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Investigating genetic factors and the effect of refined multidisciplinary clinical management on the quality of life and perceived control level of breast cancer patients undergoing surgery and its morphological diagnosis parameters

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ABSTRACT

The purpose of this study is to investigate the genetic factors and the effect of refined multidisciplinary clinical management on the quality of life and perceived control level of breast cancer patients undergoing surgery and its morphological diagnosis parameters. Breast cancer, as the most common cancer in women, requires screening, early diagnosis, prognosis, response to treatment, and choosing the appropriate treatment method. In this study, we introduced the genes involved in breast cancer BRCA1 and BRCA2 and the molecular techniques of its diagnosis. From October 2016 to July 2021, 400 patients with breast cancer were selected from the glandular surgery department of Xingtai Third Hospital. According to the method of random number table, they were divided into an observation group and a control group, with 200 cases in each group. The control group adopted the routine management scheme, while the observation group adopted the multidisciplinary refined clinical management scheme based on the control group. The quality of life, perception control level, negative psychology, upper limb lymphedema, and satisfaction with the nursing of the two groups were compared after 3 months of intervention. The results showed the scores and total scores of the quality-of-life scale for breast cancer in the observation group were higher than those in the control group (P<0.05). The scores of perceived experience and control effectiveness in the observation group were higher than those in the control group (P<0.05). The scores of the Hamilton Anxiety Scale and Hamilton Depression Scale in the observation group were lower than those in the control group (P<0.05). After nursing, the improvement of upper limb edema in the observation group was better than that in the control group (P<0.05). Nursing satisfaction in the observation group (84.50%) was higher than that in the control group (66.50%) (P<0.05). Also, the results of this research showed the multidisciplinary refined clinical management plan for breast cancer patients can effectively improve the quality of life, improve the level of perceived control, reduce negative psychology, improve the degree of upper limb edema, and increase patient satisfaction.

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Introduction

About half of breast cancers occur as a result of mutations in tumor suppressor genes (TSGs), aberrant base pair repair, cell cycle control, steroid hormone metabolism, and cell message transmission pathways. Therefore, the study of effective genes can be used as a possible marker in the early diagnosis of breast cancer (1).

According to the Consensus of Experts on Prescription Review of Antineoplastic Drugs-Breast Cancer (2) in 2020, breast cancer is the leading malignant tumor in the prevalence and case fatality rate of women in China, with 278900 new cases per year, accounting for 16.51% of all malignant tumors in women. With the progress of breast cancer surgical treatment technology optimization, cancer progression has been controlled to a certain extent and the case fatality rate has been reduced, but the importance of maintaining surgical effect has often been neglected, which leads to poor prognosis and reduces the quality of life of patients. Studies have shown (3) that perceptual control is particularly important in cancer patients, such as improving patients 'self-care ability, improving bad psychology, accelerating disease adaptation, and improving quality of life, which is a hot topic in the field of positive psychology. A multidisciplinary refined clinical management program is a multidisciplinary collaborative management program in the whole course of treatment management, which not only takes into account local treatment and systemic treatment but also takes into account standardized treatment and individualized treatment, providing patients with the best-individualized diagnosis and treatment program, improving treatment effect, ensuring medical safety, reducing the mortality rate of patients and improving long-term survival rate. At present, it is widely used in cardiogenic shock (4), neuropathic pain (5), chronic spinal pain (6), and other fields, but it is rarely reported in breast cancer patients. Therefore, in this study, 400 patients with breast cancer who were treated in the Department of Gland Surgery of the Third Hospital of Xingtai City from October 2016 to July 2021 were selected as the research objects to explore the impact of multidisciplinary refined clinical management program on the quality of life and perceived

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control level of patients with breast cancer surgery, to provide theoretical data for optimizing the prognosis of breast cancer surgery patients.

