Impact of body mass index, weight gain, and metabolic disorders on survival and prognosis in patients with breast cancer who underwent chemotherapy

Ping Yang[1,2], Yingjian He[3], Xinying Yu[3], Baohua Liu[1], Xuemei Wang[4], Xiangping Li[2], Peiyu Wang[1]

[1]School of Public Health, Peking University, Beijing 100191, China;
[2]School of Nursing, Peking University, Beijing 100191, China;
[3]Breast Cancer Center, Peking University Cancer Hospital and Institute, Beijing 100142, China;
[4]Department of Health Statistics, School of Public Health, Inner Mongolia Medical University, Hohhot 010110, China.

Abstract

Background: Weight gain during chemotherapy in patients with breast cancer contributes to their poor prognosis. However, a growing number of studies have found that metabolic disorders seem to play a more important role in breast cancer prognosis than weight gain. This study aimed to explore the prognostic effects of body mass index (BMI), weight gain, and metabolic disorders on the overall survival (OS) and prognosis of patients with breast cancer who underwent chemotherapy.

Methods: Data from the inpatient medical records of patients with breast cancer who underwent chemotherapy at the Beijing Cancer Hospital Breast Cancer Center from January to December 2010 were retrospectively collected, and the patients were followed up until August 2020.

Results: A total of 438 patients with stages I to III breast cancer met the inclusion and exclusion criteria. Forty-nine (11.19%) patients died, while 82 (18.72%) patients had tumor recurrence and metastasis at the last follow-up (August 2020). From the time of diagnosis until after chemotherapy, no significant differences were observed in the body weight ($t = 4.694$, $P < 0.001$), BMI categories ($\chi^2 = 19.215$, $P = 0.001$), and incidence of metabolic disorders ($\chi^2 = 24.841$, $P < 0.001$); the BMI categories and weight change had no effect on the OS. Both univariate ($\chi^2 = 6.771$, $P = 0.009$) and multivariate survival analyses (hazard ratio = 2.775, 95% confidence interval [CI]: 1.326–5.807, $P = 0.007$) showed that low high-density lipoprotein cholesterol (HDL-C) levels at diagnosis had a negative impact on the OS. The multivariate logistic regression analysis showed that the HDL-C level at diagnosis (odds ratio [OR] = 2.200, 95% CI: 0.996–4.859, $P = 0.051$) and metabolic disorders after chemotherapy (OR = 1.514, 95% CI: 1.047–2.189, $P = 0.028$) are risk factors for poor prognosis in patients with breast cancer.

Conclusions: Chemotherapy led to weight gain and aggravated the metabolic disorders in patients with breast cancer. Low HDL-C levels at diagnosis and metabolic disorders after chemotherapy may have negative effects on the OS and prognosis of patients with breast cancer.

Keywords: Breast cancer; Body mass index; Weight change; Metabolic disorder; Overall survival; Prognosis; High-density lipoprotein cholesterol

Introduction

Breast cancer is the most common malignant tumor in women. In 2020, 2.3 million new cases of breast cancer were reported, accounting for 11.7% of all malignancies and 685,000 deaths in women worldwide; breast cancer was also the leading cause of death, among all malignancies in women.[1] From 2000 to 2015, the incidence and mortality rate of breast cancer among women in China increased annually.[2] The latest cancer statistics showed 304,000 new cases of breast cancer and 70,000 deaths in China in 2015.[3]

Compared with that in the United States, the breast cancer mortality rate among women in China has rapidly increased in recent years.[4] Levaggi *et al*[5] found that breast cancer decreased the life expectancy and imposed a significant health burden on the female Chinese population. Chemotherapy is an important systemic treatment for patients with breast cancer, and it plays an important role in improving the long-term survival of patients with this condition.[6] However, several studies showed that patients with breast cancer gain weight gain[7,8] and develop metabolic disorders[9] after undergoing chemotherapy. These changes can lead to a poor prognosis in patients with breast cancer, such as increased risks of recurrence, metastasis, and reduced survival rates.[10]

Access this article online

Quick Response Code:	**Website:** www.cmj.org
	DOI: 10.1097/CM9.0000000000001988

Some studies analyzed the prognostic impact of obesity (OB) and metabolic disorders at diagnosis in patients with breast cancer.[11,12] However, there is a lack of evidence on the long-term prognosis due to weight gain and metabolic disorders after chemotherapy in Chinese patients with breast cancer. This study aimed to assess the body mass index (BMI), weight change, and metabolic disorders in patients with breast cancer at diagnosis and after chemotherapy, exploring the effects of these factors before and after chemotherapy on cancer recurrence, metastasis, and overall survival (OS) in patients with breast cancer.

Methods

Ethical approval

The protocol was approved by the Peking University Institutional Review Board (No. IRB00001052-16036). Informed consent was waived due to the nature of the retrospective analysis.

Patients

Inpatients diagnosed with primary breast cancer at the Breast Cancer Center of Peking University Cancer Hospital in 2010 were recruited in this retrospective cohort study. The inclusion criteria were: female patients (1) diagnosed with tumor-node-metastasis (TNM) stages I to III breast cancer confirmed by pathological examination, (2) aged >18 years, (3) who received breast cancer-related treatments (chemotherapy and surgery) at the Breast Center at Beijing Cancer Hospital, and (4) whose medical records on initial diagnosis and post-chemotherapy hospitalization were available through the hospital inpatient system (if the patient had been hospitalized several times during the course of chemotherapy, the last medical record was selected; in the case of patients who underwent neo-adjuvant chemotherapy, the pre-surgery inpatient medical records were used as the last medical records of the post-chemotherapy hospitalization). On the contrary, female patients (1) who were previously diagnosed with breast cancer or other malignant tumors and (2) whose post-chemotherapy hospitalization stay was <1 month from the initial diagnosis were excluded.

