Title: Weight and waist-to-hip ratio change pattern during the first five years of survival: data from a longitudinal observational Chinese breast cancer cohort

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Abstract

Background: Body weight management was an important component in breast cancer survivorship care. The present study described the change patterns of body weight and waist-to-hip ratio (WHR) during the first five years of survival, and investigated potential factors associated with very substantial changes.

Patients and methods: Based on a longitudinal cohort with 1462 Chinese women with breast cancer, anthropometric measurements including body weight, height, waist and hip circumferences were measured by trained interviewers following standard protocol at four time-points: baseline at study entry, 18-, 36- and 60-months follow up assessments (termed as T0, T1, T2 and T3, respectively). Body height was measured at baseline and body weight at cancer diagnosis were retrieved from medical record.

Results: Compared to weight at breast cancer diagnosis, the median weight change was -0.5kg, 0kg, +0.5kg, and +1kg at T0, T1, T2 and T3, respectively. During the first five years of survival, the proportion of women who were obese have slightly increased. At 60-months after diagnosis, only 14.3% of women had weight gain by > 5kg; and the percentage of women who had weight gain by > 10% was 10.7%. Nearly half of patients had abdominal obesity at study entry, and this proportion were gradually increased to nearly 70% at 60-months follow-up. Multivariate analysis indicated that older age, frequent sports participation and having vegetables and fruits intake ≥ 400g/day were related to lower risk of very substantial weight gain (> 10%) at 60-months follow-up; patients aged 40-49 years, having ≥ 2 comorbidities, ER negative and having vegetables and fruits intake ≥ 400g/day were associated with less likelihood of very substantial WHR substantial increase (> 10%) at 60-months follow-up.

Conclusion: Weight gain was modest in Chinese breast cancer survivors during the first five years of survival, while central adiposity has become a contemporary public health issue. The incorporation of healthy weight and abdominal circumference patient education and management has a potential to improve cancer survivorship.

Introduction

Breast cancer is the most frequent cancer among female both in Western countries and in China.[1, 2] An analysis from forty years of cancer registry data showed that the incidence of breast cancer have a tremendous increase, while the mortality rate only slightly increase in urban Chinese population.[3] This indicates that a rising number of women with breast cancer would live with the disease for longer time.

Hong Kong is a westernized and urbanized city in China, and breast cancer has also aroused heavy disease burden in local female.
According to the American Cancer Society (ACS), a cancer survivor is defined as any individual who has been diagnosed with cancer, from the time of diagnosis through the balance of life.[4] As the survival rate improves gradually, the long-term management of breast cancer survivors has been a critical issue for health professionals.

To better manage breast cancer survivors, ACS and American Society of Clinical Oncology (ASCO) established Breast Cancer Survivorship Care Guideline in 2015.
[5] It underscored that adoption of a healthy lifestyle as an essential element of survivorship care.[5] For such, body weight management is an important component, and ASCO recommended that primary care clinicians should counsel breast cancer survivors to achieve and maintain a healthy body weight.[5]

Contrary to the recommendation for cancer survivor, post-diagnosis weight gain was first described by Dixon and colleagues in 1978;[6] since then, it has been commonly reported among Western women with breast cancer, especially for those received systemic adjuvant treatment.[7] Weight gain during 1–2 year post-diagnosis was very frequent in Caucasian women, with average increase of 1.5 to 2.1 kg.[8–11] Although the prevalence of obesity was lower in Asian women,[12] weight gain has been also observed after breast cancer diagnosis. While post-diagnosis weight gain is considered common in Western countries, results from studies on Asian women have been inconsistent,[13–16] with most of them being cross-sectional with small patient number.[13, 15, 16] Two studies showed that weight gain in Asian women with breast cancer was comparable to Western counterparts.[14, 15] Another recent study observed a modest weight gain in premenopausal Hong Kong women who had completed adjuvant chemotherapy.[16] However, a study from Korea reported that weight change was not observed at 1 year after chemotherapy.[13]

The reasons for weight gain could be multifactorial. A series of factors were suggested to be associated with weight gain, including chemotherapy, use of medication in association with chemotherapy such as dexamethasone, treatment-related amenorrhea, “stress eating” and reduced physical activity.[16–19] Although not all studies have consistent findings, it has been frequently suggested that post-diagnosis weight gain was associated with inferior breast cancer prognosis.[20] In addition, weight gain after diagnosis also had a negative effect on quality of life (QoL).[21, 22] As weight management is an essential element in the long-term management of breast cancer survivors, there is still need to fully investigate the pattern of weight change and explore potential risk factors associated with very substantial weight gain among Asian women with breast cancer.

In recent decades, it has been acknowledged that the sole use of body mass index (BMI) cannot fully reflect fat distribution over body compartments;[23] therefore, other anthropometric measures, for example, waist-to-hip ratio (WHR), have been recommended in the clinical setting for the measurement of abdominal obesity.[24] Freedman et al. have reported that patients with breast cancer who had adjuvant chemotherapy would experience unfavorable changes in body composition without a significant weight change.[25] To date, two studies have suggested that central adiposity or substantial WHR change after breast cancer diagnosis correlates with mortality.[26, 27] However, the pattern of WHR change after breast cancer diagnosis was not fully illustrated. Of note, as previous study showed that Chinese and South Asian display a greater amount of visceral adipose tissue for a given waist circumference than Europeans, the measurement of WHR in Asian may need special attentation.[28]

Based on a longitudinal cohort of Chinese women with breast cancer, the present study has the following two aims: 1) to characterize the patterns of weight change from diagnosis to immediately post-diagnosis, 18-, 36- and 60-months follow up, and to identify potential socio-demographic, clinical and lifestyle factors associated with very substantial weight gain; 2) to describe the patterns of WHR change from immediately post-diagnosis to 18-, 36- and 60-months follow up, and to identify potential factors associated with very substantial WHR increase.

Patients And Methods

Study cohort

The Hong Kong NTEC-KWC Breast Cancer Survival Study (HKNKBCSS) was a prospective breast cancer cohort study, initiated to investigate the associations between lifestyle factors with breast cancer recurrence and mortality.[29–33] The inclusion criteria included patients of any age, had histologically confirmed breast cancer with American Joint Committee on Cancer (AJCC) stage 0-III diagnosed no more than 12 months before study entry,[34] female gender, mentally stable, Chinese ethnicity, able to read Chinese, and did not have prior history of breast or other cancers. Between January 2011 and February 2014, 1462 eligible patients provided written informed consent and participated in the study.

The study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee and the KWC Research Ethics Committee of the Chinese University of Hong Kong and the Hong Kong Hospital Authority.
Consented patients were interviewed at four time-points: baseline at study entry (described as T0; conducted within 12-months after breast cancer diagnosis), 18-months follow-up (T1; conducted between 12–24 months after diagnosis), 36-months follow-up (T2; which was conducted between 30–42 months after diagnosis) and 60-months follow-up (T3; 54–66 months after diagnosis).
A telephone call would be made prior to the planned interview, which would coincide with their scheduled clinic follow-up.

As of December 2017, the 60-months follow-up interview had been completed.

Among 1462 patients who completed assessment at T0, 1310, 1162 and 1171 participants completed interviews at T1, T2 and T3, respectively (follow-up rate: 89.6%, 79.5% and 80.1%, respectively).
The present study was based on the anthropometric measurements data assessed during interviews at all four time-points.

Data Collection

During each follow-up interviews, patients were assessed with structured questionnaires conducted at baseline assessment, which collected socio-demographic characteristics (education level, marital status, working status and family income), reproductive history, menopausal status, active and passive smoking, alcohol use and prior medical history (self-reported comorbidities including but not limited to diabetes, [illegible]isease and chronic kidney disease). At T0 assessment,

patients' menopause status was classified as two groups: pre-menopausal and post-menopausal. Patients who had their last menstrual period within 1 year were regarded as pre-menopausal. Post-menopausal was defined as patients who had a cessation of menstruation for 12 months or longer. From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status by T3.

