

Clinical Predictors of Weight Gain in Early Breast Cancer Survivors

Su-Ying Yu^{1,2} & Chii-Ming Chen³

¹ School of Nursing, National Taipei University of Nursing and Health Sciences, Taipei, Taiwan

² Department of Nursing, Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

³ Office of Vice and department of General surgery, Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

Correspondence: Su-Ying Yu, School of Nursing, National Taipei University of Nursing and Health Sciences, Taipei, Taiwan. Tel: 886-937-548-210.

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Abstract

Aim: To identify risk factors for weight gain after two years of a breast cancer diagnosis.

Background: Obesity in survivors of early-stage breast cancer has been associated with high disease recurrence rates and lower overall survival rates. Continuous weight gain is an indisputable phenomenon. Identifying factors at the early diagnosis and treatment phase that are associated with weight gain at 2 years later may help to develop further intervention for prevention obesity in breast cancer survivors.

Method: A retrospective study was designed to review medical records of 1901 early-stage breast cancer survivors. Extracted data included demographics, past medical history, cancer treatment, tumor characteristics, BMI at diagnosis, and 24-month weights.

Results: The sample had a mean age 50.3 (± 10.7). Most of them were premenopausal, stage II and BMI ranging from 18.5 to 24 kg/m² at diagnosis. A majority of them received mastectomy (65.9%), chemotherapy (68.8%), radiotherapy (64.6%) and hormone therapy (63%). At 24 months after surgery, the breast cancer patients gained a mean of 0.4kg; but 21.6% of them gained 5% or more. The breast cancer survivors those who were premenopausal at diagnosis, less-than-high-school education, receiving adriamycin agent, cyclophosphamide agent, and gaining 5% or more weight after surgery had significant higher risk to gain 5% or more at 2 years after diagnosis.

Conclusion: Findings from our study suggested that the premenopausal women or those who receive less formal education have higher risk to gain weight after breast cancer treatment. Engagement to healthy weight management for these high risk groups are warranted

Keywords: early-stage breast cancer, weight gain, chemotherapy

1. Introduction

In 2020 American Cancer Society, an estimated 276,480 new breast cancer will be diagnosed with a relative survival rate of up to 80% after 15 years (Siegel, Miller, & Jemal, 2020). Early diagnosis and advances of neo-adjuvant, adjuvant chemotherapy and hormone therapy utility greatly improve early breast cancer survival rates. Along with improved disease survival, advances in breast treatment have brought with them a considerable degree of adverse effects. Most of breast cancer survivors have been found to be overweight or obese (Ewertz et al., 2012; Imayama et al., 2013; Ortiz-Mendoza, de-la-Fuente-Vera, & Pérez-Chávez, 2014), especially early-stage breast cancer (EBC) survivors with significant weight gain after adjuvant treatment (Arce-Salinas et al., 2014; Vargas-Meza et al., 2017), hormone therapy (Kai Gu et al., 2010; Lorizio et al., 2012). The relationship between breast cancer recurrence and weight change was first investigated by Abe et al (Abe, Kumagai, Kimura, Hirosaki, & Nakamura, 1976); and chemotherapy (Jung, Kim, & Chung, 2020; Schwartsman et al., 2017; M. Van den Berg et al., 2017) was associated with weight gain, especially when cyclophosphamide, methotrexate and 5-fluorouracil (CMF) regiment were more obvious (Jung et al., 2020; Schwartsman et al., 2017; M. Van den Berg et al., 2017). The problem of weight gain has been around for a long time and it is still found that almost two years after the diagnosis, the weight has increased by 1.9 to 5.1 kg (Makari-Judson, Braun, Jerry, & Mertens, 2014; Reddy et al., 2013), which shows that this problem still exists and is serious. In the meta analysis review, weight gain during chemotherapy about 2.7kg, high heterogeneity (I)² 94.2% and the stratified

analysis showed that the weight of all classes increased without low heterogeneity. (M. M. G. A. van den Berg et al., 2017). Significant weight gain before 2000, the publication problem after 2000 still exists and has not improved.

Post diagnosis weight gains of 2.5 to 6.7kg was reported in Western countries (Lankester, Phillips, & Lawton, 2002; V. Vance, M. Mourtzakis, L. McCargar, & R. Hanning, 2011) and almost occurred in the 12 months after diagnosis and during adjuvant treatment period (C. L. Rock & Demark-Wahnefried, 2002; O. Trédan et al., 2010; M. Van den Berg et al., 2017) or Even as long as five years (Schmidt, Wiskemann, & Steindorf, 2018). Weight gain during adjuvant treatment may increase the risk of recurrence and mortality (Chan et al., 2014; Li et al., 2019), and decrease survival (Kroenke, Chen, Rosner, & Holmes, 2005; Shang et al., 2021) and overall health (Caan et al., 2012; Hamer & Warner, 2017; Nichols et al., 2009; M. Van den Berg et al., 2017).