Body weight

The patient's height and weight at diagnosis (body weight, BW1) and after chemotherapy (BW2) were obtained from the patient's inpatient medical records. BMI was calculated using the patient's height and weight as, BMI = BW (kg)/ height $(m)^2$. According to the recommendations of the Chinese Obesity Working Group,[13] a BMI of <18.5 kg/m^2 indicates underweight (UW), a BMI of 18.5 to 23.9 kg/m^2 indicates normal weight (NW), a BMI of 24.0 to 27.9 kg/m^2 indicates overweight, and a BMI of ≥28.0 kg/m^2 indicates OB. The weight change after chemotherapy can be calculated as, weight change = (BW2-BW1)/BW1 × 100%. According to previous studies,[14] weight change was classified as weight loss (≤−5.0%), weight stabilization (−4.9% to 4.9%), and weight gain (≥5.0%).

Metabolic disorders

According to the Chinese Diabetes Society Metabolic Syndrome (MS) criteria in 2004[15] and 2014,[16] combined with the information available in the patient's medical records, the criteria for diagnosing metabolic disorders in patients with breast cancer in this study were as follows: (1) overweight and/or obese: BMI ≥ 25.0 kg/m^2, (2) hyperglycemia: fasting plasma glucose ≥6.1 mmol/L and/or diagnosed with and treated for diabetes mellitus; (3) hypertension: blood pressure ≥ 130/85 mmHg and/or diagnosed with and treated for hypertension, (4) high triglyceride (TG) level: fasting TG ≥ 1.70 mmol/L, and (5) low high-density lipoprotein cholesterol (HDL-C) level: fasting HDL-C < 1.04 mmol/L.
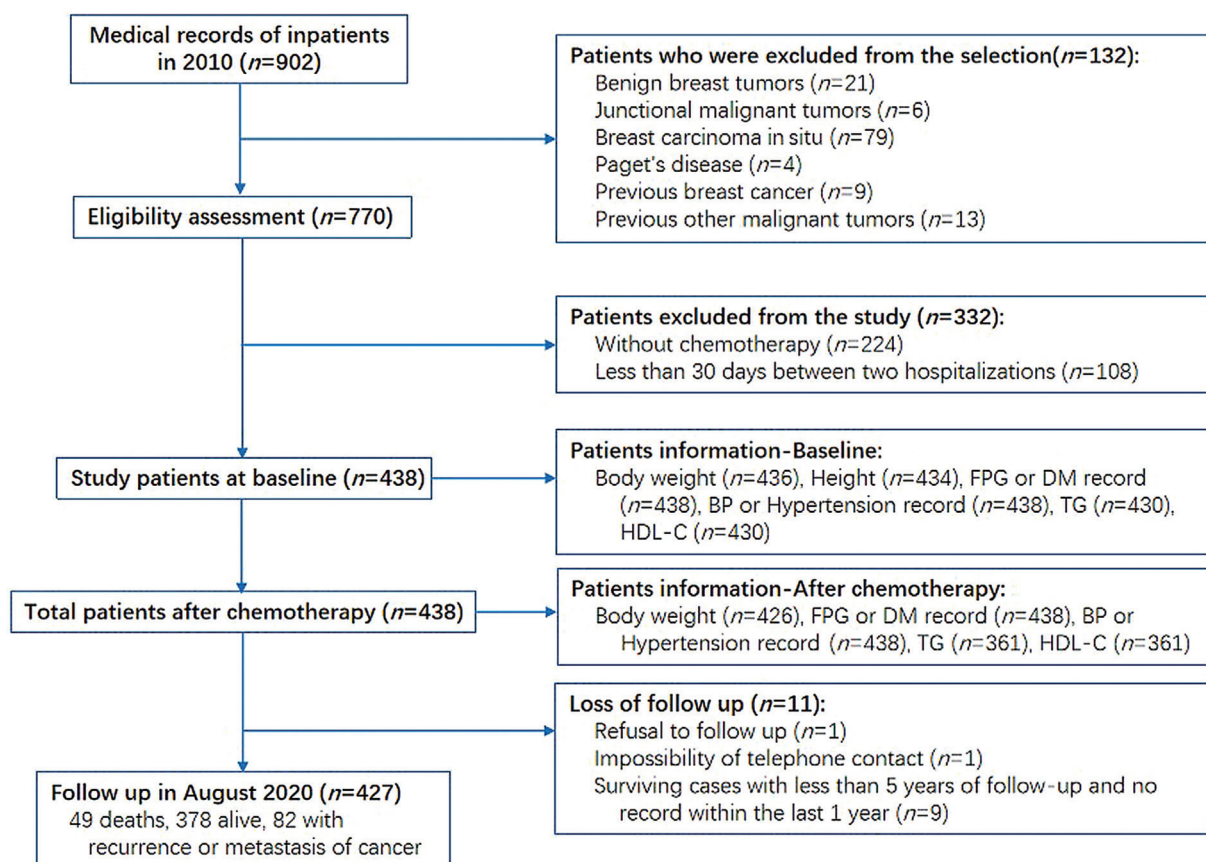
Follow-up

During follow-up, outpatient and inpatient examinations and regular telephone follow-ups were conducted until the patient's death or August 31, 2020. All patients were followed up by telephone once a year, and data on their prognosis and survival were also obtained during outpatient and inpatient visits. All patients' follow-up results were provided by the Breast Cancer Center at Beijing Cancer Hospital. The OS was defined as the period from the date of diagnosis to the date of death from any cause. Patients who were alive at the last follow-up were censored. Patients lost to follow-up were defined as surviving patients with < 5 years of follow-up and those with no record of follow-up within the last year.