General information

400 patients with breast cancer in the Department of Gland Surgery of the Third Hospital of Xingtai City from October 2016 to July 2021 were selected and divided into an observation group and a control group according to a random number table, with 200 cases in each group. In the observation group, the age was 36-59 years old, the average age was (44.60 ± 3.82) years old, the diameter of the lesion was 1-3 cm, the average diameter was (2.61 ± 0.27) cm, the pathological type was invasive ductal carcinoma in 67 cases, poorly differentiated adenocarcinoma in 78 cases and intraductal carcinoma in 55 cases, and the clinical stage was stage I in 129 cases, stage II in 39 cases and stage III in 32 cases. Education level: 60 cases of junior high school and below, 71 cases of senior high school, and 69 cases of junior college and above. In the control group, the age was 36-60 years old, the average age was (44.29 ± 3.58) years old, the diameter of the lesion was 1-3 cm, the average diameter was (2.59 ± 0.28) cm, the pathological type was invasive ductal carcinoma in 71 cases, poorly differentiated adenocarcinoma in 67 cases and intraductal carcinoma in 62 cases, and the clinical stage was stage I in 114 cases, stage II in 51 cases and stage III in 35 cases. Education level: 65 cases of junior high school and below, 68 cases of senior high school, and 67 cases of junior college and above. There was no significant difference in the general data between the two groups ($P > 0.05$).

Inclusion criteria: [1] Patients who received breast cancer surgery in the Department of Glandular Surgery of the Third Hospital of Xingtai City and were confirmed by pathology; [2] Patients who received neoadjuvant chemotherapy for breast cancer after surgery; [3] Clinical TNM stage I to III; [4] Expected survival time of more than half a year. Exclusion criteria: (i) refusal or inability to use acceptable methods of contraception during chemotherapy; (ii) pregnancy or lactation; (iii) distant metastasis of breast cancer confirmed by imaging; (iv) sensory or motor neuropathy; [5] severe cardiovascular disease, cardiopulmonary insufficiency, active infection, and human immunodeficiency virus infection; [6] Combined with other malignant tumors. This study was reviewed and approved by the Medical Ethics Committee of our hospital.

Materials and Methods

Coarse needle aspiration biopsy was performed in patients with suspected malignancy, and patients with pathologically confirmed breast cancer were randomized.

I) Patients in the control group were treated with a conventional management program after admission, including preoperative and postoperative diet management, incision management, drainage tube management, psychological management, etc. Patients were guided to carry out health education, such as breast tumor-related lectures, rehabilitation training, etc., which lasted for 3 months.

II) Based on the control group, the observation group adopted a multidisciplinary refined clinical management program to establish a multidisciplinary refined clinical management team, including an attending doctor, a nutritionist, a psychological consultant, a pharmacist, and a rehabilitation trainer. Establish a Wechat group to facilitate communication. Unified training was conducted 2 weeks before the intervention, including breast cancer diagnosis, symptomatic treatment after breast cancer surgery, postoperative drainage tube management, skin management, and so on. The attending doctor formulates the rehabilitation plan, the nutritionist, psychological consultant, and pharmacist formulate the nutrition plan, psychological consultation, and medication management, and the rehabilitation trainer formulates and guides the patient's functional exercise plan. (i) Intervention measures: The management was carried out from the aspects of individualized neoadjuvant chemotherapy, reconstructive surgery, and rehabilitation treatment. For patients receiving neoadjuvant chemotherapy according to their condition, appropriate chemotherapy regimens (such as TAC, AT, AC-TH, AC-TPH, etc.) were selected according to tumor staging and classification. During neoadjuvant chemotherapy, the evaluation was carried out at the end of each chemotherapy cycle concerning the standard of tumor shrinkage under ultrasound. For patients with tumor shrinkage area ≤ 30%, If the tumor area did not recede more than 30% after changing the protocol, the operation was performed. The tumor area of the initial chemotherapy regimen was less than 30%, surgery was performed directly, and neoadjuvant chemotherapy was performed for 2 to 5 cycles according to the specific conditions of the patients. Surgical options: standardized breast-conserving surgery or modified radical mastectomy. (ii) Rehabilitation treatment: health records were established, skin management, functional exercise, and rehabilitation guidance were carried out before the operation; After the operation, manual drainage and pressure treatment of lymphedema were carried out, and nutritional support was given to form good eating habits, psychological state of patients were assessed and targeted intervention was carried out, functional training was mainly progressive active training, and "breast cancer home guidance manual" was issued to patients to guide them to carry out systemic aerobic activities. After discharge, the patients with dysfunction were evaluated and further guided by telephone and outpatient follow-up, and the intervention lasted for 3 months.