Weight gain is a common phenomenon among breast cancer survivors who receiving adjuvant chemotherapy (Jung et al., 2020; Olivier Trédan et al., 2010), longer duration of treatment (M. Van den Berg et al., 2017), being premenopausal women (A. Gandhi et al., 2019; Wang, Cai, Wang, Zhang, & Zhang, 2014). Other factors included in age (Chen et al., 2011; da Silva, Weiderpass, Licaj, Lissner, & Rylander, 2018; Nyrop et al., 2017), advance stage (Caan et al., 2008; N. Saquib et al., 2007), and decreasing of physical activity (da Silva et al., 2018; Ferioli et al., 2018; Harvie, Howell, Thatcher, Baildam, & Campbell, 2005; Sander, Wilson, Izzo, Mountford, & Hayes, 2012), increasing of energy intake (De Vries et al., 2017; Katan & Ludwig, 2010). Physical activity and eating habits are long-term behaviors that cannot be changed in a short time. The relative weight gain is also the result of chronic energy accumulation or reduced energy consumption. Most existing research on weight gain factors of EBC survivors showed prior factors and inconsistent founding developed by Korean, Canada research (Campbell, Lane, Martin, Gelmon, & McKenzie, 2007; Han et al., 2009).

In Asian populations have different associations between BMI, percentage of body fat, and health risks than European populations have. Asian people with a high risk of type 2 diabetes and cardiovascular disease is substantial at BMIs lower than the existing WHO cut-off point for overweight (25 kg/m²) (World Health Organization. Regional Office for the Western, 2000). The past research may partly explain the large variables in weight change such as longer duration (Heideman, Russell, Gundy, Rookus, & Voskuil, 2009; Cheryl L. Rock et al., 1999; V Vance, M Mourtzakis, L McCargar, & R Hanning, 2011), a regiment of chemotherapy (such as cyclophosphamide, anthracyclines, taxane-based) (Kroenke et al., 2005; Nichols et al., 2009; Olivier Trédan et al., 2010), menopausal status (Caan et al., 2012; Liu, Lin, Miaskowski, Chen, & Chen, 2017), time of weight measurement. Despite the strong evidence linking obesity and inactivity to BC outcomes, and BC survivors with excess weight still developed. Strategies are needed to disseminate weight management and physical activity programs to these populations. If clinical predictors provided the suitable right time to intervene and weight gain should also be prevented by some weight management strategies. Many researches have discussed the causes or the treatment role of weight gain, but ignored the importance of early detection and prevention. If the clinicians can use the predictors to apply early risk assessment and planning, it may decline weight-related problems.

According to the ideal weight range defined by the WHO (BMI 18.5-24.9kg/m²) (World Health Organization. Regional Office for the Western, 2000), the risk of all-cause mortality in Taiwan people will increase with BMI, and the relative risk of overweight and obesity will increase significantly. The BMI value exceeds 25 kg/m², each increase in the value of 1 unit is relative to the relative mortality risk from all causes increase by 9%. The Asians have more body fat than whites and have a higher risk of cardiovascular disease (Goh & Hart, 2018; Misra et al., 2018). Premenopausal overweight and obesity in Asian women are associated with breast cancer (Nindrea, Aryandono, Lazuardi, & Dwiprahasto, 2019) and the incidence of BC in Asia women peaks between 40 and 50 years old (Gomez, Yao, Kushi, & Kurian, 2019). By cancer registry annual report in Taiwan, female breast cancer, 14,217 new diagnoses were documented in 2018 (Health promotion administration ministry of health and welfare Taiwan, 2020) and relative survival rate was 85% after 5 years (Yip, 2009). When the proportion of breast cancer patients who are overweight before surgery is as high as 39.3% (Feng et al., 2018), the issue of weight gain has become a very important issue.

Thus, the purposes of this study were to explore the predictors of weight gain in EBC survivors two years after diagnosis. The findings can contribute to assist breast cancer clinicians making the decision of weight management for high risk patients, help patients actively participate in weight management and EBC rehabilitation program earlier.

1.1 Background

Changes in body weight associated with cancer treatment (Vagenas et al., 2015) for a number of decades. The key research reports that 50-96% of EBC patient experience weight gain during treatment phase (Ashu Gandhi et

al., 2019) and other research showed that weight change persisted progressively for several years after diagnosis, even in patients with weight maintaining during treatment phase (Wendy Demark-Wahnefried et al., 2001). This aspect was also observed in a longitudinal study, which the risk of weight gain was positively related to the time elapsed after diagnosis (Sedjo et al., 2014). The risk factors associated with the weight gain of EBC have been investigated by several researchers. Several investigations report that the weight gain may be attributed by the effects of cancer treatment such as chemotherapy, endocrine therapy (ET) (Grace Makari-Judson, Braun, Jerry, & Mertens, 2014; Sedjo et al., 2014). However, little has been explored about the association of other clinical factors, such as surgery and tumor characteristics, and other social factors, such as education that may denote as competency for healthy weight management.