Statistical analysis

Normally distributed continuous variables were described using mean and standard deviation. Non-normally distributed variables were described using median and interquartile ranges. Categorical and counted variables were expressed using the number of cases and percentage. The differences in BW and BMI at diagnosis and after chemotherapy were determined using paired t tests. The differences in BMI categories and metabolic disorders at diagnosis and after chemotherapy were determined using McNemar χ^2 test. Survival curves were derived from the Kaplan-Meier estimates, and the curves were compared using log-rank tests. A Cox proportional hazard model was used to estimate the hazard ratios (HRs) for the OS of the patients in a multivariate analysis. A binary logistic regression model was applied to estimate the odds ratio (OR) for the prognosis of patients with breast cancer in a multivariate analysis. All statistical tests were two sided and were performed using SPSS 22.0 software (IBM Corp., Armonk, NY, USA). P values of <0.05 were considered significant.

Results

A total of 902 patients diagnosed with primary breast cancer were admitted to the Breast Cancer Center at the Peking Cancer Hospital in 2010. Twenty-one patients with benign breast tumors, six with junctional malignant tumors, seventy-nine with carcinoma *in situ* of the breast,

Figure 1: Diagram reporting the number of patients selected and follow-up In the study. BP: Blood pressure; DM: Diabetes mellitus; FPG: Fasting plasma glucose; HDL-C: High-density lipoprotein cholesterol; TG: Triglyceride.

four with Paget's disease, nine who were previously diagnosed with breast cancer, and thirteen who were previously diagnosed with other malignant tumors were excluded. Totally 224 patients who did not undergo chemotherapy and 108 patients who underwent chemotherapy for <30 days between two hospitalizations were excluded. Finally, 438 patients with stages I to III breast cancer who met the inclusion and exclusion criteria were included in the study [Figure 1].

At the end of August 2020, 49 (11.2%) patients had died, 11 (2.5%) were lost to follow-up, 378 (86.3%) survived, and 82 (18.7%) had cancer recurrence and metastasis. The 1-, 3-, 5-, and 10-year OS rates of patients with breast cancer were 97.5% (95% confidence interval [CI]: 96.0–98.9%), 94.0% (95% CI: 91.8–96.3%), 91.9% (95% CI: 89.3–94.5%), and 88.4% (95% CI: 85.3–91.5%), respectively; meanwhile, the median survival time was 109.29 (95% CI: 97.76–102.70) months.

Patients' characteristics

The 438 participants were all female patients with breast cancer, aged 47.4 ± 10.5 years (23–75 years) at diagnosis, with an average time interval of 121.4 ± 50.4 days (30–464 days) between two hospitalizations. The clinical characteristics of these patients are presented in Supplementary Table 1, http://links.lww.com/CM9/A937.

Weight and metabolic disorders in patients with breast cancer

The complete weight measurement records of 422 patients at the time of diagnosis and after chemotherapy were obtained. A total of 302 (71.6%) patients had stable weight, 30 (7.1%) had > 5% weight loss, and 90 (21.3%) had ≥ 5% weight gain. The differences in BW, BMI categories, and metabolic disorders between two hospitalizations were compared using McNemar χ^2 test. As shown in Tables 1 and 2, significant differences were observed in the BW, BMI categories, and metabolic disorders between two hospitalizations.

Risk factors for breast cancer survival time

A Kaplan-Meier analysis (log-rank method) was used to conduct a univariate analysis of the OS time of patients with breast cancer with different clinical characteristics; the variables (menopausal status, lymph node status, type of surgery, estrogen receptor [ER] status, and progesterone receptor [PR] status) with significant results are shown in Figure 2A–E.

A Kaplan-Meier analysis (log-rank method) was applied to compare the OS time of patients with breast cancer with different BMI categories, weight changes at the time of diagnosis and after chemotherapy, and different numbers

Table 1: Comparison of body weight, BMI categories, and metabolic disorders ($N = 422$).

Variables	At diagnosis	After chemotherapy	Statistics	P value
Body weight (kg)	63.73 ± 9.47	64.44 ± 9.53	4.694^*	<0.001
BMI (kg/m^2)	24.93 ± 3.55	25.23 ± 3.45	4.444^*	<0.001
<18.5	5 (1.2)	4 (0.9)		
18.5–23.9	172 (40.8)	151 (35.8)		
24.0–27.9	175 (41.5)	185 (43.8)		
≥28.0	70 (16.6)	82 (19.4)		
Metabolic disorder indicators			$19.215^\dagger$	0.001
Overweight and/or obese	196 (46.4)	216 (51.2)		0.010
Hyperglycemia	43 (9.8)	54 (12.3)		0.063
Hypertension	73 (16.7)	78 (17.8)		0.090
High TG	114 (32.1)	190 (53.5)		<0.001
Low HDL-C	24 (6.8)	61 (17.2)		<0.001
N of metabolic disorders			$24.841^\dagger$	<0.001
0	161 (36.7)	117 (26.7)		
1–2	221 (50.5)	247 (56.4)		
≥3	56 (12.8)	74 (16.9)		

Data are presented as n(%) or mean ± standard deviation. $^*t$ test. †Chi-square test. BMI: Body mass index; HDL-C: High-density lipoprotein cholesterol; TG: Triglyceride.