Observation index

(I) Assessment of quality of life: Before and 3 months after the intervention, the breast cancer quality of life scale (7) was used to assess, including physical, emotional, functional and breast cancer-specific modules, with a total score of 0-152. The higher the score, the better the quality of life. Cronbach's alpha coefficient was 0.783. (II) Assessment of perceived control: Before and 3 months after the intervention, the cancer experience and efficacy scale (8) was used to assess the level of perceived control, including 29 items of perceived experience (patients' personal, socioeconomic, emotional experience) and control efficacy (personal efficacy, collective efficacy of cooperation with family members, medical efficacy), including 16 items of perceived experience. There were 13 items of control efficacy, and each item was scored by 5 grades, with a total score of 29 to 145. The higher the score, the better the quality of life. Cronbach's alpha coefficient was 0.794.

(III) Negative psychological assessment: Before and 3 months after the intervention, the Hamilton anxiety scale

(9,10) and the Hamilton depression scale were used to assessing anxiety and depression. There were 14 items on the Hamilton anxiety scale, and the total score was 0 to 56. The higher the score, the more serious the anxiety. Cronbach's alpha coefficient was 0.844. There were 17 items on the Hamilton Depression Scale, and the total score was 0 to 54. The higher the score, the more serious the depression. Cronbach's alpha coefficient was 0.874 (11).

(IV) The degree of upper limb edema was evaluated according to the subjective symptoms of upper limb lymphedema and the increased volume of upper limbs after operation: ① None: upper limb lymphedema and increased volume of upper limbs were not found; ② Mild: slight lymphedema in the upper limbs, which was not easy to be found by naked eyes, and the volume of the upper limbs increased by less than 10%; ③ Moderate: obvious swelling of the upper limbs, involving changes in the forearm, skin, and nails, and an increase in the volume of the upper limbs by 10% to 80%, which had little effect on the movement of the upper limb; ④ Severe: obvious swelling of the upper limbs, involving a wide range, varicose veins and rubber swelling of the skin, and the volume of the upper limbs increased by more than 80%, which seriously affected the activities of upper limbs.

(V) Satisfaction evaluation: After 3 months of intervention, the satisfaction of patients with the multidisciplinary refined clinical management program was investigated and evaluated by four levels, including very satisfied, basically satisfied, general and poor. Satisfaction = (very satisfied + basically satisfied)/total number of cases × 100%

Statistical methods

All data were analyzed by SPSS24.0 software. For measurement data conforming to normal distribution, mean ± standard deviation ($\bar{x} \pm s$ Independent sample t test was used for comparison between the two groups, and χ^2test was used for comparison of enumeration data. $P < 0.05$ was considered statistically significant.

Results

Comparison of quality of life between the two groups

Before the intervention, there was no significant difference in the scores and total scores of the breast cancer quality of life scale between the two groups ($P > 0.05$). After the intervention, the scores and total scores of the breast cancer quality of life scale increased in both groups, and the scores and total scores of the scale in the observation group were higher than those in the control group ($P < 0.05$), as shown in Table 1.

Comparison of perceived control level between the two groups

Before nursing, there was no significant difference in the scores of perceived experience and control efficacy between the two groups ($P > 0.05$). After the intervention, the scores of perceived experience and control efficacy in both groups increased, and the scores of the above items in the observation group were higher than those in the control group ($P < 0.05$), as shown in Table 2.

Negative psychological comparison between the two groups

Before the intervention, there was no significant difference in the scores of HAMA and HAMD between the two groups ($P > 0.05$). After the intervention, the scores of the above scales decreased in both groups, and the decrease in the observation group was greater ($P < 0.05$), as shown in Table 3.

Comparison of the degree of upper limb edema between the two groups

After the intervention, the improvement of upper limb edema in the observation group was significantly better than that in the control group ($P < 0.05$), as shown in Table 4.

Comparison of satisfaction of two groups of management schemes

The satisfaction of the observation group (84.50%) was higher than that of the control group (66.50%) ($P < 0.05$), as shown in Table 5.