Clinical information was retrieved by reviewing hospital medical records.

These included patient's age at breast cancer diagnosis, cancer characteristics [histology, AJCC stage, estrogen receptors (ER), progesterone receptors (PR) and human epidermal-growth-factor receptor 2 (HER2) status of the breast tumor] and treatment for breast cancer (type of breast surgery, details of adjuvant radiotherapy, chemotherapy and endocrine therapy).
Physical activity was measured by a validated modified Chinese Baecke questionnaire.[35] The MET code of each sport was based on the values in the Ainsworth compendium of physical activity.[36] According to the level of sports activity, patients were categorized into 3 groups as follow: never (0 MET-hours/week), rare/occasional (< 10 MET-hours/week) and frequent (≥ 10 MET-hours/week) physical activity. The cut-off point of 10 MET-hours/week was based on the recommendations for cancer survivors.[4, 37] Habitual dietary intake was collected by a validated and interviewer-administered food frequency questionnaire (FFQ).[38] The average daily intake of nutrients, such as total energy, fat and other nutrients were calculated according to the Chinese Food Composition Table.[39] Meeting dietary recommendation on vegetables and fruits intake was defined as eating at least five servings (at least 400 gram) of nonstarchy vegetables and fruits every day according to the WCRF/AICR guidelines for cancer survivors.[37] At T0 assessment, patients were asked to recall their habitual physical activity and dietary intake in the preceding 12 months before cancer diagnosis. At T1, T2 and T3 assessments, patients were asked to report these parameters over the previous 12 months.

Anthropometric Measurements

Anthropometric measurements including body weight, height, waist and hip circumference were performed based on standard protocol. Trained interviewers measured body weight, waist and hip circumference at T0, T1, T2 and T3 assessment, respectively, and the body height was only measured at T0 assessment. Body height was measured to the nearest 0.1 cm with the patients in bare feet, back against the wall, heels together and eyes looking straight ahead.

Body weight was measured to the nearest 0.1 kg with the participant in light clothing and bare feet using a TANITA Body Fat Scale (Model BF-522, TANITA, Japan).
Weight at diagnosis was collected from hospital medical records.

Body mass index (BMI) was calculated by weight (kg) divided by the square of height (m^2). According to BMI classification of the Asia-Pacific region, patients can be categorized into 5 groups as following:

underweight < 18.5 kg/m^2, normal 18.5–22.9 kg/m^2, overweight 23-24.9 kg/m^2, obese ≥ 25 kg/m^2.[40] Compared to weight at breast cancer diagnosis, absolute weight change at T0, T1, T2 and T3 assessment was calculated (weight at T0, T1, T2 or T3 - weight at diagnosis), and then classified into five groups: substantial loss (> 5kg), moderate loss (> 2kg and ≤ 5kg), stable change (within 2kg), moderate gain (> 2 kg and ≤ 5kg) and substantial gain (> 5kg). The relative percent of weight change at T0, T1, T2 and T3 assessment was also calculated (absolute weight change at T0, T1 or T2/weight at diagnosis*100), and then classified those changes into six groups: substantial loss (> 5%), moderate loss (> 2% and ≤ 5%), stable change (within 2 %), moderate gain (> 2 and ≤ 5%), substantial gain (5–10%) and very substantial gain (> 10%).

WHR was calculated as the ratio of waist circumference to hip circumference, which is regarded as an index of abdominal obesity.[41] World Health Organization (WHO) expert consultation defines abdominal obesity as WHR above 0.85 for women;[42] patients were grouped into two categories: without abdominal obesity < 0.85 and with abdominal obesity ≥ 0.85. As WHR at diagnosis were not available, the value obtained at T0 assessment was used as reference in the measurement of post-diagnosis WHR change. Percentage of changes between T0 assessment and T1, T2 and T3 assessment were calculated (absolute WHR change at T1, T2 or T3/WHR at T0*100), and then classified those changes into six groups: substantial decrease (> 5%), moderate decrease (> 2% and ≤ 5%), stable change (within 2%), moderate increase (> 2% and ≤ 5%), substantial increase (5–10 %) and very substantial increase (> 10%).

Statistical analysis

Patients' socio-demographic, clinical and lifestyle factors described as follows: continuous variables were expressed as means with standard deviation or median with range as appropriate, and categorical variables were summarized as patient number (n) and percentage (%). Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with $P < 0.1$ in univariate analysis were included into the multivariate logistic regression model. Similar analyses were performed to identify any potential factors associated with very substantial WHR increase from T0 to T3 assessment. All analyses were performed using SPSS 26.0; and P values < 0.05 at two-sided analysis were considered statistically significant.

Results

Patients' characteristics

A total of 1462 patients who participated in this cohort were included into this analysis.
The baseline demographic, clinical and lifestyle characteristics of patients are provided in Table 1. The mean age at diagnosis was 51.9 years (SD: 9.1). The median time from diagnosis to T0 assessment was 3.2 months. Overall, 84.1% of patients had education of high school or below, 71.1% were married, 32.4% had a monthly household income of more than 30, 000 HK dollars and 50.6% had full-time or part-time employment. At study entry, most of patients (61.6%) had no comorbidity and 53.5% of women were pre-

menopausal. With regards to the clinical characteristics of breast tumor, majority of patients were staged as 0-II (80.4%), with tumor histology being invasive ductal carcinoma (83.8%) and ER positive (72.3%). The proportions of patients who received chemotherapy, radiotherapy and endocrine therapy were 75.2%, 70.6% and 72.1%, respectively.

Table 1
Patients' demographic, clinical and lifestyle characteristics collected at T0 assessment (N = 1462)

Characteristics	Number of patients	Percentage, %
Time from diagnosis to T0 assessment, median (range), months	3.2 (0.1–11.9)	
Age at diagnosis, mean (SD), years	51.9 (9.1)	
Age group at diagnosis, years	150	10.3
<40	468	32.0
40–49	552	37.7
50–59	292	20.0
≥60		
Education level	1230	84.1
High school or below	232	15.9
College or above		
Marital status	1039	71.1
Married or cohabitation	423	28.9
Unmarried or divorced or widowed		
Family income, HKD/month	683	46.7
< 15,000	452	30.9
15,000–30,000	204	14.0
30,000–50,000	123	8.4
≥50,000		
Employment status	545	37.3
Full time	195	13.3
Part time	722	49.4
Not working		

Abbreviations: SD, standard deviation; HKD, Hong Kong dollars; BMI, body mass index; AJCC, American joint Committee on cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER 2, human [illegible] metabolic equivalent of task; g, gram.

Characteristics	Number of patients	Percentage, %
Number of comorbidities	901	61.6
0	371	25.4
1	190	13.0
≥ 2		
Menopausal status at T0 assessment	782	53.5
Pre-menopausal	680	46.5
Post-menopausal		
Parity	339	23.2
0	340	23.3
1	531	36.3
2	252	17.2
≥ 3		
AJCC stage	523	35.8
0-I	652	44.6
II	276	18.9
III	11	0.8
Missing		
Histology	1225	83.8
IDC	42	2.9
ILC	94	6.3
DCIS	101	6.9
Others		
ER status, %	1057	72.3
Positive	363	24.8
Negative	42	2.9
Missing		

Abbreviations: SD, standard deviation; HKD, Hong Kong dollars; BMI, body mass index; AJCC, American joint Committee on cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER 2, human [illegible] metabolic equivalent of task; g, gram.

