

Prevalence and correlates of major depressive disorder in breast cancer survivors in Shanghai, China

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Abstract

Objective: Our objective is to measure the prevalence and correlates of major depressive disorder (MDD) among Chinese breast cancer patients after surgery, which is essential for analyzing the service needs and allocating mental health resources.

Methods: A total of 505 patients were randomly recruited from 1580 post-surgery breast cancer outpatients from one tertiary hospital in Shanghai, and the Mini International Neuropsychiatric Interview was used to assess 1-month prevalence of MDD according to the Diagnostic and Statistical Manual Fourth Edition (DSM-IV) in a two-phase design.

Results: The adjusted 1-month prevalence of MDD was 20.59% (95% CI 17.06–23.82). The risk for depression within the first year was two times as higher as that in more than 1 year. Patients within 1 year after surgery, with lower income, disrupted marriage or being single, recurrent breast cancer and psychiatric history were more likely to have MDD. There was no significant association between depression and disease stage, type of surgery, receptor status and cancer treatment.

Conclusions: Depression is quite common in Chinese breast cancer patients and survivors. A more sensitive and responsive mental health service is recommended for this population.
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Introduction

Breast cancer is by far the most frequent cancer among women worldwide, accounting for 26% of all cancers in women. It is also the leading cause of cancer mortality in women [1]. Because both cancer diagnosis and disease-related treatments can be very stressful for women, the co-morbidity of depression in breast cancer patients is very common. The prevalence of depression among this population ranged from 1% to 53%, depending on study sample, design and particularly the definition and instrument used to assess depression [2–5]. Furthermore, untreated depression has been shown in many studies to be associated with the amplification of physical symptoms, prolonged functional impairment, decreased quality of life and even negative prognosis of the disease [6–8].

In China, breast cancer is the third most frequent type of malignant cancer, and the estimated incidence rate has climbed to 30–50 per 100,000 each year now [9]. With the advances in early detection and treatment, the survival rate of this population is growing rapidly [9,10]. Studies addressing the adverse psychological impact of breast cancer, especially major depression, one of the most prevalent and disabling psychiatric

morbidities, have become increasingly important. Unfortunately to date, reliable and comparative data for depression in Chinese breast cancer patients and survivors were scarce. Moreover, the existing studies were usually handicapped by reliance on self-report measures, where rather arbitrary cut-off values on self-rating symptom scales were used to make diagnosis and to estimate the prevalence of depression. The rates cited from these studies varied quite widely from 23% to 68% [11–13]. More precise estimate of major depression based on established and validated diagnostic tools should be used to analyze the service needs of these patients and to better allocate the new and existing mental health resources.

The very limited studies that explored risk factors for depression in Chinese breast cancer patients so far had yielded inconsistent results [11–14]. Besides medical issues, breast cancer patients have to cope with the challenges from various perspectives of life, including financial and occupational strains, changes of body image, reconstructing self-concept and so on [15]. Furthermore, profound socioeconomic transformations in the past three decades in China have brought about unprecedented changes in the labor market, family structure, socio-moral values, health care and gender

roles. There is the need to clarify the detrimental factors for cancer treatment and rehabilitation.

In sum, the present study is the first of a two-phase design in China to estimate the prevalence of major depressive disorder among patients diagnosed with stage 0–IV breast cancer after surgery. The presence of major depressive disorder (MDD) was identified according to criteria set forth in the Diagnostic and Statistical Manual Fourth Edition (DSM-IV) [16]. Associations between depression and demographic and clinical characteristics were also evaluated. We predicted that major depression would be a frequent but unrecognized and undertreated condition among Chinese breast cancer patients. The risk factors identified would make an early detection of vulnerable patients possible.