Table 2: Comparisons of overall survival time among patients with different nutrition or metabolic status.

| Variables	N	Death(s)	Survival (months)	χ^2 value	P value
BMI at diagnosis (kg/m^2)				2.153	0.541
<18.5	6	1 (16.7)	111.93 (105.00–118.86)		
18.5–23.9	175	15 (8.6)	123.52 (119.81–127.24)		
24.0–27.9	181	22 (12.2)	120.13 (116.22–124.05)		
≥28.0	72	10 (13.9)	116.39 (108.69–124.09)		
BMI after chemotherapy (kg/m^2)				6.642	0.084
<18.5	4	2 (50.0)	94.30 (69.21–119.39)		
18.5–23.9	15	14 (9.2)	122.85 (118.72–126.99)		
24.0–27.9	185	21 (11.4)	120.82 (117.07–124.58)		
≥ 28.0	83	11 (13.3)	116.93 (109.86–123.99)		
Weight changes after chemotherapy (%)				3.809	0.149
≥−5.0	30	6 (20.0)	108.60 (96.28–120.92)		
−4.9 to 4.9	304	34 (11.2)	121.50 (118.35–124.64)		
≥5.0	90	7 (7.8)	123.40 (118.82–127.99)		
N of metabolic disorders at diagnosis				2.411	0.300
0	161	15 (9.3)	121.30 (117.23–125.37)		
1–2	221	25 (11.3)	122.11 (118.63–125.58)		
≥3	56	9 (16.1)	113.38 (104.78–121.98)		
N of metabolic disorders after chemotherapy				2.179	0.336
0	117	9 (7.7)	121.25 (117.28–125.21)		
1–2	247	30 (12.2)	120.63 (117.03–124.23)		
≥3	74	10 (13.5)	118.11 (111.45–124.78)		

Data are shown as n (%), median (95% confidence interval). BMI: Body mass index.

of metabolic disorders, respectively; however, it failed to confirm the effect of different BMI categories, weight changes, or different numbers of metabolic disorders on the OS time of patients with breast cancer [Table 2].

A Kaplan-Meier analysis (log-rank method) was also applied to compare the OS time of patients with breast cancer with different metabolic disorders at diagnosis and after chemotherapy. The results only showed that low HDLC levels at diagnosis resulted in lower OS time in patients with breast cancer ($\chi^2 = 6.771$, $P = 0.009$) [Figure 2F].

The multivariate Cox regression analysis (backward likelihood ratio [LR] method) was used to analyze the risk factors for the OS outcome of patients with breast cancer. Patient's age (≥ 40, 41–59, and ≥ 60 years) at diagnosis, menopausal status (premenopausal or postmenopausal) at diagnosis, TNM stage (I, II, and III), type of surgery (mastectomy or lumpectomy), lymph node status (negative or positive), ER status (negative or positive), PR status (negative or positive), and human epidermal growth factor receptor 2 (HER2) status (negative or positive) combined with the BMI categories (at diagnosis or after chemothera-
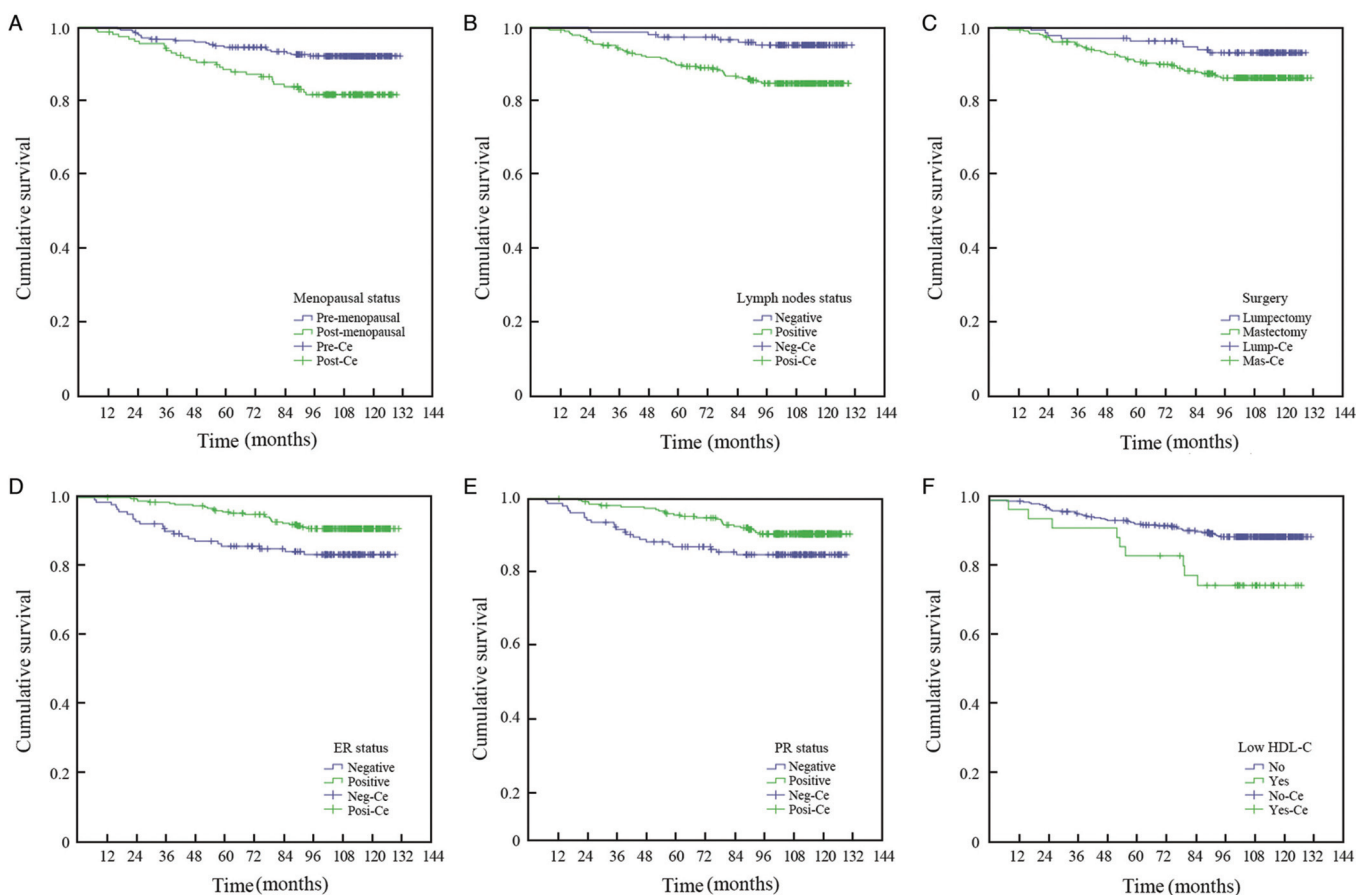
Figure 2: Kaplan-Meier curves for the overall survival of patients with breast cancer with different (A) menopausal status ($\chi^2 = 10.263$, $P < 0.001$), (B) lymph node status ($\chi^2 = 10.196$, $P = 0.001$), (C) type of surgery ($\chi^2 = 4.220$, $P = 0.040$), (D) ER status ($\chi^2 = 6.437$, $P = 0.011$), (E) PR status ($\chi^2 = 4.022$, $P = 0.045$), and (F) HDL-C level at diagnosis. ER: Estrogen receptor; HDL-C: High-density lipoprotein cholesterol; PR: Progesterone receptor.