Characteristics	Number of patients	Percentage, %
PR status, %	810	55.4
Positive	605	41.4
Negative	47	3.2
Missing		
HER 2 status, %	381	26.1
Positive	966	66.1
Negative	115	7.9
Missing		
Type of surgery	917	62.7
Mastectomy	545	37.3
Conservation		
Chemotherapy, %	1100	75.2
Yes	362	24.8
No		
Radiotherapy, %	1032	70.6
Yes	430	29.4
No		
Endocrine therapy, %	1054	72.1
Yes	408	27.9
No		
Height, median (range), cm	156 (137–177)	
Weight, median (range), kg	56.0 (33.4–111.0)	

Abbreviations: SD, standard deviation; HKD, Hong Kong dollars; BMI, body mass index; AJCC, American joint Committee on cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER 2, human [illegible] metabolic equivalent of task; g, gram.

Characteristics	Number of patients	Percentage, %
BMI at diagnosis, kg/m^2	53	3.6
Underweight (< 18.5)	713	48.8
Normal (18.5–22.9)	297	20.3
Overweight (23-24.9)	399	27.3
Obese (≥ 25)		
Waist circumference, median (range), cm	80.3 (58.5-126.5)	
Hip circumference, median (range), cm	95.0 (78.0-136.5)	
WHR at T0 assessment	391	26.7
< 0.8	765	52.3
0.8–0.89	306	21.0
≥0.9		
Sports participation 1-year before diagnosis	666	45.6
Never	487	33.1
Rarely/occasionally	309	21.1
Frequently		
Dietary energy intake 1-year before diagnosis, median (range), kcal/day	1620.3 (551.1-5787.3)	
Dietary fat intake, median (range), g/1000 kcal/day	39.1 (14.2–62.7)	
Vegetables and fruits intake 1-year before diagnosis, g/day	496	33.9
<400	966	66.1
≥400		
Ever smoking before diagnosis	22	1.5
Yes	1440	98.5
No		

Abbreviations: SD, standard deviation; HKD, Hong Kong dollars; BMI, body mass index; AJCC, American joint Committee on cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER 2, human [illegible] metabolic equivalent of task; g, gram.

Characteristics	Number of patients	Percentage, %
Ever frequent alcohol intake before diagnosis (> 4 times/week)	28	1.9
Yes	1434	98.1
No		

Abbreviations: SD, standard deviation; HKD, Hong Kong dollars; BMI, body mass index; AJCC, American joint Committee on cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-growth-factor receptor 2; MET, metabolic equivalent of task; g, gram.

According to the BMI criteria for Asian population, 3.6% were underweight, 48.8% were normal weight, 20.3% were overweight and the remaining 27.3% were obese at breast cancer diagnosis.
At study entry, the proportions of patients without or with abdominal obesity were 52.1% and 47.9%, respectively.

With regards to lifestyle factors during the proceeding one year before breast cancer diagnosis, about half of patients (45.6%) never participated in sports activity, the median dietary energy intake was 1620.3 kcal/day and median fat intake was 39.1 gram (g)/1000kcal/day.
More than half of patients (66.1%) had vegetables and fruits ≥ 400 g/day. The proportions of patients who were ever smoker or ever frequent alcohol drinker were very small.

Distribution of patients' BMI and weight change pattern from diagnosis to T0, T1, T2 and T3 assessment

The distribution of patients' BMI at each time-point (from diagnosis to 60-months post-diagnosis) were summarized in Fig. 1A.

The proportions of patients being underweight were relative stable, namely 4.0%, 5.3%, 5.2%, 4.5% and 4.5% at diagnosis, T0, T1, T2 and T3 assessment; the proportions of patients being overweight were also stable during follow-ups; the corresponding figures were 21.1%, 19.7%, 21.0%, 21.7% and 22.1% at diagnosis, T0, T1, T2 and T3 assessment, respectively.
The proportions of patients with normal BMI slightly decreased in a progressive manner during follow-ups, namely 46.4%, 48.4%, 45.6%, 43.0% and 39.5% at diagnosis, T0, T1, T2 and T3 assessment, respectively; while the proportion of patients with obesity slightly increased, namely 28.5%, 26.6%, 28.2%, 30.9% and 33.8% at diagnosis, T0, T1, T2 and T3 assessment, respectively.

Compared to weight at breast cancer diagnosis, the median weight change was − 0.5kg, 0kg, 0.5kg, and 1kg at T0, T1, T2 and T3, respectively. Absolute weight change from diagnosis to T0, T1, T2 and T3 were summarized in Fig. 1B.

Most of the women had a relative stable weight (change within ± 2kg) at T0, T1, T2 and T3 assessment (89.9%, 55%, 49.9% and 45.5%, respectively) when compared to weight at diagnosis.
The proportions of women who gained weight within 2-5kg were 2.7%, 18.7%, 20.4% and 23.4% at T0, T1, T2 and T3, respectively; and the corresponding figures for patients who had weight gain of > 5kg were 0.5%, 4.7%, 9.9% and 14.3%, respectively.

Percent of weight change from diagnosis to T0, T1, T2 and T3 were summarized in Fig. 1C. The percentage of women who gained weight by 2–5% were 4.3%, 18.7%, 19.6% and 18.1% at T0, T1, T2 and T3, respectively; the corresponding figures for weight gain 5–10% were 1.6%, 11.2%, 15.7% and 20.5% at T0, T1, T2 and T3 assessment, respectively; and the proportion of patients had weight gain > 10% were relatively low, 0.3%, 3.3%, 7.5% and 10.7% at T0, T1, T2 and T3 assessment, respectively.

Category of WHR and change pattern from T0 to T1, T2 and T3 assessment

The distribution of WHR categories at each follow-up were summarized in Fig. 2A.

The proportions of patients with WHR < 0.85 were 52.1%, 51.5%, 37.4% and 30.7% at T0, T1, T2 and T3 assessment, respectively.

With regards to percentage of WHR change, 28.3%, 21.5% and 18.8% of patients had percentage of WHR change within ± 2% from T0 to T1, T2 and T3 assessment, respectively (Fig. 2B). The percentage of women who increased WHR by 2–5% were 18.4%, 19.0% and 18.8% at T1, T2 and T3, respectively; the corresponding figures for WHR increase 5–10% were 11.4%, 21.1% and 26.6% at T1, T2 and T3, respectively; and the proportion of patients with WHR increase > 10% were 7.7%, 17.5% and 21.6% at T1, T2 and T3, respectively. Overall, more patients had WHR increase during progressive follow-up.

Analysis for risk factors associated with weight gain > 10% from diagnosis to T3 assessment

The outcomes of univariate and multivariate analyses on factors associated with very substantial weight gain (> 10%) were summarized in Table 2. Univariate analysis revealed that older age at breast cancer diagnosis (P = 0.0005), had ≥ 2 comorbidities (P = 0.007), remained post-menopausal from T0 to T3 (P = 0.009), had ≥ 1 child-birth (P = 0.009), frequent sports participation at T3 assessment (P = 0.001) as well as vegetables and fruits intake ≥ 400g/day (P = 0.001) were associated with less likelihood of weight gain. However, not working (P = 0.016) and more dietary fat intake at T3 assessment (P = 0.018) were associated with very substantial weight gain. On multivariate analysis, older age at breast cancer diagnosis [odds ratio (OR) for patients aged ≥ 60 years 0.235, 95% confidence interval (CI): 0.077–0.723; P = 0.012), frequent sports participation at T3 assessment (OR 0.475, 95%CI: 0.276–0.816; P = 0.007) and vegetables and fruits intake ≥ 400g/day (OR 0.586, 95%CI: 0.389–0.882; P = 0.010) were independent factors for less likelihood of weight gain.