Methods

Participants

The study sample was drawn from outpatients treated at the Department of Breast Care in Shanghai Longhua Hospital, a university-affiliated tertiary public hospital with 703 inpatient beds, that mainly serves people from diverse socioeconomic backgrounds in Shanghai, a city of nearly 20 million inhabitants. This department provides approximately 3200 visits of outpatient service monthly for various breast diseases. Participants eligible for this study (i) were primary, biopsy-proven breast cancer, (ii) were 18–65 years old, (iii) were selected 6–36 months after surgery, (iv) had completed radiation therapy and/or chemotherapy and (v) had no other active treatment except for hormonal therapy. Patients were excluded from the study only if they had current or past histories of other severe physical diseases, such as neurological disorder, or any acute, unstable or severe medical condition that might interfere with the interview. Our study was conducted within a 15-month period from January 2008 to March 2009. When patients attended outpatient service, eligible candidates were selected by trained research assistants according to the aforementioned inclusion and exclusion criteria. A total of 1580 women were eligible for recruitment. From this sample, one-third, 526 participants were randomly selected by a computer-generated random number table. Among them, 21(4%) refused for various reasons. In total, 505 subjects were successfully recruited. Women who refused to participate were not different from those who were recruited in terms of age, clinical stage of cancer and time after surgery ($t_{524} = 0.26$, $p = 0.80$; $\chi^2_2 = 3.77$, $p = 0.15$; $\chi^2_3 = 3.45$, $p = 0.33$, respectively).

Individual face-to-face interview of about 40 min long was conducted. The research team consisted of two psychiatrists, one gynecologist and two nurses as research assistants. After complete description of the study was given to the subjects, written informed consent was obtained. The study protocol was approved by institutional review boards of Shanghai Longhua Hospital and Shanghai Mental Health Center.

Measures

The prevalence of MDD was measured by using a two-phase design. In the first phase, we used the Chinese version of the Beck Depression Inventory (BDI) to screen for possible cases [17,18]. Scores of 5–13, 14–20 and ≥ 21 in the Chinese version of the BDI suggested mild, moderate and severe depression, respectively. In our study, we used the cut-off score of 5 to identify possible cases of depression.

In the second phase, Mini International Neuropsychiatric Interview (MINI) [19] was used to identify the major depressive disorder patients according to DSM-IV criteria. The MINI is a short structured diagnostic interview for DSM-IV and International Classification of Disease, Tenth Edition (ICD-10) for psychiatric disorders. The validity and applicability test of the Chinese version of MINI has been conducted [20]. Although MINI is a semi-structured interview, additional questions could be used to inquire about metaphors of distress that are specific to the local context. This ensures that the diagnostic interview in our study is culturally informed. We used Modules A (major depressive episode), Module D (manic episode and hypomanic episode) and Module L (psychotic disorders) of MINI in this study. Module D and L were administered to exclude bipolar and psychotic disorders. In our study, only current (within 1 month) diagnosis of major depressive disorder was made.

In the second phase, all participants with high scores on BDI (5 or higher) were assessed by MINI to make the diagnosis of MDD. Ten per cent of the participants with low scores (4 or lower) on the BDI were randomly selected to receive the MINI assessment to determine the rate of false negatives. For patients diagnosed with MDD, the 17-item Hamilton Depression Scale (HAMD) was used to assess the severity of major depressive episode. Scores of 17–24 and >24 on the Chinese version of HAMD were defined as mild to moderate and severe depression, respectively [17]. MINI was administered by one of the authors (Weijun Chen), who is a psychiatrist and completed the training for using MINI. HAMD rating was conducted by another independent psychiatrist.

After the recruitment, research assistants collected socio-demographic and medical data from the participants in a semi-structured interview. Socio-demographic data included age, education, occupational status, monthly income and marital status. Medical data included time after surgery, state of tumor–node metastasis (TNM) at the time of primary diagnosis, type of surgery, estrogen receptor and progesterone receptor status, chemotherapy, radiotherapy and immunotherapy and recurrence. Medical records were reviewed under the supervision of the gynecologist in our team to verify the accuracy of collected data. Information of past psychiatric history and family history of mental illness were also collected.