py), weight changes after chemotherapy, or indicators or numbers of metabolic disorders (at diagnosis or after chemotherapy) were included as independent variables. The results are shown in Table 3.

Risk factors for breast cancer prognosis

A multivariate logistic regression model was used to predict the risk factors for cancer recurrence or metastasis (0 = no, 1 = yes) using patient's age (≥ 40, 41–59, and ≥ 60 years) at diagnosis, menopausal status (premenopausal or postmenopausal) at diagnosis, TNM stage (I, II, and III), type of surgery (mastectomy or lumpectomy), lymph node status (negative or positive), ER status (negative or positive), PR status (negative or positive), and HER2 status (negative or positive) combined with the indicators of metabolic disorder (at diagnosis or after chemotherapy) or weight changes as the related factors. The results are shown in Table 4.

Discussion

In this study, 86.3% of patients with breast cancer achieved an OS of almost 10 years. Their 1-, 3-, 5-, and 10-year survival rates were 97.5%, 94.0%, 91.9%, and 88.4%, respectively. Li et al[17] followed up 3470 female patients with breast cancer from four hospitals in Beijing and reported a 5-year survival rate of 90.72%. Chen et al[18] followed up 13,297 female patients with primary breast cancer in Guangzhou from 2008 to 2017, and reported 1-, 3-, and 5-year survival rates of 99.0%, 95.3%, and 92.1%, respectively. The 5-year survival rate of patients with breast cancer in these studies was similar to that in our study. This finding suggests that in some developed Chinese cities, such as Beijing and Guangzhou, patients with breast cancer achieve a better survival after undergoing systematic standard treatments. Compared with the 5-year relative survival rate (73.0%) of patients with breast cancer in China reported by Chen and Zheng[19] in 2015, the current survival status of patients with breast cancer has significantly improved. The survival rate of patients with breast cancer from China is also similar to the 5-year survival rate (92.0%; 95% CI: 91.6%–92.4%) of patients from the United States.[20]

Weight gain is a very common problem in patients with breast cancer who undergo chemotherapy; moreover, obese patients with breast cancer have poorer survival than those without OB.[21,22] In this study, 422 patients with breast cancer had increased BW ($P < 0.001$); the

Table 3: Multivariate Cox regression analysis of risk factors for overall survival.

	At diagnosis		After chemotherapy	
Variables	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Menopausal status, Post *vs.* Pre	2.204 (1.219–3.982)	0.009	2.589 (1.369–4.895)	0.003
Lymph node status, Positive *vs.* Negative	3.253 (1.451–7.292)	0.004	3.134 (1.311–7.492)	0.010
ER status, Positive *vs.* Negative	0.529 (0.292–0.957)	0.035	0.538 (0.286–1.014)	0.055
Low HDL-C at diagnosis, No *vs.* Yes	2.775 (1.326–5.807)	0.007	NA	NA

CI: Confidence interval; ER: Estrogen receptor; HDL-C: High-density lipoprotein cholesterol; HR: Hazard ratio; NA: Not available.

Table 4: Multivariate logistic regression analysis to predict the risk factors of recurrence or metastasis.