Table 2
Univariate and multivariate analysis on factors associated with weight gain > 10% from diagnosis to T3 assessment, by stepwise logistic regression (n = 1171)

	Univariate analysis			Multivariate analysis		
	OR	**95%CI for OR**	**P**	**OR**	**95%CI for OR**	**P**
Age group at diagnosis	1	-	0.0008	1	-	0.032
< 40	0.848	0.474–1.516	-	0.973	0.507–1.869	-
40–49	0.555	0.306–1.007	0.587	0.561	0.236–1.332	0.935
50–59	**0.235**	**0.104–0.528**	0.053	**0.235**	**0.077–0.723**	0.190
≥60			**0.0005**			**0.012**
Education level	1	-	0.260			
High school or below	1.314	0.817–2.115				
College or above						
Marital status	1	-	0.445			
Married or cohabitation	1.169	0.783–1.748				
Unmarried or divorced or widowed						
Family income, HKD/month	1	-	0.419			
< 30,000	1.193	0.778–1.828				
≥30,000						
Employment status	1	-	**0.016**	1	-	0.626
Working	**1.590**	**1.088–2.323**		1.109	0.731–1.684	
Not working						

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with P < 0.1 in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, employment status, number of comorbidities, menopausal status from T0 to T3 assessment, parity, sports participation at T3 assessment, dietary fat intake at T3 assessment and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-quivalent of task; g, gram.

	Univariate analysis			Multivariate analysis		
	OR	**95%CI for OR**	**P**	**OR**	**95%CI for OR**	**P**
Number of comorbidities	1	-	0.026	1	-	0.159
0	0.932	0.609–1.428	0.747	1.046	0.663–1.650	0.847
1	**0.312**	**0.134–0.727**	**0.007**	0.433	0.177–1.059	0.067
≥ 2						
Menopausal status from T0 to T3 assessment	1	-	0.033	1	-	0.161
Pre-menopausal	0.688	0.421–1.124	0.135	0.866	0.494–1.519	0.617
Peri-menopausal	**0.521**	**0.319–0.851**	**0.009**	1.575	0.717–3.458	0.257
Post-menopausal						
Parity	1	-	**0.009**	1	-	0.298
0	**0.586**	**0.393–0.873**		0.793	0.513–1.227	
≥ 1						
AJCC stage	1	-	0.810			
0-I	0.881	0.586–1.327	0.545			
II	0.993	0.583–1.691	0.980			
III						
ER status, %	1	0.870–1.959	0.198			
Positive	1.305					
Negative						

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with $P < 0.1$ in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, employment status, number of comorbidities, menopausal status from T0 to T3 assessment, parity, sports participation at T3 assessment, dietary fat intake at T3 assessment and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-quivalent of task; g, gram.

	Univariate analysis			Multivariate analysis		
	OR	95%CI for OR	P	OR	95%CI for OR	P
PR status, %	1	0.716–1.515	0.831			
Positive	1.042					
Negative						
HER 2 status, %	1	0.614–1.416	0.743			
Positive	0.932					
Negative						
Type of surgery	1	-	0.584			
Mastectomy	0.898	0.612–1.319				
Conservation						
Chemotherapy, %	1	-	0.166			
No	0.751	0.500-1.127				
Yes						
Radiotherapy, %	1	0.568–1.255	0.403			
No	0.844					
Yes						
Endocrine therapy, %	1	0.562–1.290	0.448			
No	0.852					
Yes						

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with $P < 0.1$ in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, employment status, number of comorbidities, menopausal status from T0 to T3 assessment, parity, sports participation at T3 assessment, dietary fat intake at T3 assessment and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-quivalent of task; g, gram.

	Univariate analysis			Multivariate analysis		
	OR	**95%CI for OR**	**P**	**OR**	**95%CI for OR**	**P**
Sports participation at T3 assessment	1	-	0.002	1	-	0.024
Never	0.828	0.548–1.249	0.368	0.869	0.570–1.327	0.517
Rarely/occasionally	**0.396**	**0.234–0.670**	**0.001**	**0.475**	**0.276–0.816**	**0.007**
Frequently						
Dietary energy intake at T3 assessment	1	-	0.501			
≤median	1.136	0.783–1.647				
>median						
Dietary fat intake at T3 assessment, g/1000 kcal/day	1	-	**0.018**	1	-	0.375
≤median	**1.577**	**1.081–2.301**		1.199	0.803–1.791	
>median						
Vegetables and fruits intake at T3 assessment, g/day	1	-	**0.001**	1	-	**0.010**
<400	**0.508**	**0.344–0.750**		**0.586**	**0.389–0.882**	
≥400						
Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with P < 0.1 in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, employment status, number of comorbidities, menopausal status from T0 to T3 assessment, parity, sports participation at T3 assessment, dietary fat intake at T3 assessment and vegetables and fruits intake at T3 assessment.						
From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.						
Abbreviations: OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-growth-factor receptor 2; MET, metabolic equivalent of task; g, gram.						

Analysis for risk factors associated with WHR increase > 10% from T0 to T3 assessment

Table 3 illustrates the outcomes of univariate and multivariate analyses on factors associated with WHR increase > 10% from T0 to T3 assessment. Univariate analysis revealed that older age at breast cancer diagnosis (patients aged 40–49 years, $P = 0.024$ patients aged ≥ 60 years, $P = 0.016$), had ≥ 2 [illegible].019) and vegetables and fruits intake ≥ 400g/day ($P =$

0.007) were associated with less likelihood of very substantial WHR increase. On multivariate analysis, older age at breast cancer diagnosis (OR for patients aged 40–49 years 0.599, 95% CI: 0.367–0.977; P = 0.040), had ≥ 2 comorbidities (OR 0.224, 95% CI: 0.602–0.695; P = 0.001), ER negative (OR 0.620, 95% CI: 0.437–0.881; P = 0.008) and vegetables and fruits intake ≥ 400g/day (OR 0.614, 95% CI: 0.448–0.840; P = 0.002) were all independent factors for very substantial WHR increase.

Table 3
Univariate and multivariate analysis on factors associated with WHR increase > 10% from diagnosis to T3 assessment, by stepwise logistic regression (n = 1171)

	Univariate analysis			Multivariate analysis		
	OR	**95%CI for OR**	**P**	**OR**	**95%CI for OR**	**P**
Age group at diagnosis, year	1	-	0.031	1	-	0.023
< 40	**0.572**	**0.352–0.927**	-	**0.599**	**0.367–0.977**	-
40–49	0.774		**0.024**	0.984		**0.040**
50–59	**0.520**	0.486–1.233	0.281	0.711	0.606–1.597	0.946
≥60		**0.305–0.886**	**0.016**		0.404–1.251	0.237
Education level	1	-	0.200			
High school or below	1.272	0.881–1.836				
College or above						
Marital status	1	-	0.522			
Married or cohabitation	1.105	0.814–1.501				
Unmarried or divorced or widowed						
Family income, HKD/month	1	-	0.310			
< 30,000	1.184	0.855–1.638				
≥30,000						
Employment status	1	-	0.150			
Working	1.228	0.928–1.625				
Not working						

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with P < 0.1 in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, number of comorbidities, ER status and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: WHR, waist-to-hip ratio; OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, [illegible]; MET, metabolic equivalent of task; g, gram.

	Univariate analysis			Multivariate analysis		
	OR	**95%CI for OR**	**P**	**OR**	**95%CI for OR**	**P**
Number of comorbidities	1	-	0.006	1	-	0.006
0	0.878	0.633–1.217	0.434	1.279	0.603–1.199	0.355
1	**0.418**	**0.245–0.713**	**0.001**	**0.224**	**0.602–0.695**	**0.001**
≥ 2						
Menopausal status from T0 to T3 assessment	1	-	0.445			
	1.146	0.760–1.727	0.515			
Pre-menopausal	0.941		0.768			
Peri-menopausal		0.629–1.409				
Post-menopausal						
Parity	1	-	0.259			
0	0.832	0.605–1.145				
≥ 1						
AJCC stage	1	-	0.203			
0-I	0.840	0.620–1.136	0.258			
II	0.691	0.452–1.057	0.089			
III						
ER status, %	1	**0.471–0.933**	**0.019**	1	**0.437–0.881**	**0.008**
Positive	**0.663**			**0.620**		
Negative						

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with $P < 0.1$ in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, number of comorbidities, ER status and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: WHR, waist-to-hip ratio; OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, [illegible]; MET, metabolic equivalent of task; g, gram.