Statistical analysis

According to the diagnoses by MINI, the adjusted 1-month prevalence of MDD and the corresponding

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95% CI were estimated. Chi-squared test was conducted to examine differences in the prevalence of MDD across socio-demographic and clinical characteristics. The multivariate logistic regression analysis was performed to identify socio-demographic and clinical variables associated with MDD. Adjusted odds ratios with 95% CIs were presented for each variable based on the logistic regression analysis. All the statistical analyses were performed with SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of the participants

Of a total of 505 study participants, the mean age was 52.02 years (SD=4.55, range 23–65) and the mean time after surgery was 17.6 months (SD=9.0, range 6–36). Of these, 469 (93%) were married. Nearly half of them were retired or unemployed. Three hundred and thirty-two (66%) participants had monthly income not higher than RMB 2000. Four hundred and thirty-one (85.7%) participants had stage 0-II breast cancer. Three hundred and fourteen (62.2%) finished their surgery for more than 1 year. Mastectomy (88.9%) was the most prevalent type of operation. No participant reported a history of schizophrenia and other psychotic disorders, bipolar disorder or substance and alcohol abuse, whereas 43 (8.5%) reported previous depressive or anxiety disorder. The mean BDI score of the participants was 7.50 (SD=7.00, range 0–36). The socio-demographic and clinical characteristics of 505 participants are summarized in Tables 1 and 2, respectively.

Prevalence of major depression

There were 505 participants who received the BDI assessment, and 205 (40.59%) scored above the cut-off. Then all these 205 participants were interviewed by means of MINI. Ninety-four (45.85%) was diagnosed as MDD cases. Three hundred participants scored lower than the cut-off score 5, of whom 30 (10%) were randomly chosen to respond to the MINI. One (0.20%) met the criteria of MDD. Table 3 showed a total of 95 patients diagnosed as MDD. The adjusted 1-month prevalence is 20.59% (95% CI: 17.06–23.82). The mean 17-item HAMD score was 20.99 (SD=3.22, range 17–29). Of these, 73 (76.8%) had mild to moderate depression, and 22 (23.2%) were severe. Twenty-three (24.2%) patients had past psychiatric history: 15 (15.79%) for depressive episode, 3 (3.16%) for dysthymia, 3 (3.16%) for anxiety disorders and 2 (2.10%) for mixed anxiety–depressive disorder.

Correlates of depression

Table 1 showed that post-surgery breast cancer patients with disrupted marital status (being separated, divorced or widow) or being single were 2.8 times in average

more likely to have MDD than those who were still married. Those in the lowest income band (less than RMB 2000) were nearly two times more likely to have MDD than those in the higher income bands. The risk of MDD in patients with past psychiatric history was 11 times higher than those without past psychiatric history. These effects were adjusted for other demographic and clinical factors. Age, occupation status, education and family history of mental illness did not show significant association with MDD.

Results in Table 2 suggested that higher risk of MDD was reported within 12 months after surgery. After 12 months of surgery, the diagnosis of MDD was reduced by half. In addition, patients with recurrent breast cancer had much higher risk (15 times) of MDD than those without such condition. However, types of operation, TNM stage, estrogen receptor and progesterone receptor status, radiation, chemotherapy and immunotherapy did not correlate with MDD.

Discussion

The demographic and clinical characteristics of our sample were similar to that of a previous 'Shanghai Breast Cancer Survival Study' in terms of mean age, percentage of being married, TNM stage 0–II, mastectomy and chemotherapy (52.0 vs 53.6 years; 92.9% vs 87.2%; 85.7% vs 89%; 88.9% vs 95.1%; 93.1% vs 91.8%, respectively, with the first of the two numbers representing the present study and the second number the previous study) In that study, a population-based cohort of breast cancer survivors ($n=2232$) 3 years after diagnosis was recruited through the Shanghai Cancer Registry from 2002 to 2004 [22]. Considering the different recruitment time (17.6 months after surgery versus 3 years after diagnosis), the mean age of diagnosis of our sample was very close to that of the representative cohort.