1.1.1 Weight Gain

Women tend to gain weight after breast cancer diagnosis and during chemotherapy, which may increase risk of poor outcomes. EBC survivors BMI increase of more than 0.5kg/m^2 compared to maintaining BMI was marginally associated with increased loco-regional recurrence risk (HR: 2.53; 95% CI, 1.18-5.45; $P = 0.017$) (Schvartsman et al., 2017). EBC survivors with overweight or obese measured as 68% at 72 months after surgery (Vagenas et al., 2015) and overweight or obese are a severe health issue for EBC survivors. Previous research on weight change and health implications reported that a weight change of greater than 5% might be considered clinically relevant (Ball, Brown, & Crawford, 2002; Caan et al., 2006).

1.1.2 Chemotherapy

Receipt of chemotherapy has been linked to weight gain since the 1970's in EBC survivorship (W. Demark-Wahnefried, Winer, & Rimer, 1993) and weight changes excess 8-10 kg with CMF regiment, prednisone for one year regiment (Puckett, Gabbar, & Bokhari, 2018; Verhaegen & Van Gaal, 2019). The CMF regiment showed weight gain worse than others regiment (M. Van den Berg et al., 2017; Park et al., 2018) and taxane, anthracycline regiment are associated with less weight gain (M. Van den Berg et al., 2017). However, premenopausal women receiving taxanes/anthracycline regimen chemotherapy with significant weight gain on different study (Ashu Gandhi et al., 2019) and it shows that adjuvant chemotherapy regimen have different conclusion, founding on weight gain problems. Impacting weight gain after diagnosis and included chemotherapy regiment, premenopausal, ET, younger, initially weight or BMI at diagnosis. EBC weight change with greater than 5% of their baseline weight at 18 months (Chen et al., 2011; K. Gu et al., 2010) and weight change factor as previous studies except socio-demographics, lifestyle factors.

1.1.3 Endocrine Treatment

In current clinical treatment guidelines recommended that adjuvant therapy includes endocrine therapy in postmenopausal EBC at least five years to improve their overall prognosis and survival. (Dowsett et al., 2010; Schiavon & Smith, 2014). For postmenopausal EBC survivors, ET was recommended with aromatase inhibitor (AI) (Eisen et al., 2015; Taylor & Muss, 2010), exemestane, anastrozole, or letrozole (Burstein, Griggs, Prestrud, & Temin, 2010) and tamoxifen or an AI plus was suggested to premenopausal survivors. It is believed that long-term ET contributes to EBC weight change; but conflicting and inconsistent findings are reported (Howell et al., 2005; Saquib et al., 2007). Further studies are needed.

1.1.4 Initially Body Weight or BMI

Chemotherapy was strongly significantly associated with EBC weight gain and only 10% of EBC survivors returned to their pre-diagnosis weight after follow-up (Saquib et al., 2007). Lower BMI at diagnosis showed higher risk for greater subsequent weight gain after treatment (Ashu Gandhi et al., 2019). EBC women weight gain was significantly associated with BMI and weight at diagnosis.

1.1.5 Surgical Node Dissection or Hormone Receptors

Patient and treatment related weight gain occurred multicollinearity and mastectomy, stage, node dissection presented significant in separate multivariable models of adjuvant treatment (Nyrop et al., 2017). EBC survivor weight gain associations were observed between weight change and tumor stage but not associated with nodal stage, grading, hormone receptor status, or histologic cell subtype (Mutschler et al., 2018).

1.1.6 Menopausal Status

The weight gain observed in health women or undergoing menopause and a prospectively studies showed aged 45 to 55 years gained 0.79kg, aged 55 years and older lost weight (Williamson, Kahn, Remington, & Anda, 1990). In a prospective study, a third of premenopausal EBC underwent adjuvant chemotherapy with significant weight gain and over 40% EBC developed central obesity at 12 months after diagnosis (A. Gandhi et al., 2019). Another

long term study reported premenopausal EBC with weight gain of $\geq 5\%$ after 5 years of ET and premenopausal of EBC patient at diagnosis were 1.4 times then women who were postmenopausal at diagnosis (Mutschler et al., 2018; Raghavendra et al., 2018). In the new publication, it can be seen that in the first 2 years of breast cancer survivors, 49% of premenopausal survivors and 38% of postmenopausal survivors still account for a large proportion of their body weight >2 kg after two years of treatment (Nyrop et al., 2018). Women's menopausal status included variable list.

2. Method

2.1 Aim

The aim of the study was to identify factors that are associated with the development of weight gain greater than 5% 2 years after surgery for early-stage breast cancer.

2.2 Design

This study was based on a retrospective cohort. Data were collected from electronic medical records of early-stage breast cancer survivors at a cancer center in northern Taiwan.