	Univariate analysis			Multivariate analysis		
	OR	95%CI for OR	P	OR	95%CI for OR	P
PR status, %	1	0.674–1.189	0.444			
Positive	0.895					
Negative						
HER 2 status, %	1	0.814–1.554	0.478			
Positive	1.124					
Negative						
Type of surgery	1	-	0.143			
Mastectomy	1.236	0.931–1.640				
Conservation						
Chemotherapy, %	1	-	0.118			
No	0.780	0.571–1.065				
Yes						
Radiotherapy, %	1	0.794–1.472	0.621			
No	1.081					
Yes						
Endocrine therapy, %	1	-	0.223			
No	1.229	0.882–1.712				
Yes						

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with $P < 0.1$ in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, number of comorbidities, ER status and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: WHR, waist-to-hip ratio; OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, [illegible]; MET, metabolic equivalent of task; g, gram.

	Univariate analysis			Multivariate analysis		
	OR	95%CI for OR	P	OR	95%CI for OR	P
Sports participation at T3 assessment, MET-hour/week	1	-	0.387			
Never	1.239	0.888–1.730	0.207			
Rarely/occasionally	1.032	0.721–1.477	0.864			
Frequently						
Dietary energy intake at T3 assessment, kcal	1	-	0.831			
≤median	0.970	0.734–1.282				
>median						
Dietary fat intake in 1000kcal at T3 assessment, g/day	1	-	0.618			
≤median	1.074	0.812–1.419				
>median						
Vegetables and fruits intake at T3 assessment, g/day	1	-	**0.007**	1	-	**0.002**
<400	**0.656**	**0.482–0.892**		**0.614**	**0.448–0.840**	
≥400						
Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with P < 0.1 in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, number of comorbidities, ER status and vegetables and fruits intake at T3 assessment.						
From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.						
Abbreviations: WHR, waist-to-hip ratio; OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-growth-factor receptor 2; MET, metabolic equivalent of task; g, gram.						

Discussion

Based on a longitudinal breast cancer cohort, the present study prospectively measured anthropometric parameters during the first five years of survival. The results showed that weight gain was not common er. Over the first 12-months and at 18-months post-diagnosis,

the median weight change was − 0.5 kg and 0 kg, respectively. At 36-months to 60-months after diagnosis, it observed a modest weight gain with a medium value of 0.5 and 1 kg, respectively. At 60-months after diagnosis, only 14.3% of women had weight gain by > 5kg; and the percentage of women who had weight gain by > 10% was 10.7%. Of note, nearly half of patients had abdominal obesity at study entry, and this figure gradually increased to nearly 70% at 60-months after diagnosis.

Being older and having frequent sports participation were independent protective factors for very substantial weight gain in multivariate analysis.
Additionally, aged 40–49 years at diagnosis, had ≥ 2 comorbidities, ER negative and higher vegetables and fruits intake after breast cancer diagnosis are independently associated with less likelihood of very substantial WHR increase.

The weight change pattern in the current study were inconsistent with findings from Western countries, which have generally reported weight gain following adjuvant treatment. Goodwin et al. reported the weight change from baseline to 1 year post-diagnosis among 535 women with newly diagnosed breast cancer in Canada, and showed that about 84% of women gained weight with a mean value of 1.6 kg.[8] Another study which included 185 women in United States (US) with early stage breast cancer, showed that the mean weight gain was 1.5 kg, 2.7 kg and 2.8 kg at 1 year, 2 year and 3 year after diagnosis, respectively.[11] Rock et al. examined the weight change from diagnosis to study enrollment (mean time since diagnosis: 26 months) among 1116 US breast cancer patients, showing that the mean weight gain was 2.7 kg and 60% of the participants reported weight gain.[43] In contrast to data from Western women, weight gain after breast cancer diagnosis among Asian women has been relatively modest. The Shanghai Breast Cancer Survival Study (SBCSS) reported that the median weight change from diagnosis to 6, 18 and 36 months post-diagnosis were 1.0, 2.0 and 1.0 kg, respectively; about 26%, 37% and 33% of gained weight by ≥ 5% at 6, 18 and 36 months post-diagnosis, respectively.[14] It is noted that the magnitude of weight gain in the SBCSS was slightly greater than that obtained in the present study. Although the study design of the SBCSS was similar to the present cohort, the two studies enrolled patients diagnosed at different times; with the present study having enrolled patients who were diagnosed nearly 10 years later than the SBCSS (from 2011 to 2014). In a study of 260 Korean women with early stage breast cancer who received adjuvant treatment, the investigators reported that no weight gain was found after treatment, and the mean weight change was − 0.3 and − 0.4 kg at 1- and 2- year after treatment, respectively.[13] Another cross-sectional study included 280 premenopausal women (median age at diagnosis was 41 year) with breast cancer after chemotherapy in Hong Kong and reported similar weight change pattern: the median weight gain from diagnosis to 5 years after diagnosis was 1.8 kg, with 63.2% of women gaining weight by > 2%.[16] The varied results among studies in Asian women may be explained by difference in study design, variations in time interval for assessment since initial diagnosis, as well as diverse lifestyle habits.

Several previous studies have tried to investigate the associations between socio-demographic and clinical factors and weight change after diagnosis. In the Health, Eating, Activity and Lifestyle (HEAL) [illegible]sal women at diagnosis had greater weight gain than pre-

menopausal women or women who had menopausal transition after diagnosis.[10] However, in the SBCSS, more weight gain was observed among women who were premenopausal during the first 6 months.[14] The present study supports the SBCSS findings that women who were pre-menopausal at study entry had higher risk of substantial weight gain than those who were postmenopausal in univariate analysis. Findings from studies in Western populations reported an association between chemotherapy and weight gain.[8, 9, 11, 18] However, this finding was not confirmed in Asian population. For example, the Korean study and the SBCSS did not find a weight gain after adjuvant chemotherapy.[13, 14] Similarly, the present study did not show chemotherapy to be associated with the risk of very substantial weight gain. On the other hand, the present study found that older age was associated with reduced risk of weight gain even in multivariate analysis, which was supported by two previous studies in Chinese women with breast cancer. [14, 16]

Several studies have reported a significant decrease in physical activity during and after treatment, and this lifestyle change may be another reason for post-diagnosis weight gain.[9, 44, 45] Chen et al. explored the potential predictors of weight change in SBCSS and reported that higher exercise level was marginally related to weight loss.[19] Similar relationship was observed in the current study, higher level of physical activity was statistically associated with lower risk of very substantial weight gain in both univariate and multivariate analysis. Those findings suggested that high level of physical activity might prevent post-diagnosis weight gain. The results from SBCSS suggested that higher energy intake was related to greater weight gain;[19] while findings from the present study and Yaw et al' s study showed that total energy intake was not associated with weight change.[15]

A number of reports have investigated the relationship between post-diagnosis weight gain and breast cancer prognosis, and strongly supported that post-diagnosis weight gain was related to higher risk of mortality among breast cancer survivors. In 2015, Playdon et al. systematically summarized these data, including 12 studies and a total of 23,832 breast cancer patients.[20] The meta-analysis showed that patients who gained weight by ≥ 5% was associated with increased risk of overall mortality compared with patients who maintained their body weight (defined as weight change < ± 5%).[20] However, it should be noted that evidence from Chinese women with breast cancer has been limited, with only one study showing that women who gained ≥ 5 kg had higher mortality than those who maintained their weight. [46]

WHR was regarded as an index for the measurement of central adiposity.[42] In general population, abdominal adipose tissue (which is positively associated with waist circumference and waist-hip ratio) is associated with a range of metabolic abnormalities, including decreased glucose tolerance, reduced insulin sensitivity and adverse lipid profiles.[42] The present study found that nearly half of women with breast cancer had central adiposity and this phenomenon is more severe as survival time increased. To our knowledge, this is the first study to describe the change pattern of WHR. Multivariate analysis showed that higher vegetables and fruits intake was related to lower risk of substantial WHR increase. In addition, patients aged 40–49 years and had ≥ 2 comorbidities were less likely to had very substantial WHR

years and those had no comorbidity, respectively; suggesting

that those patients may be more cared about abdominal obesity. Moreover, the present study suggested that patients with ER-negative disease was associated with less likelihood of very substantial WHR increase when compared to patients with ER positive; this may be related to use of adjuvant endocrine therapy, in particular, tamoxifen.