In our study, the overall 1-month prevalence of MDD in patients with breast cancer in the time of 6–36 months post-surgery was 20.59%. Most (77%) were with mild to moderate depression, and 23% were severe. Regarding the varied prevalence at different time points after surgery, in our study sample the prevalence of MDD in 6–12 months post-surgery was 27.2%, whereas the risk for depression within the first year was two times as higher as that in more than 1 year. Our findings suggested that the highest risk for depression in breast cancer patients is in the first year after diagnosis and primary treatment. On the basis of diagnostic interviews, some previous studies focusing on the assessment within the first year post-surgery also demonstrated elevated rates of major depression. The prevalence of 15–30% was reported in studies [23–27].

Some studies showed that for breast cancer patients, depression will improve significantly after the typically higher vulnerability first year following cancer diagnosis and initial treatment [5]. For example, using the eight-item Center for Epidemiological Studies Depression Scale (CES-D), Bardwell *et al.* reported that the

Table 1. Prevalence of major depressive disorder (MDD) by demographic characteristics

Characteristic	Number (%)	MDD number (%)	p-value of χ^2	Adjusted OR (95% CI) ^a	p-value of MLR
Age (years)					
<36	20 (4.0)	3 (15.0)	0.31	1.00	0.16
36–45	93 (18.4)	14 (15.1)		0.40 (0.07–2.22)	
46–55	233 (46.1)	52 (22.3)		0.87 (0.40–1.90)	
56–65	159 (31.5)	26 (16.4)		0.50 (0.26–0.95)	
Marriage status					
Married	469(92.9)	83(17.7)	0.02	1.00	0.03
Unmarried/separated/divorced/widowed	36 (7.1)	12 (33.3)		2.84(1.13–7.13)	
Occupation status					
Employed	246 (52.3)	48 (18.3)	0.92	1.00	0.99
Retirement	207(41.0)	40 (19.3)		0.96 (0.51–1.81)	
Unemployed	34 (6.7)	7 (20.0)		0.98 (0.35–2.73)	
Education					
Primary school	21 (4.2)	6 (28.6)	0.18	1.00	0.76
Junior middle school	155 (30.7)	33 (21.3)		1.79 (0.54–5.92)	
High middle school	180 (35.6)	36 (20.0)		1.15 (0.62–2.14)	
≥College	149 (29.5)	20 (13.4)		0.90 (0.41–1.97)	
Monthly income^b					
≤2000	332 (68.2)	77 (23.2)	0.06	1.00	0.11
>2000, ≤5000	121 (24.8)	13 (10.7)		0.43 (0.20–0.95)	
>5000	34 (7.0)	4 (11.8)		0.61 (0.17–2.28)	
Family history of mental disorder					
No	492 (97.4)	92 (18.7)	0.69	1.00	0.94
Yes	13 (2.6)	3 (23.1)		1.06 (0.26–4.33)	
Past psychiatric history					
No	462 (91.5)	71 (15.4)	0.00	1.00	0.00
Yes	43 (8.5)	24 (55.8)		10.83(4.93–23.78)	

^aAdjusted OR (95% CI) was calculated in multivariate analysis with logistic regression method.

^bThe per capita disposable monthly income for Shanghai residents in 2008 was RMB ¥ 2200, US\$1.00 = RMB ¥ 6.8 [21].