Morphological diagnosis parameters

Morphological diagnosis parameters of breast cancer include tumor size and grade and positive or negative status of Immunohistochemistry (IHC) markers such as Estrogen Receptor (ER) Progesterone Progesterone Receptor (PR), Human Epidermal Growth Factor Receptor 2 (HER2) and Ki68 marker. The use of these markers and diagnostic parameters has led to the division of breast cancer with distinct clinical symptoms, which include 5 groups: Luminal A, Luminal B, Normal-Like, Basal-Like, and HER2 Overexpression. The molecular classification of breast cancer is based on gene expression profile, chromosomal changes, mutation status, proteomics, DNA copy number changes, methylation, and miRNAs and has been expanding for years and is reviewed by the International Consortium of Molecular Taxonomy of Breast Cancer (12).

Key genes effective in causing breast cancer

The *BRCA1* gene is located on chromosome 17 and encodes a nuclear phosphoprotein of 190 kDa and is known as the most susceptible and influential gene related to breast cancer (Table 1). The *BRCA1* gene acts as a tumor suppressor and plays a role in maintaining genomic stability. The *BRCA1* gene contains 22 exons that cover about 110 kb of DNA. The encoded protein combines with other tumor suppressors, DNA sensors, and other signals and forms a BRCA1-associated genome surveillance complex (BASC). This gene product is related to histone deacetylase complexes through interaction with RNA polymerase II and the C-terminal domain. Therefore, this protein plays a role in transcription, DNA repair of double-strand breaks, and recombination. More than 500 different types of mutations have been identified in this gene, which includes single nucleotide substitutions, deletions, and accessions. Mutations in this gene are responsible for approximately 40% of hereditary breast cancers and more than 80% of hereditary breast and ovarian cancers (13,14).

The *BRCA2* gene is located on chromosome 13 and inherited mutations in the *BRCA2* gene increase the lifetime risk of developing breast or ovarian cancer (Table 6). *BRCA2* plays a role in maintaining genome stability, especially the homologous recombination pathway for double-stranded DNA repair. The largest exon in both *BRCA1* and *BRCA2* genes is exon 11, which harbors the most criti-

Table 1. Comparison of quality of life between the two groups (points, $\bar{x} \pm s$).

Group	Physical condition		Emotional status		Functional status		Breast cancer specific module		Total score	
	Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention
Observation group (n = 200)	17.12±2.10	27.43±2.65*	17.83±1.54	24.54±2.10*	19.74±1.76	28.10±2.76*	25.10±2.73	34.98±2.85*	81.43±9.10	113.43±13.65*
Control group (n = 200)	17.15±2.14	23.54±2.21*	17.87±1.51	22.21±1.87*	19.83±1.65	22.57±2.35*	25.31±2.83	31.43±2.76*	80.54±9.43	101.54±12.65*
t	0.141	15.943	0.262	11.718	0.527	21.574	0.755	12.654	0.960	9.035
P	0.887	<0.001	0.793	<0.001	0.598	<0.001	0.450	<0.001	0.337	<0.001

Note: * indicates comparison with pre-nursing within the group, P < 0.05

Table 2. Comparison of perceptual control level between the two groups (scores, $\bar{x} \pm s$).

Group	Perceptual experience		Control efficiency	
	Before the intervention	After the intervention	Before the intervention	After the intervention
Observation group (n = 200)	61.83±6.00	72.24±6.79*	43.79±4.17	58.49±6.23*
Control group (n = 200)	61.59±5.92	65.13±6.24*	43.49±4.11	49.23±6.78*
t	0.402	10.903	0.724	14.222
P	0.687	<0.001	0.469	<0.001

Note: * indicates comparison with pre-nursing within the group, P < 0.05.

Table 3. Comparison of negative psychology between the two groups.

Group	Hamilton Anxiety Scale		Hamilton Depression Scale	
	Before the intervention	After the intervention	Before the intervention	After the intervention
Observation group (n = 200)	25.21±3.21	15.24±1.87*	23.65±2.65	19.43±2.10*
Control group (n = 200)	25.32±5.92	18.10±1.67*	23.98±2.55	21.21±2.37*
t	0.231	16.132	1.269	7.949
P	0.817	<0.001	0.205	<0.001

Note: * indicates comparison with pre-nursing within the group, P < 0.05.