Of interests, a few studies have investigated whether central adiposity status after breast cancer diagnosis was associated with detrimental outcomes of breast cancer.[26, 27, 47, 48] For a given BMI, it has been widely reported that Asians tend to have a higher fat percentage and a higher proportion of abdominal adiposity than western populations, [49, 50] it highlights the need to address this issue in specific ethnic groups.

This study was based on data from a longitudinal cohort study with a large sample size, with quantitatively compared the changes of body weight and WHR from immediately post-diagnosis to five years of survival. However, a few limitations should be noted. Firstly, the change pattern was not compared with cancer-free women of similar age; it is, therefore, unclear whether these observed changes can be attributed to aging perse or to breast cancer and its treatment. Secondly, the baseline measurements of WHR were conducted within one year after breast cancer diagnosis; with no data captured right after diagnosis. However, the interval between diagnosis to study entry was relatively short (with median time of 3.2 months), significant WHR changes would not be expected. Thirdly, the multivariate analysis for potential predictive factors could only be regarded as an exploratory analysis given that no clear hypothesis had been stated at priori.

Conclusion

Based on a longitudinal observational cohort of Chinese female patients with early stage breast cancer in Hong Kong, this study compared the change pattern of body weight and WHR during the first five years of survival, and explored the potential factors related to very substantial changes. The study identifies that breast cancer patients in Hong Kong experienced a modest weight gain over the first 5 years of survival, with only about 10% of women gained weight by > 10%. WHR analysis found that nearly half of patients had central adiposity at breast cancer diagnosis, but the proportion increased to nearly 70% at 60-months follow-up. Multivariate analyses indicated that frequent sports participation was significantly associated with lower risk of great weight gain after diagnosis; while higher vegetables and fruits intake decrease the risk of post-diagnosis WHR increase.

Weight management in breast cancer survivorship is an essential component and should be integrated into the survivorship care.
Furthermore, central adiposity has become a contemporary public health issue especially for Asians, and the incorporation of healthy abdominal circumference education and management has the potential to improve the length and quality of cancer survivorship.

Abbreviations

WHR: waist-to-hip ratio

ACS: American Cancer Society

ASCO: American Society of Clinical Oncology

QoL: quality of life

HKNKBCSS: The Hong Kong NTEC-KWC Breast Cancer Survival Study

AJCC: American Joint Committee on Cancer

ER: estrogen receptors

PR: progesterone receptors

HER2: human epidermal-growth-factor receptor 2

BMI: body mass index

OR: odds ratio

SBCSS: Shanghai Breast Cancer Survival Study

Declarations

Ethical approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the Joint CUHK-NTEC Clinical Research Ethics Committee and the KWC Research Ethics Committee of the Chinese University of Hong Kong and the Hong Kong Hospital Authority and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Consent to publication: Not Applicable.

Availability of data and materials: All analyzed data during the current study were presented in the main manuscript. The original datasets are available from the corresponding author on reasonable request.

Competing interest: The authors declare that they have no competing interests.

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Author Contributions

YYL, SCH and WY designed the study. YYL and FM performed the statistical analysis. AC, CK, KLC, RL collected data. YYL, SCH and WY wrote the first draft of the manuscript, to which all authors subsequently contributed. All authors read and approved the final manuscript.

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Tables

Table 1. Patients’ demographic, clinical and lifestyle characteristics collected at T0 assessment (N=1462)

Characteristics	Number of patients	Percentage, %
Time from diagnosis to T0 assessment, median (range), months	3.2 (0.1-11.9)	
Age at diagnosis, mean (SD), years	51.9 (9.1)	
Age group at diagnosis, years		
<40	150	10.3
40-49	468	32.0
50-59	552	37.7
≥60	292	20.0
Education level		
High school or below	1230	84.1
College or above	232	15.9
Marital status		
Married or cohabitation	1039	71.1
Unmarried or divorced or widowed	423	28.9
Family income, HKD/month		
<15,000	683	46.7
15,000-30,000	452	30.9
30,000-50,000	204	14.0
≥50,000	123	8.4
Employment status		
Full time	545	37.3
Part time	195	13.3
Not working	722	49.4
Number of comorbidities		
0	901	61.6
1	371	25.4
≥2	190	13.0
Menopausal status at T0 assessment		
Pre-menopausal	782	53.5
Post-menopausal	680	46.5
Parity		
0	339	23.2
1	340	23.3
2	531	36.3
≥3	252	17.2
AJCC stage		
0-I	523	35.8
II	652	44.6
III	276	18.9
Missing	11	0.8
Histology		
IDC	1225	83.8
ILC	42	2.9
DCIS	94	6.3
Others	101	6.9
ER status, %		
Positive	1057	72.3
Negative	363	24.8
Missing	42	2.9
PR status, %		
Positive	810	55.4
Negative	605	41.4
Missing	47	3.2
HER 2 status, %		
Positive	381	26.1
Negative	966	66.1
Missing	115	7.9
Type of surgery		
Mastectomy	917	62.7
Conservation	545	37.3

Yes	1100	75.2
No	362	24.8
Radiotherapy, %		
Yes	1032	70.6
No	430	29.4
Endocrine therapy, %		
Yes	1054	72.1
No	408	27.9
Height, median (range), cm	156 (137-177)	
Weight, median (range), kg	56.0 (33.4-111.0)	
BMI at diagnosis, kg/m^2		
Underweight (<18.5)	53	3.6
Normal (18.5-22.9)	713	48.8
Overweight (23-24.9)	297	20.3
Obese (≥25)	399	27.3
Waist circumference, median (range), cm	80.3 (58.5-126.5)	
Hip circumference, median (range), cm	95.0 (78.0-136.5)	
WHR at T0 assessment		
< 0.8	391	26.7
0.8-0.89	765	52.3
≥0.9	306	21.0
Sports participation 1-year before diagnosis		
Never	666	45.6
Rarely/occasionally	487	33.1
Frequently	309	21.1
Dietary energy intake 1-year before diagnosis, median (range), kcal/day	1620.3 (551.1-5787.3)	
Dietary fat intake, median (range), g/1000 kcal/day	39.1 (14.2-62.7)	
Vegetables and fruits intake 1-year before diagnosis, g/day		
<400	496	33.9
≥400	966	66.1
Ever smoking before diagnosis		
Yes	22	1.5
No	1440	98.5
Ever frequent alcohol intake before diagnosis (> 4 times/week)		
Yes	28	1.9
No	1434	98.1

Abbreviations: SD, standard deviation; HKD, Hong Kong dollars; BMI, body mass index; AJCC, American joint Committee on cancer; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-growth-factor receptor 2; MET, metabolic equivalent of task; g, gram.