2.3 Participants

All patients with newly diagnosed early-stage breast cancer, who were diagnosed, treated and followed up at the research institute for two years, were screened for this study. The recruitment of patients was based on the following criteria: (1) stage 0 to III breast cancer was confirmed by tissue diagnosis and deemed operable, (2) surgical intervention for breast cancer with regular follow-up care at the center, and (3) age of 18 to 75 years at the time of diagnosis. The exclusion criteria were (1) history of multiple cancers, (2) recurrent or metastatic disease, (3) lack of weight or height records at diagnosis or during follow-up, and (4) history of renal or heart failure. A total of 1956 patients' medical records with newly diagnosed breast cancer and have had follow-up care for 2 years were extracted between 2010 and 2014. Of these, the study excluded 55 patients, because they either had incomplete weight or height data after surgery or loss follow up after surgery ($n = 47$), passed away ($n = 2$), received adjuvant cancer treatment or follow-up care at another hospital ($n = 7$), were undergoing hemodialysis treatment ($n = 1$). The final sample was 1901 patients with breast cancer (Figure1).

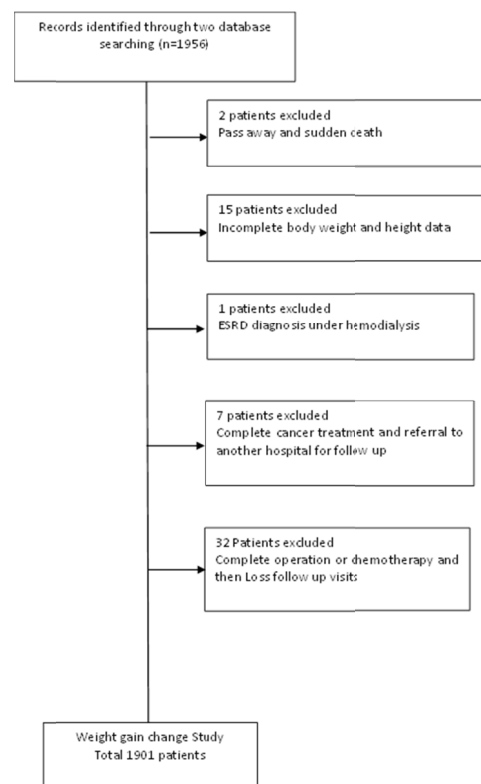


Figure 1. Recruitment of patients for study of weight gain

2.4 Data Collection

Data pertaining to potential risk factors associated with the development of weight gain after surgery were extracted from electronic medical records. Clinical data included age at diagnosis (years), menopausal status at diagnosis, American Joint Committee on Cancer (AJCC) stage (I, II, III, 0), joint estrogen receptor(ER)/progesterone receptor (PR)/Her-2 status, surgery method(wide excision, mastectomy), adjuvant therapy (none, chemotherapy, cortisol agent, radiotherapy, endocrine treatment) and chronic personal medical history (diabetes, hypertension, dyslipidemia). Sociodemographic at diagnosis were also documented, including education and menopausal status. The weight and height of patients were obtained from their records at baseline before surgery, and 24 months after surgery. While the standard practice of this center, weight is measured and recorded by nursing staff. Nursing staff are required to weigh patients in light clothing without shoes, accessories, or additional items on their person. The body weight in kg, one decimal. The uniform weight machine used at the hospital is regularly adjusted by the Public Works Department for precise measurement.

2.5 Ethical Considerations

Research was approved by the internal review board of the hospital (2011104A) .

2.6 Data Analysis

Statistics were performed with SPSS 23.0 for Windows. The *p* value less than 0.05 indicate significant difference. Multivariate logistic regression was used to analyze significant factors in univariate analysis. As considering to test for the gap of previous studies, education and endocrine therapy were still included into adjusted model in multivariate analysis, though they did not yield significant difference in univariate analysis. Weight gain was grouped into one of two categories (<5% and ≥5%). The weight change (percentage) before surgery and 24 months after surgery was calculated as $100 \times (\text{weight at 24 months after surgery} - \text{weight before surgery}) \div (\text{weight before surgery})$.

2.7 Validity, Reliability and Rigour

The validity and reliability were ensured via a rigorous process of data collection from e-medical records. A standardized protocol of collecting patient's personal information, disease, treatment and weight from patients' e-medical records was established by the research team, and was verified for its content availability, accuracy and feasibility by one nursing research, one breast cancer nurse practitioner and one medical informatics professional. The researcher proceeded to collect the data after a series of training, verification and test-retest process. She was trained by the rest of research team members. A performance test was conducted to check the concordance of data collection process with the protocol during the training section. Finally, the information from the first 10 medical records were re-collected two-week apart to check the test-retest reliability; and the agreement between the two times of data collection reached to 100% of 24 items.