	At diagnosis		After chemotherapy	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Lymph nodes status	2.603 (1.462–4.634)	0.001	2.634 (1.482–4.679)	0.001
Low HDL-C level at diagnosis	2.200 (0.996–4.859)	0.051	NA	NA
N of post-chemotherapy metabolic disorders	NA	NA	1.514 (1.047–2.189)	0.028

CI: Confidence interval; HDL-C: High-density lipoprotein cholesterol; NA: Not available; OR: Odds ratio.

proportion of OW and obese ($P < 0.001$) patients who received chemotherapy was higher compared with that at the time of diagnosis. Of these patients, 90 (21.30%) had a weight gain of $> 5\%$, while 30 (7.10%) experienced a weight loss of $> 5\%$. A total of 1080 patients who completed adjuvant chemotherapy were analyzed in the ADEBAR study[10]; of the 307 (24.8%) patients who had a weight change of $\geq 5\%$, 120 (11.1%) lost weight and 187 (17.3%) gained weight. The two weight change groups had a significant independent negative effect on the OS ($P = 0.039$) compared with the stable weight group. A systematic review of BMI and survival in patients with breast cancer showed that those who were UW, overweight, and obese prior to the diagnosis had a higher overall risk of death than NW women.[23] However, a weight change of $\geq 5\%$ was not found to have the same effect on OS in this study. This could be due to the fact that most of the studies included in this systematic review were conducted in Western populations and most of the studies were published 10 years ago; hence, the characteristics of the patients included in these studies may differ from those of current studies. This study also failed to determine the effect of BMI categories and weight change on patient's survival at diagnosis and after chemotherapy. The follow-up study of patients with breast cancer in Shanghai,[7] which began in 2002, found that those who gained $> 5\%$ of weight 18 months after diagnosis had an overall mortality risk of 1.54 (95% CI: 1.03–2.29) and a risk of recurrent metastasis of 1.30 (95% CI: 0.88–1.92). That study included all patients with breast cancer, not just patients with breast cancer who received chemotherapy; moreover, the post-treatment weight was collected from > 6 months after the time of diagnosis, whereas the post-chemotherapy weight was measured within 4 months after diagnosis in our study. Fang *et al*[24] conducted a retrospective study in 409 patients with breast cancer and received new adjuvant chemotherapy and found that initial BMI was a risk factor for poor disease-free survival but not for OS. However, Schvartsman *et al*[25] found that

a BMI increase of > 0.5 kg/m^2 after chemotherapy was a predictive factor for an increase in the locoregional recurrence risk (HR: 2.53; 95% CI: 1.18–5.45; $P = 0.017$) when compared with stable BMI. The effects of BMI or weight gain on the prognosis of patients with breast cancer before and after chemotherapy have been investigated in many studies, but the conclusions are not entirely consistent. Some studies consider body fat distribution to be more important than BMI as a metabolic risk factor.[26] In the Nurses' Health Study, abdominal fat was strongly and positively associated with all-cause, cardio-vascular disease and cancer mortality but not with BMI. Even among normal-weight women, increased waist circumference was associated with significantly increased mortality from cardiovascular disease.[27]

In this study, 277 (63.3%) patients with breast cancer had metabolic disorders at diagnosis, of whom 56 (12.8%) had more than three metabolic disorders. After chemotherapy, 321 (73.3%) patients developed metabolic disorders, of whom 74 (16.9%) had more than three metabolic disorders. The metabolic disorders in patients with breast cancer were exacerbated after chemotherapy ($\chi^2 = 177.069$, $P < 0.001$). The Kaplan-Meier analysis found that patients with breast cancer wo had low HDL-C levels at diagnosis had a shorter survival time ($\chi^2 = 6.771$, $P = 0.009$). After controlling for patient age and clinical characteristics, Cox regression still showed that a low HDL-C level at diagnosis (HR = 2.775, 95% CI: 1.326–5.807) was a risk factor for OS in patients with breast cancer. The multiple logistic regression analysis also showed the same result; that is, low HDL-C level at diagnosis (OR = 2.200, 95% CI: 0.996–4.859) and metabolic disorders after chemotherapy (OR = 1.514, 95% CI: 1.047–2.189, $P = 0.028$) were risk factors for tumor recurrence or metastasis, and a low HDL-C level at diagnosis (OR = 4.010, 95% CI: 1.657–9.709) was a risk factor for death in patients with breast cancer. Results of nine cohort studies pooling the data of 17,892 patients

with breast cancer showed that patients with MS at diagnosis had a significantly increased risk of cancer recurrence (relative risk = 1.52, $P = 0.02$).[28] In a retrospective study of 1391 patients with breast cancer in Beijing, Fan et al[11] analyzed the relationship between the MS and its components (BMI, HDL, and TG) and their clinical outcomes, and found that low HDL at diagnosis was a significant independent risk factor of poor relapse-free survival (HR = 3.266, 95% CI: 2.087–5.112) and OS (HR = 3.071, 95% CI: 1.732–5.445). This may be because low HDL-C level is associated with a more aggressive tumor profile.[29] In addition, a low level of HDL-C is negatively correlated with the activity of the pro-inflammatory cytokine interleukin (IL)-6, and IL-6 and IL-8 may promote the spread and metastasis of breast cancer tumor cells.[30,31]