Table 2. Univariate and multivariate analysis on factors associated with weight gain >10% from diagnosis to T3 assessment, by stepwise logistic regression (n=1171)

	Univariate analysis			Multivariate analysis		
	OR	95%CI for OR	P	OR	95%CI for OR	P
Age group at diagnosis			0.0008			0.032
<40	1	-	-	1	-	-
40-49	0.848	0.474-1.516	0.587	0.973	0.507-1.869	0.935
50-59	0.555	0.306-1.007	0.053	0.561	0.236-1.332	0.190
≥60	**0.235**	**0.104-0.528**	**0.0005**	**0.235**	**0.077-0.723**	**0.012**
Education level						
High school or below	1	-				
College or above	1.314	0.817-2.115	0.260			
Marital status						
Married or cohabitation	1	-				
Unmarried or divorced or widowed	1.169	0.783-1.748	0.445			
Family income, HKD/month						
<30,000	1	-				
≥30,000	1.193	0.778-1.828	0.419			
Employment status						
Working	1	-		1	-	
Not working	**1.590**	**1.088-2.323**	**0.016**	1.109	0.731-1.684	0.626
Number of comorbidities			0.026			0.159
0	1	-		1	-	
1	0.932	0.609-1.428	0.747	1.046	0.663-1.650	0.847
≥2	**0.312**	**0.134-0.727**	**0.007**	0.433	0.177-1.059	0.067
Menopausal status from T0 to T3 assessment			0.033			0.161
Pre-menopausal	1	-		1	-	
Peri-menopausal	0.688	0.421-1.124	0.135	0.866	0.494-1.519	0.617
Post-menopausal	**0.521**	**0.319-0.851**	**0.009**	1.575	0.717-3.458	0.257
Parity						
0	1	-		1	-	
≥1	**0.586**	**0.393-0.873**	**0.009**	0.793	0.513-1.227	0.298
AJCC stage			0.810			
0-I	1	-				
II	0.881	0.586-1.327	0.545			
III	0.993	0.583-1.691	0.980			
ER status, %						
Positive	1					
Negative	1.305	0.870-1.959	0.198			
PR status, %						
Positive	1					
Negative	1.042	0.716-1.515	0.831			
HER 2 status, %						
Positive	1					
Negative	0.932	0.614-1.416	0.743			

Mastectomy Conservation	1 0.898	- 0.612-1.319	0.584			
Chemotherapy, % No Yes	1 0.751	- 0.500-1.127	0.166			
Radiotherapy, % No Yes	1 0.844	0.568-1.255	0.403			
Endocrine therapy, % No Yes	1 0.852	0.562-1.290	0.448			
Sports participation at T3 assessment Never Rarely/occasionally Frequently	1 0.828 **0.396**	- 0.548-1.249 **0.234-0.670**	0.002 0.368 **0.001**	1 0.869 **0.475**	- 0.570-1.327 **0.276-0.816**	0.024 0.517 **0.007**
Dietary energy intake at T3 assessment ≤median >median	1 1.136	- 0.783-1.647	0.501			
Dietary fat intake at T3 assessment, g/1000 kcal/day ≤median >median	1 **1.577**	- **1.081-2.301**	**0.018**	1 1.199	- 0.803-1.791	0.375
Vegetables and fruits intake at T3 assessment, g/day <400 ≥400	1 **0.508**	- **0.344-0.750**	**0.001**	1 **0.586**	- **0.389-0.882**	**0.010**

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with P < 0.1 in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, employment status, number of comorbidities, menopausal status from T0 to T3 assessment, parity, sports participation at T3 assessment, dietary fat intake at T3 assessment and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-growth-factor receptor 2; MET, metabolic equivalent of task; g, gram.

Table 3. Univariate and multivariate analysis on factors associated with WHR increase >10% from diagnosis to T3 assessment, by stepwise logistic regression (n=1171)

	Univariate analysis			Multivariate analysis		
	OR	95%CI for OR	P	OR	95%CI for OR	P
Age group at diagnosis, year			0.031			0.023
<40	1	-	-	1	-	-
40-49	**0.572**	**0.352-0.927**	**0.024**	**0.599**	**0.367-0.977**	**0.040**
50-59	0.774	0.486-1.233	0.281	0.984	0.606-1.597	0.946
≥60	**0.520**	**0.305-0.886**	**0.016**	0.711	0.404-1.251	0.237
Education level			0.200			
High school or below	1	-				
College or above	1.272	0.881-1.836				
Marital status						
Married or cohabitation	1	-				
Unmarried or divorced or widowed	1.105	0.814-1.501	0.522			
Family income, HKD/month						
<30,000	1	-				
≥30,000	1.184	0.855-1.638	0.310			
Employment status						
Working	1	-				
Not working	1.228	0.928-1.625	0.150			
Number of comorbidities			0.006			0.006
0	1	-		1	-	
1	0.878	0.633-1.217	0.434	1.279	0.603-1.199	0.355
≥2	**0.418**	**0.245-0.713**	**0.001**	**0.224**	**0.602-0.695**	**0.001**
Menopausal status from T0 to T3 assessment			0.445			
Pre-menopausal	1	-				
Peri-menopausal	1.146	0.760-1.727	0.515			
Post-menopausal	0.941	0.629-1.409	0.768			
Parity			0.259			
0	1	-				
≥1	0.832	0.605-1.145				
AJCC stage			0.203			
0-I	1	-				
II	0.840	0.620-1.136	0.258			
III	0.691	0.452-1.057	0.089			
ER status, %						
Positive	1			1		
Negative	**0.663**	**0.471-0.933**	**0.019**	**0.620**	**0.437-0.881**	**0.008**
PR status, %						
Positive	1					
Negative	0.895	0.674-1.189	0.444			
HER 2 status, %						
Positive	1					
Negative	1.124	0.814-1.554	0.478			

Mastectomy Conservation	1 1.236	- 0.931-1.640	0.143			
Chemotherapy, % No Yes	1 0.780	- 0.571-1.065	0.118			
Radiotherapy, % No Yes	1 1.081	0.794-1.472	0.621			
Endocrine therapy, % No Yes	1 1.229	- 0.882-1.712	0.223			
Sports participation at T3 assessment, MET-hour/week Never Rarely/occasionally Frequently	1 1.239 1.032	- 0.888-1.730 0.721-1.477	0.387 0.207 0.864			
Dietary energy intake at T3 assessment, kcal ≤median >median	1 0.970	- 0.734-1.282	0.831			
Dietary fat intake in 1000kcal at T3 assessment, g/day ≤median >median	1 1.074	- 0.812-1.419	0.618			
Vegetables and fruits intake at T3 assessment, g/day **<400** **≥400**	1 **0.656**	- **0.482-0.892**	**0.007**	1 **0.614**	- **0.448-0.840**	**0.002**

Univariate logistic regression was performed to identify any potential factors associated with very substantial weight gain from diagnosis to T3 assessment. The potential variables with P < 0.1 in univariate analysis were included into the multivariate logistic regression model, including age group at diagnosis, number of comorbidities, ER status and vegetables and fruits intake at T3 assessment.

From T0 to T3 assessment, patients' menopause status could be classified as three groups: pre-menopausal, peri-menopausal and post-menopausal. Peri-menopausal was defined as pre-menopausal patients at T0 who described a change in menopause status at T3.

Abbreviations: WHR, waist-to-hip ratio; OR, odds ratio; CI, confidence interval; HKD, Hong Kong dollars; AJCC, American joint Committee on cancer; ER, estrogen receptor; PR, progesterone receptor; HER 2, human epidermal-growth-factor receptor 2; MET, metabolic equivalent of task; g, gram.

