Obesity Does Not Influence Management of Advanced Breast Cancer in the Elderly

Laurel L. Tangalakis,[1] Chandler S. Cortina,[1] Jennifer D. Son,[1] Jennifer Poirier,[1] Andrea Madrigrano[2]

Abstract

A retrospective review of patients age 70 years and greater with advanced breast cancer shows that body mass index does not impact surgical management or adjuvant treatment.

Background: Obesity is becoming increasingly common in the elderly population, and it adds to the complexity of treatment decisions in this population. We aimed to investigate whether body mass index (BMI) affects care in this subset of patients. **Patients and Methods:** We performed a retrospective chart review on 118 patients over the age of 70 years diagnosed with breast cancer and pathologically proven axillary disease over an 8-year period at an urban academic hospital and compared BMI to treatment received, clinical stage, and hormone receptor status. **Results:** Performance of radiation therapy, axillary surgery, and chemotherapy was compared in the elderly population over lower and higher BMI, and no significant difference was detected. Although there was a trend for increasing clinical stage to be associated with a lower BMI, this was not statistically significant ($P = .06$). **Conclusion:** Obesity does not appear to influence treatment decisions in patients over the age of 70 years. Breast cancer providers should turn to other patient and clinical factors when deciding treatment plans in this patient population. Further investigation is needed to examine how obesity influences tumor biology, diagnosis, and treatment decisions.

Clinical Breast Cancer, Vol. 19, No. 3, 197-9 © 2019 Published by Elsevier Inc.
Keywords: Axillary dissection, Chemotherapy, Radiation therapy, Sarcopenia, Surgical management

Background

Obesity is defined by the Centers for Disease Control and Prevention as a body mass index (BMI) equal to or greater than 30 kilograms per meters squared (kg/m^2).[1] Over the past several decades, the rate of obesity in the United States has continued to increase in both the general population and the elderly.[2] Obesity has been directly correlated with an increased risk of breast cancer, and the incidence of breast cancer peaks at the ages of 75 to 79 years.[3,4] Both the elderly and obese are unique patient populations, and often their care deviates from typical treatment protocols.[5-7] Elderly patients with breast cancer are less likely to receive standard surgical care, and many do not receive radiation therapy after breast conserving surgery, despite having disease that does not fall under the Cancer and Leukemia Group B (CALGB) 9434 criteria.[4,8,9] Adjuvant therapy can be omitted in this age group owing to age bias, concerns for toxicity, presence of comorbidities, and effects on quality of life.[10,11]

As obesity is becoming increasingly more common in the elderly population, these patients bring on new challenges in the treatment of breast cancer. Discussions about quality of life, presence of comorbidities, and postoperative complications become increasingly more critical. Our study aimed to investigate whether there is an association between BMI and a decrease in the type of specific therapies (radiation therapy, axillary dissection, and chemotherapy) used to treat advanced breast cancer.

Patients and Methods

A single institution retrospective chart review was performed on patients diagnosed with breast cancer who were age 70 years or older with pathologically proven positive axillary lymph nodes with or without metastatic disease from April 2008 through September 2016. Patients were categorized into 5 categories: normal weight, overweight, and class I, class II, and class III obesity. These categories are defined by BMI and corresponding health risk. Mean and standard deviations of BMI were calculated for each category

[1]Department of Surgery
[2]Division of Surgical Oncology, Department of Surgery, Rush University Medical Center, Chicago, IL

Submitted: Jul 26, 2018; Revised: Nov 9, 2018; Accepted: Dec 28, 2018; Epub: Jan 12, 2019

Address for correspondence: Laurel L. Tangalakis, MD, Rush University Medical Center, Department of Surgery, 1750 W Harrison St, 791 Jelke, Chicago, IL 60612
E-mail contact: laurel_l_tangalakis@rush.edu

1526-8209/$ - see frontmatter © 2019 Published by Elsevier Inc.
https://doi.org/10.1016/j.clbc.2018.12.020

Table 1 Number of Women (Percentages) in Different Body Mass Index Categories

	Normal Weight	Overweight	Obesity Class I	Obesity Class II	Obesity Class III
Frequency	41 (35)	37 (32)	23 (20)	12 (10)	4 (3)

(Table 1). Whether BMI was related to treatment received, cancer stage, and hormone receptor status was examined using Kruskal-Wallis analyses of variance and Welch t tests, depending on whether the predictor was categorical or binary, respectively. BMI was further assessed as a binary variable (with a cutoff of 30), and the same questions were addressed using Fisher exact tests. All statistical analyses were done in R 3.3.2.[12] This study underwent Institutional Review Board (IRB) approval prior to collection of any data, data analysis, or publication.