A systematic review noted that lymph node status, tumor size, age at diagnosis, and ER status were the most commonly used predictors in the models of breast cancer death or recurrence.[32] Age is an important risk factor for death in patients with breast cancer; the European Society of Breast Cancer Specialists working group defined "young patients with breast cancer" as women aged < 40 years.[33] Li et al[34] found a non-linear J-shaped dose-response relationship between age at breast cancer onset and risk of breast cancer death ($P < 0.001$), with HRs of 1.72 (95% CI: 1.06–2.81) and 1.89 (95% CI: 1.43–2.49), respectively. However, no age-related differences were found in the OS of patients with breast cancer in this study, which may be attributed to the fact that the majority of the patients in this study were aged 41 to 59 years, with a smaller proportion of people aged < 40 years or > 60 years. Results of the univariate analysis showed that menopausal status, lymph node status, extent of surgical resection, ER status, and PR status affected the OS of patients with breast cancer in this study, while further Cox regression analysis found that only menopausal status, lymph node status, and ER status affected the OS. These results are consistent with those of a previous study.[18]

This was a retrospective study; although post-chemotherapy time was defined as at least 1 month after chemotherapy, the time after chemotherapy in patients with breast cancer ranged from 1 to 15 months, which may be the reason why the impact of post-chemotherapy weight changes on long-term survival and prognosis of patients was not identified in this study. Hence, regular follow-up should be conducted in the future in patients with breast cancer who will undergo chemotherapy to further understand the pattern of weight changes and metabolic disturbances during chemotherapy in patients with this condition. In addition, the information in this study was obtained from the patients' hospital records; therefore, only simple OB indicators such as BMI were available, and there was a lack of information that could more accurately reflect the OB status of patients such as body fat distribution. The medical records of patients with breast cancer should include indicators that reflect central OB, such as abdominal circumference and waist-to-hip ratio, in order to provide more information for future studies.

Conclusions

Chemotherapy causes an increase in the proportion of overweight and obese patients with breast cancer and worsening of metabolic disorders. More evidence is needed to clarify the impact of BMI categories and post-chemotherapy weight changes on the survival and prognosis of Chinese patients with breast cancer. Low HDL-C level at diagnosis and metabolic disorder after chemotherapy may have negative effects on the OS or prognosis of patients with breast cancer.

Conflicts of interest

None.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209–249. doi: 10.3322/caac.21660.
2. Zhang S, Sun K, Zheng R, Zeng H, Wang S, Chen R, et al. Cancer incidence and mortality in China, 2015. J Natl Cancer Center 2021;1:2–11. doi: 10.1016/j.jncc.2020.12.001.
3. Sun K, Zheng R, Zhang S, Zeng H, Zou X, Chen R, et al. Report of cancer incidence and mortality in different areas of China, 2015 (in Chinese). China Cancer 2019;28:1–11. doi: 10.11735/j.issn.1004-0242.2019.01.A001.
4. Wang Z, Bao J, Yu C, Wang J, Li C. Secular trends of breast cancer in China, South Korea, Japan and the United States: application of the age-period-cohort analysis. Int J Environ Res Public Health 2015;12:15409–15418. doi: 10.3390/ijerph121214993.
5. Levaggi A, Poggio F, Lambertini M. The burden of breast cancer from China to Italy. J Thorac Dis 2014;6:591–594. doi: 10.3978/j.issn.2072-1439.2014.06.21.
6. Gray R, Clarke M, Collins R, Peto R. The EBCTCG overview of adjuvant therapy of breast cancer. What are the implications for future studies? Early Breast Cancer Trialists' Collaborative Group. Ann N Y Acad Sci 1993;698:339–348. doi: 10.1111/j.1749-6632.1993.tb17224.x.
7. Gu K, Chen X, Zheng Y, Chen Z, Zheng W, Lu W, et al. Weight change patterns among breast cancer survivors: results from the Shanghai breast cancer survival study. Cancer Causes Control 2010;21:621–629. doi: 10.1007/s10552-009-9491-z.
8. Vance V, Mourtzakis M, McCargar L, Hanning R. Weight gain in breast cancer survivors: prevalence, pattern and health consequences. Obes Rev 2011;12:282–294. doi: 10.1111/j.1467-789X.2010.00805.x.
9. Lu LJ, Gan L, Hu JB, Ran L, Cheng QF, Wang RJ, et al. On the status of β-cell dysfunction and insulin resistance of breast cancer patient without history of diabetes after systemic treatment. Med Oncol 2014;31:9562. doi: 10.1007/s12032-014-0956-x.
10. Mutschler NS, Scholz C, Friedl TWP, Zwingers T, Fasching PA, Beckmann MW, et al. Prognostic impact of weight change during adjuvant chemotherapy in patients with high-risk early breast cancer: results from the ADEBAR study. Clin Breast Cancer 2018;18:175–183. doi: 10.1016/j.clbc.2018.01.008.
11. Fan Y, Ding X, Wang J, Ma F, Yuan P, Li Q, et al. Decreased serum HDL at initial diagnosis correlates with worse outcomes for triple-negative breast cancer but not non-TNBCs. Int J Biol Markers 2015;30:e200–e207. doi: 10.5301/jbm.5000143.
12. Li X, Tang H, Wang J, Xie X, Liu P, Kong Y, et al. The effect of preoperative serum triglycerides and high-density lipoprotein-cholesterol levels on the prognosis of breast cancer. Breast 2017;32:1–6. doi: 10.1016/j.breast.2016.11.024.
13. The Working Group on Obesity in China (WGOC). Predictive values of body mass index and waist circumference to risk factors of related diseases in Chinese adult population (in Chinese). Chin J Prev Med 2002;23:5–10. doi: 10.3760/j.issn:0254-6450.2002.01.003.
14. Playdon MC, Bracken MB, Sanft TB, Ligibel JA, Harrigan M, Irwin ML. Weight gain after breast cancer diagnosis and all-cause mortality: systematic review and meta-analysis. J Natl Cancer Inst 2015;107:djv275. doi: 10.1093/jnci/djv275.