Figures

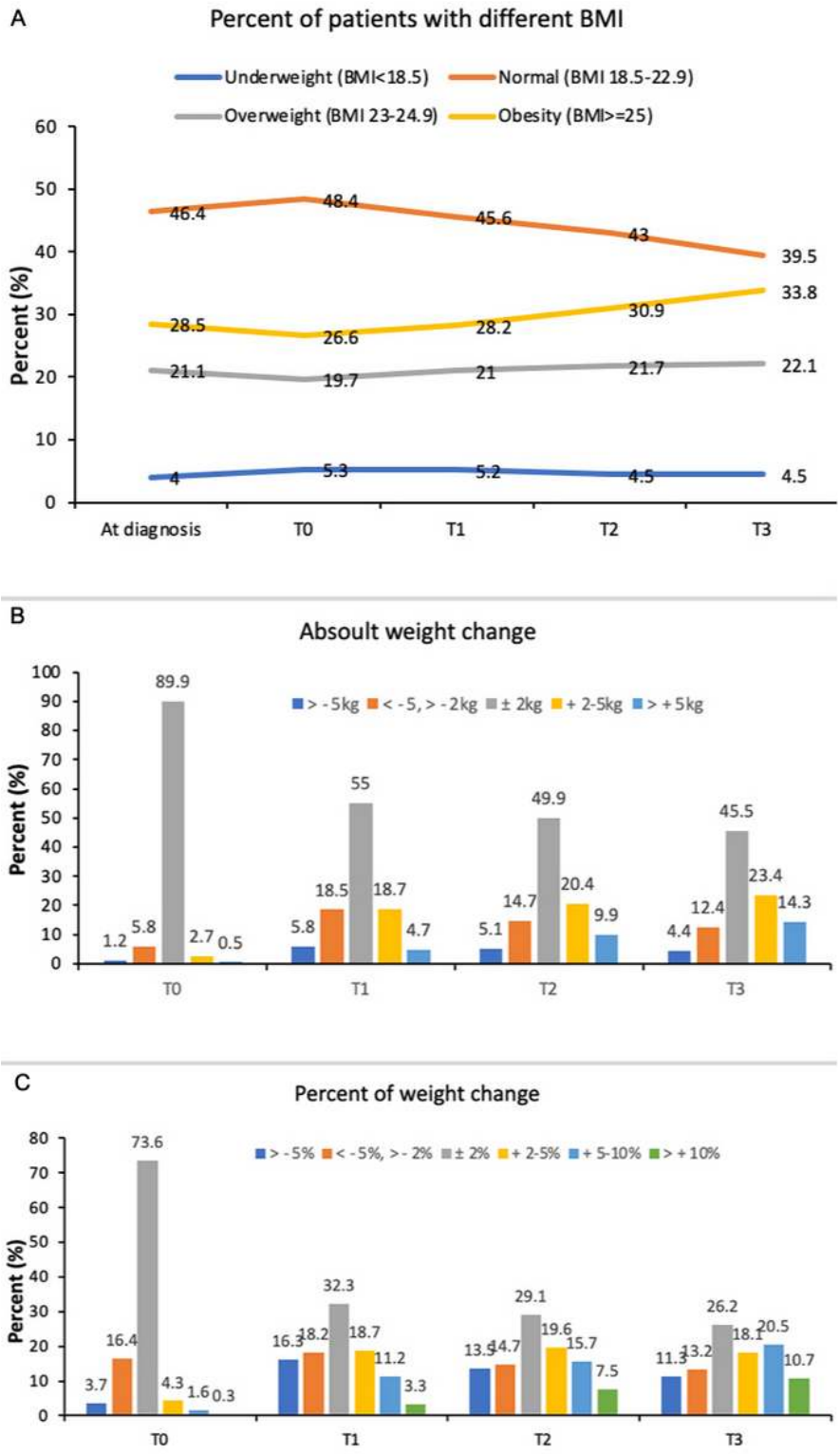

Figure 1

Distribution of patients by BMI or weight change. A) Distribution of patients by BMI at diagnosis, T1, T2 and T3 assessment; B) Distribution of patients by absolute weight change categories from diagnosis to T0, T1, T2 and T3 assessment; C) Distribution of patients by percent of weight change categories from diagnosis to T0, T1, T2 and T3 assessment. Abbreviation: BMI, body mass index.

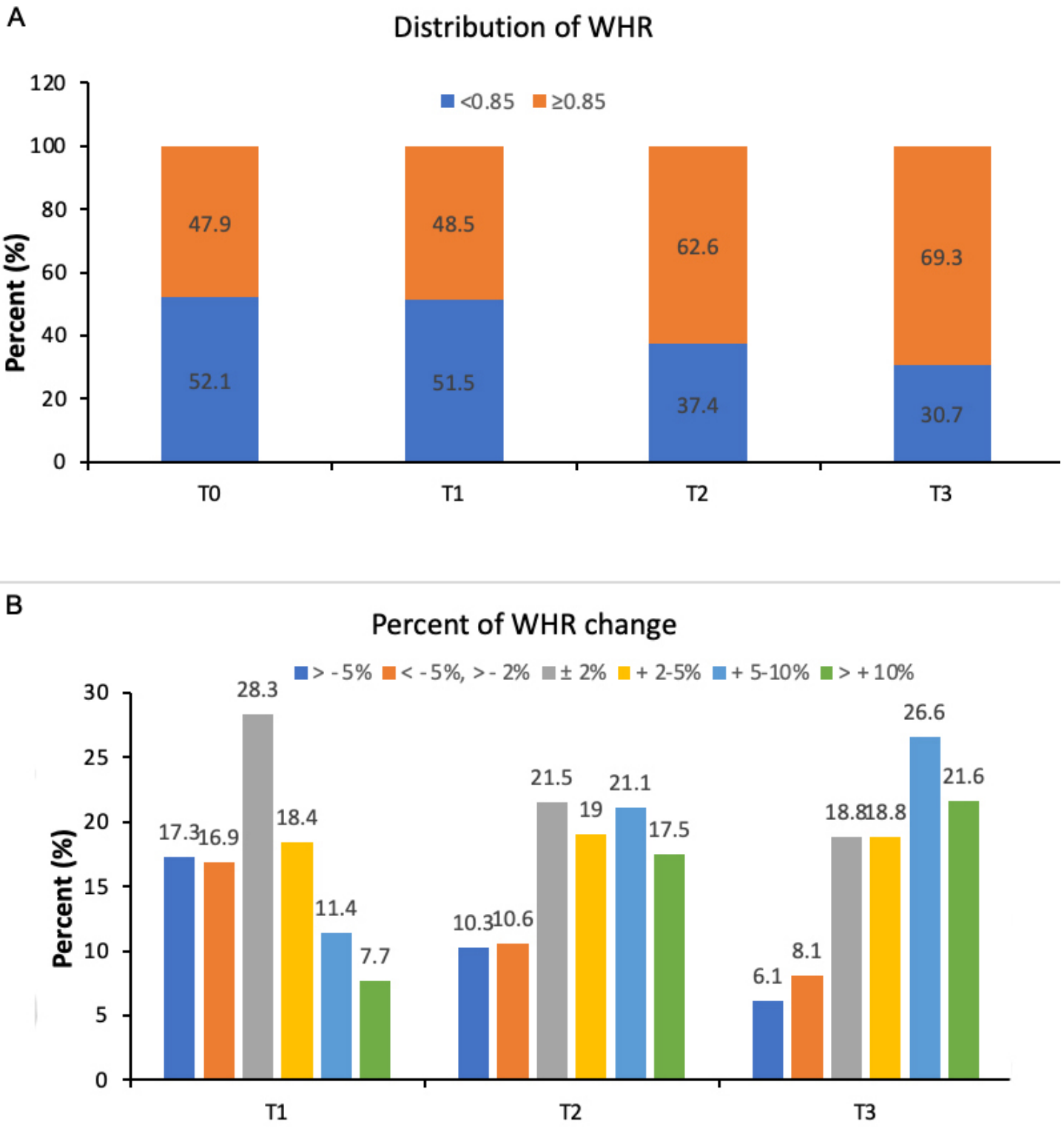

Figure 2

Distribution of patients by BMI or weight change. A) Distribution of patients by BMI at diagnosis, T1, T2 and T3 assessment; B) Distribution of patients by absolute weight change categories from diagnosis to T0, T1, T2 and T3 assessment; C) Distribution of patients by percent of weight change categories from diagnosis to T0, T1, T2 and T3 assessment. Abbreviation: BMI, body mass index.