Results

In total, 118 patients (116 women and 2 men) met inclusion criteria. Thirty-four percent of patients had normal weight (BMI, < 25), 32% were overweight (BMI, 25-30), 20% were class I obesity (BMI, 30-35), 10% were class II obesity (BMI, 35-40), and only 3% were class III obesity (BMI, > 40) (Table 1). BMI association with chemotherapy, radiation therapy, or axillary surgery was performed, and there was no statically significant difference between each of the 5 categorical groups. The mean BMI for patients that received chemotherapy was 28.1, and those who did not receive chemotherapy was 28.8 ($P = .51$). Patients who underwent radiotherapy had a BMI of 27.9 compared with 28.9 for those that did not ($P = .40$). The BMI for patients who had axillary surgery was 27.9, and the BMI for those who did not was 28.8 ($P = .41$) (Table 2).

Although there was a trend for increasing clinical stage to be associated with a lower BMI, this was not statistically significant ($P = .06$). TNM stage also was analyzed but was not statistically significant ($P = .09$). There was no statistically significant relationship to estrogen receptor status ($P = .86$), progesterone receptor status ($P = .55$), or human epidermal growth factor receptor 2 status ($P = .93$) (Table 3). Controlling for obese versus non-obese patients (BMI below or above 30), all analysis remained statically nonsignificant, with P-values being greater than 0.05.

Table 2 Mean (SD) of BMI by Therapy

	Mean BMI (SD)	*P* Value
Chemotherapy		.51
No	28.1 (6.3)	
Yes	28.8 (6.1)	
Radiation therapy		.40
No	27.9 (6.2)	
Yes	28.9 (6.2)	
Axillary dissection		.41
No	27.9 (6.0)	
Yes	28.8 (6.3)	
Operation type		.12
Lumpectomy	32.4 (5.9)	
Lumpectomy and sentinel node biopsy	29.4 (6.4)	
Lumpectomy and axillary dissection	29.5 (4.8)	
Mastectomy	31.8 (4.4)	
Mastectomy and sentinel node biopsy	29.0 (6.9)	
Mastectomy and axillary dissection	28.5 (6.9)	
No surgery	24.9 (3.9)	
Axillary dissection only	21.0 (NA, n = 1)	

Abbreviations: BMI = body mass index; NA = not available; SD = standard deviation.

Discussion

There is an elevated probability of developing breast cancer and an escalation in overall mortality when BMI is greater than 40 kg/m^2.[13] Increasing BMI is also associated with an increased risk for breast cancer recurrence.[14] Furthermore, adiposity is a key risk factor for breast cancer in postmenopausal females, with a relative risk of 1.12 compared with non-obese patients.[13,15] Obesity can also promote tumor carcinogenesis through sex hormone metabolism, deregulated insulin signaling, chronic low-grade inflammatory state, and altered adipokine expression.[15]

BMI greater than 30 is a documented risk factor for postoperative complications after mastectomy, and these patients are also at an increased risk for lymphedema after axillary surgery.[16,17] Chemotherapy dosing can be complex owing to the dosing changes related to overall body weight versus ideal body weight.[18] Although healthy dietary habits and physical exercise are commonly emphasized for obese individuals after receiving a breast cancer diagnosis, data are inconsistent on whether this actually helps to improve outcomes.[19]

Treatment of breast cancer in the elderly and obese populations commonly diverges from standard treatment algorithms. At our institution, there were no statistical differences in BMI and treatment patterns in elderly patients over the age of 70 years with advanced breast cancer. Furthermore, neither clinical stage nor TNM stage nor hormone receptor status was associated with a patient's BMI in our cohort. Given that this is a single-institution study, our sample size was small, and this is a limitation of the study. Perhaps a larger population-based analysis could reveal significant differences based on BMI or obesity classification, but this has yet to be performed.

Considerations that are specific to this unique subset of patients include quality of life and increased risks for complications and toxicities during treatment. Obese populations undergoing mastectomies and axillary lymph node dissections are at increased risk for both surgical complications and lymphedema.[19] Chemotherapy dosing in this population is often complex secondary to fear of elevated toxicity hazard. Previous authors have revealed that these patients receiving chemotherapy are commonly underdosed and therefore have suboptimal outcomes.[18,19] Lastly, owing to the effect of obesity on hormonal status, endocrine therapy also can differ in this population. Data from the Breast International Group (BIG) 1-98 trial supported the use of letrozole versus anastrozole in this subset with superior outcomes.[19,20]

After a diagnosis of breast cancer, lifestyle modifications for obese individuals include weight loss, engaging in moderate physical