3. Results

3.1 Baseline and Treatment Characteristics of Patients

All woman included in this study (n=1901) and clinical and tumor characteristics of the study population all shown (table 1). Mean age at surgery was 50.3 (± 10.7) years. Regarding education level, 566 patients (30.1%) had a junior high school degree, 590 patients (31.4%) had a high school degree, and 723 patients (38.5%) had a college degree or higher. (Participants had more than a high school education). A total of 1091 patients (57.6%) were undergoing menopause before surgery, and 806 patients (42.4%) were postmenopausal. In total, 648 patients (34.1%) underwent wide excision, and 1253 patients (65.9%) underwent mastectomy. In total, 864 (45.4%) patient had DCIS or stage I, 1037 patients (54.6%) stage II, III disease, 1359 (71.5%), 1144 (60.2%) tested positive for estrogen, progesterone receptors, and 1255 (66%) tested positive for Her-2 receptors. The majority received chemotherapy (68.8%), radiation therapy (64.6%) and 63% of participants received hormone therapy. At the time of breast cancer surgery, 42.1% of women was overweight or obese (BMI ≥ 24 kg/m²). The mean body weight before surgery was 58.2 kg (standard deviation [SD] 9.5) and mean body weight was 58.6 kg (SD 9.5) 24 months after surgery. However, 22% of patients' weight gained more than 5% at the second years. The weight gain <5% groups and $\geq 5\%$ groups reached the crossover point in the first year after the operation (Figure 2). The weight gain of less than 5% groups developed decreased slightly, and weight gain of more than or equal to 5% groups developed increased slightly and two groups resulting in two weight gain trend.

Table 1. Weight gain and clinical characteristics

	All patients (n=1901)	24-month Weight Gain		p
		<5% (n=1490)	≥ 5% (n=411)	
Age at diagnosis,				<0.0001
mean(SD)	50.3(10.7)	50.9(10.7)	48.4(10.7)	
Weight				
At diagnosis				
mean(SD)	58.2(9.5)	59.1(9.7)	55.3(8.0)	
24 months				
mean(SD)	58.6(9.5)	58.1(9.6)	60.3(8.9)	
Baseline BMI				<0.0001
<18.5	73(3.8)	53(3.6)	20(4.9)	
18.5-24	1027(54)	750(50.3)	277(67.4)	
≥24	801(42.1)	687(46.1)	114(27.7)	
AJCC stage				
DCIS/ I	864(45.4)	685(46)	179(43.6)	
II/ III	1037(54.6)	805(54)	232(56.4)	
Menopausal status				<0.001
postmenopausal	806(42.4)	671(45)	135(32.8)	
premenopausal	1094(57.6)	819(55)	276(67.2)	
Education				
< high school	566(30.1)	441(29.6)	125(30.4)	
high school	590(31.4)	473(31.7)	117(28.5)	
≥college	723(38.5)	556(37.3)	167(40.6)	
Past medical history				0.02
None	1463(77)	1129(75.8)	334(81.3)	
Yes	438(23))	361(24.2)	77(18.7)	
Breast surgery				NS
WE	648 (34.1)	518(34.8)	130(31.6)	
Mastectomy	1253(65.9)	972(65.2)	281(68.4)	
ER receptor				
Negative	542(28.5)	433(29.1)	109(26.5)	
positive	1359(71.5)	1057(70.9)	302(73.5)	
PR receptor				
Negative	757(39.8)	590(39.6)	167(40.6)	
positive	1144 (60.2)	900(60.4)	244(59.4)	
HER2 receptor				
Negative	646(34)	525(35.2)	121(29.4)	

	positive	1255(66)	965(64.8)	290(70.6)
Chemotherapy				
	No	594(31.7)	486(32.6)	108(26.3)
	Yes	1307(68.8)	1004(67.4)	303(73.7)
Adriamycin agent				
	No	679(35.7)	551(3.7)	128(6.8)
	Yes	1222(64.3)	939(63)	283(20.2)
Taxane-base agent				
	No	1328(69.9)	1046(70.2)	282(68.6)
	Yes	573(30.1)	444(29.8)	129(31.4)
Cyclophosphamide agent				
	No	662(73.5)	649(43.6)	132(32.1)
	Yes	1239(65.2)	841(56.4)	279(67.9)
Dexamethasone agent				
	No	599(31.5)	490(33)	109(26.5)
	Yes	1302(68.5)	1000(67)	302(73.5)
Radiation				
	No	673(35.4)	536(36)	137(33.3)
	Yes	1228(64.6)	954(64)	274(66.7)
Endocrine therapy				
	None	703(37)	560(37.6)	143(34.8)
	Yes	1198(63)	930(62.4)	268(65.2)

Note: DCIS=ductal carcinoma in situ; ER = estrogen receptor; PR = progesterone receptor; HER2 = human epithelial growth factor-2; WE=wide excision