Table 4. Comparison of upper limb edema degree between the two groups [n (%)].

Group	None	Mild	Moderate	Severe
Observation group (n = 200)	122 (61.00)	63 (31.50)	15 (7.50)	0
Control group (n = 200)	55 (27.50)	118 (59.00)	16 (8.00)	11 (5.50)
χ^2	53.106			
P	<0.001			

Table 5. Comparison of satisfaction with the two management programs [n (%)].

Group	Very satisfied	Basically satisfied	General	Poor	Satisfaction
Observation group (n = 200)	110 (55.00)	59 (29.50)	24 (12.00)	7 (3.50)	169 (84.50)
Control group (n = 200)	60 (30.00)	73 (36.50)	43 (21.50)	27 (13.50)	133 (66.50)
χ^2					19.329
P					<0.001

Table 6. the genetic information of BRCA1 and BRCA2 in the study.

Name	*BRCA1*	*BRCA2*
ORGANISM	Homo sapiens (Human)	Homo sapiens (Human)
Accession number nucleotide	NM_007294	NM_000059.4
Accession number protein	NP_009225.1	NP_000050.3
Gene ID	672	675
Chromosome	17	13
Inheritance	Autosomal dominant	Autosomal dominant
Cytogenetic location	17q21.31	13q13.1
Chromosome location bp	43044295-43125364	32315508-32400268
nucleotide length	7088 bp	11954 bp
protein length	1863 aa	3418 aa
Molecular weight (Da)	207720.85	384230.28
Isoelectric point	5.29	6.29
Total Exon	22	26

cal and frequent mutations in breast cancer patients. The *BRCA2* protein contains multiple copies of a 70-amino acid motif called the BRC motif, and these motifs mediate binding to RAD51 recombinase, which functions in DNA repair. *BRCA2* is considered a tumor suppressor gene and more than 300 different types of mutations have been identified in this gene, generally termed codon types (13,14).

Epigenetic mechanisms

Today, epigenetic mechanisms are known as an important factor in the development of breast cancer, which means a change in gene expression without a change in the gene sequence. As we know, the increase in methylation in CpG Island Hyper methylation is one of the important mechanisms in the silencing of specific genes. In many cancers, especially breast cancer, this mechanism is involved in the negative regulation of the cell cycle by affecting the genes through the effect of Retinoblastoma factors and P53 factors (15).

LncRNAs and miRNAs

LncRNAs and miRNAs are effective sites outside the protein-coding regions that are expressed in cancer tissues and can be used as molecular markers. One of the advantages of lncRNAs is their high stability and presence in body fluids, which can be measured using the Real time-PCR method. MiRNAs are among the epigenetic factors effective in gene regulation, which play a fundamental role in various biological processes such as the development of angiogenesis, growth, and differentiation. Different types of miRNAs such as miR16, miR-183, miR-200c, miR-34c, Let7, and lncRNAs such as HOTAIR, H19, GAS5, and ARIL can act in different stages of breast cancer by affecting several cellular and molecular targets and can be used as diagnostic biomarkers for breast cancer (16–18).

Discussion

According to the epidemiological investigation (19), breast cancer accounts for about 10% of all malignant tumors, which seriously affects the physical and mental health and economic level of patients, and brings a great burden to society, patients, and their families. At present, the main treatment for breast cancer is surgery, but the physical trauma after surgery will bring a great psychological impact, and long-term adjuvant treatment is needed to avoid recurrence and metastasis. In addition, axillary lymph node dissection may be required, which can easily cause lymphatic reflux disorders in the upper limb of the patient. Studies have shown that (20) scientific and reasonable clinical management programs for breast cancer patients can reduce the occurrence of negative psychology and postoperative adverse reactions, and improve the quality of life. A multidisciplinary refined clinical management scheme is a management scheme throughout the whole course of treatment, which takes into account both local and total, coordinates standardized treatment and individualized treatment carries out the best-individualized diagnosis and treatment scheme around patients, strengthens discipline construction and promotes discipline integration under the premise of ensuring treatment effect and medical safety, which is conducive to reducing the mortality rate of breast cancer and improving long-term survival rate (21).

