve SS [28]. In the process of psychological counseling and meticulous care, medical staff and family members communicated with patients frequently, leading to the increase in PSSS score in the observation group. This is also one of the reasons why patients in the observation group recovered better and were less anxious and depressed. Disappointing diagnosis, treatment and survival of BC patients inevitably induces negative emotions in the patients and bring burdens to their family. After a period of effective care, both physical and mental growth of patients will be enhanced. This growth not only reduces or eliminates the depression and anxiety of patients, but also alleviates their illness and improves their quality of life, and helps the families to a certain

extent [29]. It was shown in our study that psychological counseling plus meticulous care better promoted the PTG of patients and improved their SS.

There is still room for improvement in this study. Firstly, we have failed to evaluate intraoperative cooperation and postoperative compliance of patients. Secondly, how the quality of life of patients has improved during the follow-up has not been investigated. These limitations will be addressed in the future clinical nursing research to better serve the patients and slow down disease progression.

To sum up, psychological counseling plus meticulous care is conducive to PTG and SS of chemotherapy-treated BC patients, which is worthy of clinical promotion.

### Acknowledgements

This study was financially supported by the Effect of group counseling on social support and post-traumatic growth of breast cancer patients undergoing chemotherapy, Project of Wenzhou science and Technology Bureau of Zhejiang Province (Y20180473).

### Disclosure of conflict of interest

None.

**Address correspondence to:** Shenshen Pan, Department of Thyroid and Breast Surgery, The First Affiliated Hospital of Wenzhou Medical University, No. 2, Fuxue Lane, Wenzhou 325000, Zhejiang Province, China. Tel: +86-0577-55579461; E-mail: panshenshen2010@163.com

### References

- [1] McGuire S. World Cancer Report 2014. Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer, WHO Press, 2015. *Adv Nutr* 2016; 7: 418-419.
- [2] Sachs N, de Ligt J, Kopper O, Gogola E, Bounova G, Weeber F, Balgobind AV, Wind K, Gracanin A, Begthel H, Korving J, van Boxtel R, Duarte AA, Lelieveld D, van Hoeck A, Ernst RF, Blokzijl F, Nijman IJ, Hoogstraat M, van de Ven M, Egan DA, Zinzalla V, Moll J, Boj SF, Voest EE, Wessels L, van Diest PJ, Rottenberg S, Vries RGJ, Cuppen E and Clevers H. A living biobank of breast cancer organoids captures disease heterogeneity. *Cell* 2018; 172: 373-386, e310.
- [3] Riaz M, van Jaarsveld MT, Hollestelle A, Prager van der Smissen WJ, Heine AA, Boersma AW, Liu J, Helmijr J, Ozturk B, Smid M, Wiemer EA,