OR, odds ratio; MLR, multiple linear regression.

rates of depressive symptoms in breast cancer survivors within 4 years since diagnosis were comparable with women in the general population [28]. In our study although the prevalence of MDD decreased significantly after 1 year of surgery, nearly 16% of patients did suffer from major depression in the years after surgery and similar to that reported by Gandubert *et al.* [29]. By the same instrument of MINI, they found 19.4% of patients were diagnosed as MDD following breast cancer diagnosis, and 16.0% were diagnosed more than 1.75 years after surgery. Some other studies even suggested there were no significant decrease of depression for years after surgery [27,30]. With Structured Clinical Interview For DSM-III-R Axis I Disorders (DSM-III-R/SCID) administered, Burgess *et al.* did not observe any decrease in prevalence of depressive disorder in more than 1 year after diagnosis in a cohort of 222 early breast cancer patients. Given the difference in study methods, and particularly the instrument for assessing depression, such cross-study variation of prevalence at different times during the cancer trajectory is expected. However, studies already suggested that prevalence estimates based on self-report screening instruments were usually much more variable than those based on structured diagnostic interview [31]. Our findings are consistent with others and suggest that a significant number of patients will still suffer from depression in years to come after treatment and they will need ongoing attention and care.

This study is the first attempt to use diagnostic instruments to detect major depressive disorder in breast

cancer patients in China. The results demonstrated an equally high rate of major depression in Chinese patients compared with their counterparts in Western countries. A recent population-based epidemiological study in four Chinese provinces suggested that the adjusted 1-month prevalence of DSM-IV/SCID MDD was 1.57% (95% CI: 1.29–1.91) in urban and 2.6% (95% CI: 2.28–2.97) in women [32]. Compared with the general population, breast cancer patients and survivors had a much higher risk of depression. Because the prevalence of depression found in Chinese surveys in general population remains in the low-average range of worldwide estimates [33,34], it would appear that there are ethnic differences in prevalence of depression. To make things worse, with the lack of knowledge on depression, breast cancer patients and their families may misconstrue the experience of major depression as a 'normal' psychological reaction to diagnosis of cancer. Fear of stigmatization and psychological denial may further delay these patients from seeking proper treatment. In China, depression still is an under-diagnosed and undertreated illness [35]. A recent study in five Chinese cities reported that the prevalence of depressive disorders (including MDD and dysthymic disorder) among outpatients in general hospital was 12.0%, but the recognition rate was quite low [36]. The results of this study highlighted the importance to develop a mental health care system that is sensitive to the needs of breast cancer patients. On the other hand, the MDD cases identified in our study may only represent the 'tip of the iceberg'.

Prevalence and correlates of MDD

Table 2. Prevalence of major depressive disorder (MDD) by disease characteristics

Characteristic	Number (%)	MDD number (%)	p-value of χ^2	Adjusted OR (95% CI) ^a	p-value of MLR
Months after surgery					
>6, ≤ 12	191 (37.8)	43 (22.5)	0.25	1.00	0.02
>12, ≤ 24	192 (38.0)	32 (16.7)		0.47(0.25–0.86)	
>24, ≤ 36	122 (24.2)	20 (16.4)		0.45 (0.23–0.87)	
Types of operation					
Breast conserving	56(11.1)	9 (16.1)	0.60	1.00	0.80
Mastectomy	448(88.9)	85 (19.0)		1.14 (0.42–3.11)	
TNM stage					
0–I	251(49.9)	52(20.7)	0.42	1.00	0.58
II	180(35.8)	33(18.3)		0.94 (0.50–1.76)	
III–IV	72(14.3)	10(13.9)		0.58 (0.20–1.66)	
ER and PR status					
ER/PR positive	269 (53.3)	44 (16.4)	0.19	1.00	0.54
ER/PR negative	153 (30.3)	36 (23.5)		1.89 (0.49–7.26)	
ER/PR mixed	83 (16.4)	15 (18.1)		1.36 (0.65–2.82)	
Radiation therapy					
No	308 (61.0)	66(21.4)	0.06	1.00	0.23
Yes	197 (39.0)	29(14.7)		0.64 (0.31–1.33)	
Chemotherapy					
No	34 (6.7)	8(23.5)	0.47	1.00	0.80
Yes	471 (93.3)	87(18.5)		1.15 (0.39–3.33)	
Immunotherapy					
Yes	164(32.5)	37(22.6)	0.14	1.00	0.85
No	341(67.5)	58(17.0)		1.14 (0.37–4.16)	
Recurrence					
No	495 (95.6)	88 (17.8)	0.00	1.00	0.00
Yes	10 (2.0)	7 (70.0)		19.95(3.85–103.33)	

^aAdjusted OR (95% CI) was calculated in multivariate analysis with logistic regression method.