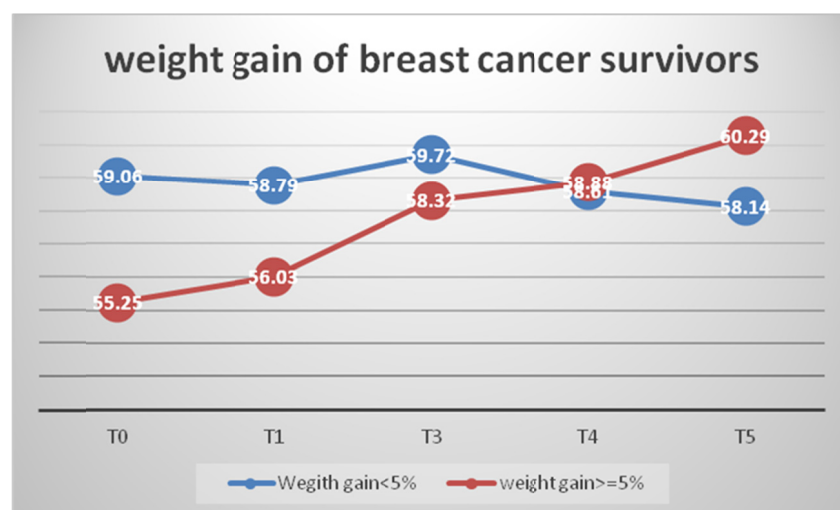


Figure 2. BC survivor weight gain ≥ 5% and < 5% curve

Note: T0=Baseline weight, T1= 1 month after diagnosis, T2= 3months, T3=5 months, T4=1 year, T5=2 years after diagnosis

3.2 Correlates of Weight Gain

The univariate analysis of associations between weight gain, clinical and participant characteristics factors were shown in Table 2. In univariate analysis, age at surgery (OR=0.978, p=.0001), menopausal status (OR=1.675, p=.0001), personal medical history (OR=0.72, p=.02), baseline BMI \geq 24 (OR=0.44, p=.003), baseline weight (OR= 0.95, p=.001), weight gain \geq 5% after one month (OR= 4.745, p=.0001), chemotherapy (OR=1.358, p=.01), adriamycin-based regiment (OR=1.297, p=.029), taxane-based regiment (OR=1.078, p=.535), cyclophosphamide-based regiment (OR= 1.63, p=.0001), dexamethasone agent (OR=1.358, p=.01) were associated with weight gain.

3.3 Multivariate Model of Weight Gain

Before the process of multivariate statistics, we evaluated weight gain and sociodemographic characteristic factors, clinical factors and we checked for multicollinearity first. The variance inflation factors (VIF) and condition index (CI) were used for detection of potential clinical multicollinearity problems between weight gain and variables. Due to multi-collinearity between age and menopausal status at diagnosis, and among adriamycin, cyclophosphamide, taxane and dexamethasone, only menopausal status, Adriamycin and cyclophosphamide were included for adjusted model.

We entry baseline BMI, education level , A agents, C agents, personal medical history, weight gain \geq 5% after one month, menopausal status, hormone therapy in the final model. Thus, eight factors derived from univariate analysis into the multivariate model simultaneously. The overall final model exhibited a good fit with well explanation date ($\chi^2= 190.28$, p=<0.0001, Nagelkerke R²=.148). In multivariate logistic regression analysis disclosed menopausal status (OR=1.48, p=.03), education level (high school OR=.611, p=.003; college OR=.679, P=.016), chemotherapy with A (OR=.584, p=.011), C agent (OR=2.0, p=.001) (Table 3).

Table 2. Univariate analysis for associations between clinical characteristics and 5% 24-month weight gain

Variable	OR	95% CI	p
Age at diagnosis	0.978	0.968-0.988	<0.0001
Weight			
at diagnosis	0.951	0.937-0.964	<0.0001
24 months	1.023	1.012-1.035	<0.0001
BMI at diagnosis			
<18.5	ref		
\geq 18.5<24	0.979	0.575-1.667	0.937
\geq 24	0.440	0.253-0.763	0.003
AJCC stage of BC			
DCIS/ I	ref		
II/III	1.103	0.885-1.374	0.383
Menopausal status			
postmenopausal	ref		
premenopausal	1.675	1.331-2.108	<0.0001
Education			
< high school	ref		
high school	0.873	0.657-1.159	0.346
\geq college	1.060	0.814-1.379	0.666
Past medical history			
None			

Variable	OR	95% CI	<i>p</i>
Yes	0.721	0.548-0.949	0.020
Breast surgery			
WE			
Mastectomy	1.152	0.912-1.455	0.235
ER receptor			
Negative			
positive	0.550	0.1-3.016	0.492
PR receptor			
Negative			
positive	0.550	0.100-3.016	0.492
HER2 receptor			
Negative			
positive	1.419	0.775-2.599	0.257
Chemotherapy			
None			
Yes	1.358	1.063-1.736	0.014
Adriamycin agent			
No			
Yes	1.297	1.027-1.639	0.029
Taxane-base agent			
No			
Yes	1.078	0.851-1.365	0.535
Cyclophosphamide agent			
No			
Yes	1.631	1.295-2.055	<0.0001
Dexamethasone agent			
No			
Yes	1.358	1.063-1.733	0.01
Radiation			
None			
Yes	1.124	0.892-1.415	0.322
Endocrine therapy			
None			
Yes	1.129	0.898-1.418	0.300