15. Metabolic Syndrome Research Collaborative Group of Chinese Diabetes Society. Recommendations on the metabolic syndrome from the Chinese Diabetes Society (in Chinese). Chin J Diabetes 2004;12:156–161. doi: 10.3321/j.issn:1006-6187.2004.03.002.

16. Chinese Diabetes Society. Guidelines for the prevention and treatment of type 2 diabetes in China (2013 edition) (in Chinese). Chin J Diabetes Mellitus 2014;6:447–498. doi: 10.3760/cma.j. issn.1674-5809.2014.07.004.

17. Li H, Zuo TT, Zeng HM, Zheng RS, Yang L, Li HC, et al. Clinical features and prognostic analysis of female breast cancer in different diagnosed ages (in Chinese). Chin J Oncol 2021;43:126–131. doi: 10.3760/cma.j.cn112152-20191212-00801.

18. Chen QX, Zhang YX, Li K, Dong H, Xu H, Lin GZ, et al. Characteristics and prognosis of female breast cancer in Guangzhou, 2008-2017 (in Chinese). Chin J Epidemiol 2020;41:1831–1835. doi: 10.3760/cma.j.cn112338-20191012-00731.

19. Chen W, Zheng R. Incidence, mortality and survival analysis of breast cancer in China (in Chinese). Chin J Clin Oncol 2015;42:668–674. doi: 10.3969/j.issn.1000-8179.20150571.

20. Emanuel EJ, Gudbranson E, Parys JV, Gortz M, Helgeland J, Skinner J. Comparing health outcomes of privileged US citizens with those of average residents of other developed countries. JAMA Intern Med 2021;181:339–344. doi: 10.1001/jamainternmed.2020.7484.

21. Protani M, Coory M, Martin JH. Effect of obesity on survival of women with breast cancer: systematic review and meta-analysis. Breast Cancer Res Treat 2010;123:627–635. doi: 10.1007/s10549-010-0990-0.

22. Lee K, Kruper L, Dieli-Conwright CM, Mortimer JE. The impact of obesity on breast cancer diagnosis and treatment. Curr Oncol Rep 2019;21:412. doi: 10.1007/s11912-019-0787-1.

23. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol 2014;25:1901–1914. doi: 10.1093/annonc/mdu042.

24. Fang Q, Huang J, Gan L, Shen K, Chen X, Wu B. Weight gain during neoadjuvant chemotherapy is associated with worse outcome among the patients with operable breast cancer. J Breast Cancer 2019;22:399–411. doi: 10.4048/jbc.2019.22.e37.

25. Schvartsman G, Gutierrez-Barrera AM, Song J, Ueno NT, Peterson SK, Arun B. Association between weight gain during adjuvant chemotherapy for early-stage breast cancer and survival outcomes. Cancer Med 2017;6:2515–2522. doi: 10.1002/cam4.1207.

26. Dulloo AG, Jacquet J, Solinas G, Montani JP, Schutz Y. Body composition phenotypes in pathways to obesity and the metabolic syndrome. Int J Obes (Lond) 2010;34 (Suppl 2):S4–S17. doi: 10.1038/ijo.2010.234.

27. Zhang C, Rexrode KM, van Dam RM, Li TY, Hu FB. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. Circulation 2008;117:1658–1667. doi: 10.1161/CIRCULATIONAHA.107.739714.

28. Li P, Wang T, Zeng C, Yang M, Li G, Han J, et al. Association between metabolic syndrome and prognosis of breast cancer: a meta-analysis of follow-up studies. Diabetol Metab Syndr 2020;12:102. doi: 10.1186/s13098-019-0514-y.

29. Flote VG, Vettukattil R, Bathen TF, Egeland T, McTiernan A, Frydenberg H, et al. Lipoprotein subfractions by nuclear magnetic resonance are associated with tumor characteristics in breast cancer. Lipids Health Dis 2016;15:56. doi: 10.1186/s12944-016-0225-4.

30. Holven KB, Retterstol K, Ueland T, Ulven SM, Nenseter MS, Sandvik M, et al. Subjects with low plasma HDL cholesterol levels are characterized by an inflammatory and oxidative phenotype. PLoS One 2013;8:e78241. doi: 10.1371/journal.pone.0078241.

31. Hartman ZC, Poage GM, den Hollander P, Tsimelzon A, Hill J, Panupinthu N, et al. Growth of triple-negative breast cancer cells relies upon coordinate autocrine expression of the proinflammatory cytokines IL-6 and IL-8. Cancer Res 2013;73:3470–3480. doi: 10.1158/0008-5472.CAN-12-4524-T.

32. Phung MT, Tin ST, Elwood JM. Prognostic models for breast cancer: a systematic review. BMC Cancer 2019;19:230. doi: 10.1186/s12885-019-5442-6.

33. Cardoso F, Loibl S, Pagani O, Graziottin A, Panizza P, Martincich L, et al. The European Society of Breast Cancer Specialists recommendations for the management of young women with breast cancer. Eur J Cancer 2012;48:3355–3377. doi: 10.1016/j.ejca.2012.10.004.

34. Li H, Zuo TT, Zeng HM, et al. Clinical features and prognostic analysis of female breast cancer in different diagnosed ages (in Chinese). Chin J Oncol 2021;43:126–131. doi: 10.3760 /cma.j.cn112152-20191212-00801.