The results of this study showed that the scores and total scores of the breast cancer quality of life scale in the observation group were higher than those in the control group. The author believes that patients with breast cancer surgery have more problems due to the disease, limited movement of upper limbs after surgery, appearance, etc., coupled with the fear of recurrence of cancer, lack of correct understanding of the disease, most patients 'enthusiasm for treatment will be significantly reduced, resulting in irregular medication, reexamination, inadequate nutrition and lack of functional exercise, which is not conducive to the prognosis and quality of life of patients. The multidisciplinary refined clinical management program is formulated on the premise of fully grasping the basic information of patients by attending doctors, nutritionists, psychological consultants, pharmacists, and rehabilitation trainers, giving full play to the professional advantages of various disciplines, highlighting the feasibility and comprehensiveness of the program, improving the overall clinical management effect, and making patients feel high-quality. Shachar et al. (22) and Buchholz et al. (23) also concluded that it can improve the treatment enthusiasm, promote the prognosis recovery, and then improve the quality of life.

Multidisciplinary clinical management has achieved significant results in a variety of diseases (24,25).

Through the clear and effective division of labor, mutual management, and coordination of team members, combined with the specific situation of patients, the professional knowledge of various disciplines is scientifically and effectively applied to the whole process of patient intervention management, and effective clinical management programs are formulated to maximize the role of intervention. The multidisciplinary team management mode is not only a simple gathering of multidisciplinary personnel but also a scientific integration of various disciplines so that patients can enjoy more comprehensive and standardized clinical management in the whole process of diagnosis and treatment (26,27). In this study, the perceived control level of the observation group was significantly higher than that of the control group, and the scores on Hamilton Anxiety Scale and Hamilton Depression Scale were lower than those of the control group. It is suggested that a multidisciplinary refined clinical management program can enhance the level of perceived control and reduce the negative psychology of patients with breast cancer surgery. The reason is that the perception experience and control efficacy of breast cancer patients are greatly affected by education, family monthly income, and perioperative psychological care, coupled with the unpredictability and uncontrollability of their diseases, which easily lead to negative emotions and affect the prognosis. In routine clinical management, the main intervener is the attending physician, who often only pays attention to the degree of disease and neglects the psychological state of patients. The multidisciplinary refined clinical management program is highly professional, according to the individual situation of different patients, follow-up and intervention are carried out from the aspects of medical treatment, changes in disease indicators, medication, and psychological changes, to put forward targeted prevention strategies and improve the physiological, psychological and social status of patients individually. Jin Qunlong et al. (28) pointed out that the multidisciplinary collaboration model has a significant effect on improving the prognosis of locally advanced rectal cancer, which is similar to the conclusion of this study. The results of this study showed that the improvement and satisfaction of upper limb edema in the observation group were significantly better than those in the control group, which was consistent with the results of Alhazmi et al. (29) and Wu et al. (30). It is further confirmed that the multidisciplinary refined clinical management program can help patients correctly understand the disease, improve the quality of cooperation, and effectively improve the upper limb edema, so the satisfaction is high.

To sum up, the implementation of the multidisciplinary refined clinical management program for patients with breast cancer surgery can effectively improve the quality of life, improve the level of perceptual control, reduce negative psychology, improve the degree of upper limb edema, and increase patient satisfaction. The shortcomings of this study are that the follow-up time is short, the long-term prognosis of breast cancer patients is not analyzed, and the follow-up time will be extended to deepen the study.

Considering the limitations of traditional breast cancer detection methods, their sensitivity, pain, and anxiety, and the risks of imaging techniques, the use of biomarkers can play an effective step in the treatment of this type of cancer. Protein and nucleic acid tumor markers are the most important molecular markers involved in the occurrence and progression of breast cancer.

Today, various techniques such as Microarray, CGH, FISH, IHC, and molecular techniques such as QPCR, MLPA, RT-PCR, and NGS are used to measure tumor markers (31). These techniques promise to improve diagnosis and help to choose the right treatment method for patients and are widely used.

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Interest conflict
The authors declare that they have no conflict of interest.

Author's contribution
LY, RD, YL: have made research design, data collection; SSh, HX, JM: did the data analysis and drafted the paper; JM, JY: revising and rewriting the manuscript. All the authors have approved the final version of the manuscript.

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