Table 3. Multivariate analysis for clinical predictors of weight gain at 24 months

Variable	Adju. OR	95% CI	<i>p</i>
BMI at Diagnosis			
<18.5	ref		
18.5-24	1.162	0.659-2.050	0.604

	≥24	0.592	0.325-1.079	0.087
Menopausal status				
	postmenopausal	ref		
	premenopausal	1.48	1.038-2.127	0.03
Education				
	< high school	ref		
	high school	0.611	0.443-0.843	0.003
	≥ college	0.679	0.496-0.929	0.016
Past medical history				
	None	ref		
	YES	1.081	0.784-1.490	0.636
Adriamycin agent				
	No	ref		
	Yes	0.584	0.584-0.886	0.011
Cyclophosphamide agent				
	No			
	Yes	2.001	1.326-3.020	0.001
Endocrine therapy				
	None			
	Yes	0.945	0.735-1.213	0.656

4. Discussion

In this large,-cohort study, we disclosed twenty-two percent of EBC survivors gained body weight after surgery and the mean weight gain from surgery to 24 months after surgery was 5kg in weight gain $\geq 5\%$ group, weight loss 1kg in weight gain $< 5\%$ group. Overall mean weight gained 0.4kg only and the weight trends of the two groups are different. This study investigated risk factors associated with weight gain of EBC patient which the predictors factor of weight changes critical point. Fourteen potential factors were collected from 1901 EBC patient's e-medical records. This study used univariate logistic regression analysis of fourteen factors for making decision which factors was predictor of weight change. Most previous research evaluated weight gain in EBC only one year after diagnosis has found that the time of weight change occurs after EBC diagnosis, and even 10 years after diagnosis. The phenomenon of weight change continues to progress and the study looking for critical moment of weight change. This concept of prevention should be extension to blueprint for breast cancer care.

Studies have shown that breast cancer survivors gained significantly more weight from diagnosis to the third year of life in women with more advanced breast cancer, younger, postmenopausal, and less physically active age (da Silva et al., 2018; Nyrop et al., 2017; Schiavon & Smith, 2014). Weight gain has been observed to occur after diagnosis (M. M. G. A. van den Berg et al., 2017) and associated with combined systemic treatment (Chen et al., 2011). Prevalence rates differ by country (Dow, Ferrell, Leigh, Ly, & Gulasekaram, 1996; K. Gu et al., 2010; O. Trédan et al., 2010; Tremblay, Pérez, Ardern, Bryan, & Katzmarzyk, 2005; V. Vance et al., 2011). Breast cancer survivors still have 32% of patients with weight problems until five years after diagnosis (Schmidt et al., 2018). The impact of the weight problem is very long-lasting. Although past studies have shown that the weight has stabilized two years after diagnosis. The study reveals that weight gain within 24 months after breast cancer surgery is common among Taiwanese women and sustained afterwards. An association with chemotherapy effects was observed in univariate analysis and multivariate analysis. In total, 21.6% of survivors gained more than 5% body weight from baseline to 24 months after surgery. This is like finding in the literature in the past that it is rare to return to the starting weight after gaining weight (Nazmus Saquib et al., 2007). This percentage is similar to those obtained in Western studies and weight issue associated with chronic disease was worth observance.

In Korea study reported the significant decrease in average weight was mainly diagnosed after 12 months and the younger age group gained significant weight after 36 months (Min, Lee, Chung, & Ahn, 2017). Some studies have found that the degree of weight gain caused by the use of different chemotherapy drug formulations is different. The adjuvant chemotherapy regimens incorporated anthracyclines and / or taxanes in the past few years and weight gain change was lesser than past. The current use of taxanes-based and other drugs still cause a slight weight gain problem and weight reverse after 1 year after chemotherapy (A. Gandhi et al., 2019). This issue must be time observation confirms the seriousness of this problem. In our study, the chemotherapeutics effects disappeared 12 months after surgery and this may be due to limited changes in body weight following the changes in hormone metabolism during early menopause.