OR, odds ratio; MLR, multiple linear regression; TNM, tumor–node metastasis; ER, estrogen receptor; PR, progesterone receptor.

Besides depression, other types of psychiatric morbidities, such as dysthymia, anxiety disorder and psychosomatoform disorder in breast cancer patients could easily slip through the net of the existing health care service.

Past psychiatric history is a risk factor identified in our study for depression in breast cancer patients. This robust association was also found in the study of Gandubert *et al.* [29], which suggested that a breast cancer diagnosis and treatment could reactivate a previous depressive disorder or trigger a new onset episode. Regarding socio-demographic correlates and risk factors, our findings were consistent with most other findings [5,11]. Patients with low income were more likely to have MDD than patients with higher income in our study. A considerable body of studies has already showed the relationship between economic hardship and psychological distress [36]. We also found depression was significantly correlated to the disrupted marriage or being single. Being widow, separated, divorced and single frequently related to more household strain, financial strain and lack of support, which significantly influenced the psychological

well-being [35,36]. Among clinical characteristics, only the factor of cancer recurrence was found to be associated with depression in our study. We did not find any relationship between depression and disease stage, type of surgery, receptor status and cancer treatment. The majority of existing studies also suggested that the occurrence of depression in breast cancer patients is more strongly influenced by psychosocial factors, rather than the severity of disease or types of treatment [5,28]. However, the aforementioned results should be interpreted with caution as they could be attributed to substantive and/or methodological effects, because most studies mainly recruited early-stage breast cancer patients [28]. In contrast, there were increasing studies that demonstrated the biologic factors in breast cancer relating to the mechanism of depression, for example, elevated pro-inflammatory cytokines, dysfunctional hypothalamic–pituitary–adrenal axis, neuro-toxic effects of chemotherapy and so on [37–39]. A bio-psycho-social approach to understanding the depression in breast cancer is needed for future studies.

Table 3. Prevalence of major depressive disorder

Major depressive disorder	n	Prevalence	
		Unweighted (%)	Weighted % (95% CI)
Total	95	18.1	20.6 (17.06–23.8)
>6, ≤ 12 months post-surgery	43	22.5	27.2 (20.9–33.6)
>12, ≤ 24 months post-surgery	32	16.7	16.7 (11.4–22.0)
>24, ≤ 36 months post-surgery	20	16.4	16.4 (9.8–23.0)

Several limitations in this study need to be discussed here. First, although the demographic and clinical features of our sample were similar to that of a population-based study in Shanghai, there was likely some sampling bias in this study as the study sample came from one hospital. In Shanghai, tertiary hospitals have the most advanced technologies and can provide high quality diagnoses and treatment. It is possible that the hospital in the present study was referred some of the more difficult patients with more complex presentations. Also it is known that patients' help-seeking behavior might bias the prevalence rate [40]. Second, in this study we only provided the diagnosis of one type of mood disorder, which may possibly increase the false positives cases from those screened with the BDI test. Other common mental disorders in breast cancer patients such as anxiety disorder and adjustment disorder should be studied in future. Third, some other important variables should be further explored in future studies, for example, time after chemo/radiotherapy.

In conclusion, the results of this cross-sectional two-phase study underline the fact that psychiatric morbidities, such as MDD were very common in Chinese breast cancer women. The results highlight the necessity to recognize the high prevalence of depression and the need to provide mental health service to this patient population. Additionally, the potential risk factors identified in our study could be used to facilitate early detection of vulnerable members which could be followed by the development of a comprehensive bio-psycho-social rehabilitation program for their adaptation and rehabilitation.

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