- Foekens JA and Martens JW. miRNA expression profiling of 51 human breast cancer cell lines reveals subtype and driver mutation-specific miRNAs. *Breast Cancer Res* 2013; 15: R33.
- [4] Dai X, Cheng H, Bai Z and Li J. Breast cancer cell line classification and its relevance with breast tumor subtyping. *J Cancer* 2017; 8: 3131-3141.
- [5] Thomson CA. Diet and breast cancer: understanding risks and benefits. *Nutr Clin Pract* 2012; 27: 636-650.
- [6] Xiao Y, Xia J, Li L, Ke Y, Cheng J, Xie Y, Chu W, Cheung P, Kim JH, Colditz GA, Tamimi RM and Su X. Associations between dietary patterns and the risk of breast cancer: a systematic review and meta-analysis of observational studies. *Breast Cancer Res* 2019; 21: 16.
- [7] Shah N, Mohammad AS, Saralkar P, Sprowls SA, Vickers SD, John D, Tallman RM, Lucke-Wold BP, Jarrell KE, Pinti M, Nolan RL and Lockman PR. Investigational chemotherapy and novel pharmacokinetic mechanisms for the treatment of breast cancer brain metastases. *Pharmacol Res* 2018; 132: 47-68.
- [8] Chen W, Qin Y, Wang D, Zhou L, Liu Y, Chen S, Yin L, Xiao Y, Yao XH, Yang X, Ma W, Chen W, He X, Zhang L, Yang Q, Bian X, Shao ZM and Liu S. CCL20 triggered by chemotherapy hinders the therapeutic efficacy of breast cancer. *PLoS Biol* 2018; 16: e2005869.
- [9] Hughes R, Qian BZ, Rowan C, Muthana M, Keklikoglou I, Olson OC, Tazzyman S, Danson S, Addison C, Clemons M, Gonzalez-Angulo AM, Joyce JA, De Palma M, Pollard JW and Lewis CE. Perivascular M2 macrophages stimulate tumor relapse after chemotherapy. *Cancer Res* 2015; 75: 3479-3491.
- [10] Daenen LG, Houthuijzen JM, Cirkel GA, Roodhart JM, Shaked Y and Voest EE. Treatment-induced host-mediated mechanisms reducing the efficacy of antitumor therapies. *Oncogene* 2014; 33: 1341-1347.
- [11] De Palma M and Lewis CE. Macrophage regulation of tumor responses to anticancer therapies. *Cancer Cell* 2013; 23: 277-286.
- [12] Roodhart JM, He H, Daenen LG, Monvoisin A, Barber CL, van Amersfoort M, Hofmann JJ, Radtke F, Lane TF, Voest EE and Iruela-Arispe ML. Notch1 regulates angio-supportive bone marrow-derived cells in mice: relevance to chemoresistance. *Blood* 2013; 122: 143-153.
- [13] Karagiannis GS, Pastoriza JM, Wang Y, Harney AS, Entenberg D, Pignatelli J, Sharma VP, Xue EA, Cheng E, D'Alfonso TM, Jones JG, Anampa J, Rohan TE, Sparano JA, Condeelis JS and Oktay MH. Neoadjuvant chemotherapy induces breast cancer metastasis through a TMEM-mediated mechanism. *Sci Transl Med* 2017; 9: ean0026.
- [14] Wang J. Perioperative nursing effect of refined nursing intervention plan based on clinical nursing pathway for patients with coronary heart disease and lung cancer. *Invest Clin* 2020; 61: 1549-1555.
- [15] Yin G, Li Y, Xu W and Han N. Chart review of patients receiving valsartan-amlodipine single-pill combination versus valsartan and amlodipine combination for blood pressure goal achievement and effects on the Hamilton anxiety rating/Hamilton depression rating scales. *Medicine (Baltimore)* 2019; 98: e18471.
- [16] Chung K, Jeon MJ, Park J, Lee S, Kim CO and Park JY. Development and evaluation of a mobile-optimized daily self-rating depression screening app: a preliminary study. *PLoS One* 2018; 13: e0199118.
- [17] Cheng CH, Ho SM and Rochelle TL. Psychometric properties of the Chinese post-traumatic growth inventory in patients with chronic diseases. *Hong Kong Med J* 2018; 24 Suppl 4: 16-19.
- [18] Wang L, Wang H, Shao S, Jia G and Xiang J. Job burnout on subjective well-being among Chinese female doctors: the moderating role of perceived social support. *Front Psychol* 2020; 11: 435.
- [19] Gluck S, Ross JS, Royce M, McKenna EF Jr, Perou CM, Avisar E and Wu L. TP53 genomics predict higher clinical and pathologic tumor response in operable early-stage breast cancer treated with docetaxel-capecitabine ± trastuzumab. *Breast Cancer Res Treat* 2012; 132: 781-791.
- [20] Masuda H, Baggerly KA, Wang Y, Zhang Y, Gonzalez-Angulo AM, Meric-Bernstam F, Valero V, Lehmann BD, Pietenpol JA, Hortobagyi GN, Symmans WF and Ueno NT. Differential response to neoadjuvant chemotherapy among 7 triple-negative breast cancer molecular subtypes. *Clin Cancer Res* 2013; 19: 5533-5540.
- [21] Lehmann BD, Jovanovic B, Chen X, Estrada MV, Johnson KN, Shyr Y, Moses HL, Sanders ME and Pietenpol JA. Refinement of triple-negative breast cancer molecular subtypes: implications for neoadjuvant chemotherapy selection. *PLoS One* 2016; 11: e0157368.
- [22] Bonechi M, Galardi F, Biagioni C, De Luca F, Bergqvist M, Neumuller M, Guarducci C, Boccacini G, Gabellini S, Migliaccio I, Di Leo A, Pestrin M and Malorni L. Plasma thymidine kinase-1 activity predicts outcome in patients with hormone receptor positive and HER2 negative metastatic breast cancer treated with endocrine therapy. *Oncotarget* 2018; 9: 16389-16399.
- [23] Ehira N, Oshiumi H, Matsumoto M, Kondo T, Asaka M and Seya T. An embryo-specific expressing TGF-beta family protein, growth-differentiation factor 3 (GDF3), augments progres-

- sion of B16 melanoma. *J Exp Clin Cancer Res* 2010; 29: 135.
- [24] Yang Y, Zhang H, Zhang M, Meng Q, Cai L and Zhang Q. Elevation of serum CEA and CA15-3 levels during antitumor therapy predicts poor therapeutic response in advanced breast cancer patients. *Oncol Lett* 2017; 14: 7549-7556.
- [25] Perrier A, Boelle PY, Chretien Y, Gligorov J, Lotz JP, Brault D, Comperat E, Lefevre G and Boissan M. An updated evaluation of serum sHER2, CA15.3, and CEA levels as biomarkers for the response of patients with metastatic breast cancer to trastuzumab-based therapies. *PLoS One* 2020; 15: e0227356.
- [26] Abrahams HJG, Gielissen MFM, Verhagen CAH-HVM and Knoop H. The relationship of fatigue in breast cancer survivors with quality of life and factors to address in psychological interventions: a systematic review. *Clin Psychol Rev* 2018; 63: 1-11.
- [27] Thompson T, Rodebaugh TL, Perez M, Schoutman M and Jeffe DB. Perceived social support change in patients with early stage breast cancer and controls. *Health Psychol* 2013; 32: 886-895.
- [28] Thompson T, Rodebaugh TL, Perez M, Struthers J, Sefko JA, Lian M, Schoutman M and Jeffe DB. Influence of neighborhood-level factors on social support in early-stage breast cancer patients and controls. *Soc Sci Med* 2016; 156: 55-63.
- [29] Gesselman AN, Bigatti SM, Garcia JR, Coe K, Cella D and Champion VL. Spirituality, emotional distress, and post-traumatic growth in breast cancer survivors and their partners: an actor-partner interdependence modeling approach. *Psychooncology* 2017; 26: 1691-1699.