The past literature appears regarding weight gain (A. Gandhi et al., 2019; Schwartsman et al., 2017) or weight maintenance in premenopausal women. Premenopausal status was related to weight gain in univariate analysis, and no significant difference was observed, which is consistent with other results (Irwin et al., 2005; Nyrop et al., 2018). Premature menopausal effects associated with weight change and fat tissue development were significant factors. Objective assessment of the menstrual periods of survivors of breast cancer was not completely accurate because it was based only on a case review. Menstrual status after chemotherapy might be affected, and the influence of menstrual status on subsequent weight changes might be underestimated (Kapoor, Collazo-Clavell, & Faubion, 2017). Weight gain after chemotherapy was reported and even obesity is less prevalent in Asian countries (Chen et al., 2011; Kai Gu et al., 2010). In the reports of China, the weight gain was only 1.8 kg, but 60% of breast cancer patients had abnormal BMI (Yeo et al., 2017). Those researchs showed that weight problems caused by treatment factors declining over time. That what factors still affect EBC women are the main points and even they implement weight management measures. In a few studies, whether physical symptoms and psychological distress have an impact on weight change and those studies also found that cancer patients with psychological disease significantly increased body change compared to patient without cancer (Vance, Mourtzakis, & Hanning, 2019). Weight management attitudes and belief disordered eating and exercise behaviors and some factors was contributed excess weight as current, past history of weight and psychological distress (Pila, Sabiston, Taylor, & Arbour-Nicotopoulos, 2018). Weight management failures associated with negative social experiences (Pila et al., 2018), inherently distress of weight management. EBC women reported feeling distress when these weight management were not successful or uncontrollable (Pedersen, Groenkjaer, Falkmer, Mark, & Delmar, 2016).

Social pressure for weight management impacts EBC women attitudes and beliefs toward obesity, and caused by psychological distress, maladaptive eating patterns or behaviors (Carels et al., 2010). EBC patient suffered from systemic adjuvant treatment followed by 5 or 10 years ET, nature metabolic change, psychologic distress, impairment of quality of life. This finding highlights the nature of excess weight as a chronic condition after anti-cancer treatment that needs to be managed in light of other co-occurring illnesses. The present study extended current weight change exclusively as anti-cancer treatment induced, and highlights the considerable impact of pre-cancer weight concerns, and the nature of menopausal status. The weight problems worse than pre-diagnosis developed progressively and weight gain pathophysiology needs exploratory for evidence of weight management strategies. If initially identification of predictor risk factors was used on clinically assessment and it will be help for prevention of weight gain.

Weight gain after 2 years EBC women, it may be a highlighted the failure of weight loss or the cycle consistent of weight gain leading to subsequent distress, thwarting efforts for weight management. EBC survivors identified as high risk of developing weight gain after diagnosis may potentially benefit from interventions. Early assessment followed by health weight management can be helping health promotion early on high risk of EBC survivors. The research reported that a telephone based health lifestyle intervention program resulted in weight loss and demonstrated an opportune approach to weight management, improvements in metabolic parameters, and reduction in the risk of comorbidities for EBC survivor (Ligibel, Basen-Engquist, & Bea, 2019).

5. Limitation

There are some limitations in this study and was a retrospective cohort study at the same cancer center. They may not be representative of the overall population of EBC survivors in Taiwan. Due to limitation in data collected by e-medical record and dietary intake, physical activity was not included this study. However, large sample sizes in this study and EBC patient, clinical characteristics, potential risk factors, cancer-related information for weight gain were included. Those data will provide us with reasonably predictable factors for weight change.

As a result, a negative effect on survival and disease recurrence was noted (Tessomboon & Chompoonuch, 2019),

but study method unfortunately cannot predict the magnitude of risk, which hindered identification of high-risk characteristics. This is one of the limitations in this study.

6. Conclusion

This study understands the predictors of weight change in 2 years after surgery for breast cancer. In the past literature, prediction models have been used for the recurrent, overall survivor of breast cancer. Rarely, they have been used to examine the changes in body weight using prediction models. The change in body weight is different from the Westerners. Although Asia women weight gains less than Westerners, the percentage of weight change is the same. It shows that problems of weight gain are more serious than the Westerners.

A weight change of more than 5% of initial body weight during adjuvant chemotherapy worsens the prognosis of patients with breast cancer in terms of overall survivors (OS) (Mutschler et al., 2018). EBC survivors should be advised to maintain a stable weight after diagnosis, receiving C/T and should receive guidance on adequate nutrition and physical activity during C/T. Specific attention of weight change was considered

6.1 Recommendations for Practice

This study shed initially weight change after chemotherapy might have an influence on further weight change and also advised to attention in regard to their weight change during therapy. The etiology of weight change in EBC women is complex, this study suggests that changes in food intake and psychosocial challenges may play an important role for EBC women. Weight management strategies for EBC survivor has been conducted and considering the founding of the current study, weight management interventions may have to be sustained over a long-term period, especially in women who were diagnosed of EBC.

6.2 Recommendations for Further Research

This retrospective study on weight change predictors with newly EBC revealed that weight change associated with adjuvant cancer treatment at 5, 12 months after surgery. The influence of weight change has decreased after two years of diagnosis. What causes the weight change of EC survivors after diagnosis is still influential, which is worth further research and understanding it. In further, considering the fundamental challenges of weight management, improving weight related psychological effects should be a clinical priority to improve the well-being of women in survivorship.

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