Table 3 Mean (SD) of BMI by Staging and Hormone Receptor Status

	Mean BMI (SD)	*P* Value
Clinical stage		.06
1	32.4 (6.5)	
2	28.5 (5.0)	
3	28.2 (8.2)	
4	26.8 (4.5)	
TNM stage		.09
1	34.7 (4.9)	
2	22.4 (2.5)	
3	28.7 (6.5)	
4	27.4 (4.9)	
ER^+ status		.86
Not ER^+	28.7 (6.3)	
ER^+	28.4 (6.2)	
PR^+ status		.55
Not PR^+	28.9 (6.8)	
PR^+	28.2 (5.9)	
Her2Neu status		.93
Not Her2Neu	28.5 (6.3)	
Her2Neu	28.3 (5.2)	

Abbreviations: BMI = body mass index; ER^+ = estrogen receptor-positive; Her2Neu = human epidermal growth factor receptor 2; PR^+ = progesterone receptor-positive; SD = standard deviation.

activity, and limiting alcohol consumption.[15] These adjustments, especially physical activity, can be more difficult in the aging population. Furthermore, it is not clear whether any weight loss post-diagnosis will help to improve outcomes.[19] Sarcopenia, the decline in skeletal muscle associated with the aging process, is an underinvestigated component of the obese elderly population and may contribute to worse outcomes and treatment complications.[21,22] Both elderly and obese populations are individually at risk for sarcopenia, and further exploration is warranted as to whether post-diagnosis intervention could be helpful to reverse these negative effects.

Conclusion

The elderly obese population is a distinctive subset of patients who are at high risk for breast cancer secondary to numerous risk factors. At our institution, BMI does not currently affect treatment patterns in obese patients over the age of 70 years with advanced breast cancer. When considering treatment options for elderly obese patients, patient comorbidities, quality of life, and tumor biology should all be considered in the collaborative approach to selecting treatment(s) between patients and providers. Given the increasing incidence of elderly obese patients in the United States, further investigation is needed to examine how both obesity and age influences tumor biology, diagnosis, and treatment decisions.

Clinical Practice Points

- Age and obesity are definable patient characteristics that may influence treatment decisions by providers.
- There were no statistical differences in BMI and treatment patterns in elderly patients with advanced cancer at our institution, and neither stage nor hormone receptor status was associated with a patient's BMI.
- Breast cancer providers should turn to other patient and clinical factors when deciding treatment plans in this patient population. Further investigation is needed to examine how obesity influences tumor biology, diagnosis, and treatment decisions.

Acknowledgments

The authors thank Karen Ohara for her dedication and assistance in facilitating institutional approval of the study.

Disclosure

The authors have stated that they have no conflicts of interest.

References

1. Centers for Disease Control and Prevention. Defining adult overweight and obesity, Available at: www.cdc.gov/obesity/adult/defining.html. Accessed: March 15, 2018.
2. Better Policies for a Healthy America. Obesity rates & trends, Available at: www.stateofobesity.org/rates. Accessed: March 15, 2018.
3. Sweeney C, Blair CK, Anderson KE, Lazovich D, Folsom AR. Risk factors for breast cancer in elderly women. *Am J Epidemiol* 2004; 160:868-75.
4. National Comprehensive Cancer Network. The complete library of NCCN clinical practice guidelines in oncology, Available at: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#breast. Accessed: March 7, 2018.
5. Tesarova P. Breast cancer in the elderly – should it be treated differently. *Rep Pract Oncol Radiother* 2013; 18:26-33.
6. Tesarova P. Specific aspects of breast cancer therapy of elderly women. *Biomed Res Int* 2016; 2016:1381695.
7. Deglise C, Bouchardy C, Burri M, et al. Impact of obesity on diagnosis and treatment of breast cancer. *Breast Cancer Res Treat* 2010; 120:185-93.
8. Giordano SH, Hortobagyi GN, Kau SW, Theriault RL, Bondy ML. Breast cancer treatment guidelines in older women. *J Clin Oncol* 2005; 23:783-91.
9. Hughes KS, Schnaper LA, Bellon JR, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. *J Clin Oncol* 2013; 19:2382-7.
10. Karuturi M, VanderWalde N, Hyman M. Approach and management of breast cancer in the elderly. *Clin Geriatr Med* 2016; 32:133-53.
11. National Cancer Institute. SEER cancer statistics factsheets: breast cancer, Available at: http://seer.cancer.gov/statfacts/html/breast.html. Accessed: August 5, 2017.
12. R Core Team. *R: a language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing; 2016. Available at: https://www.R-project.org. Accessed: January 22, 2018.
13. Esfahlan RJ, Zarghami N, Esfahlan AJ, Mollazadeh M, Nejati K, Nasiri M. The possible impact of obesity on androgen, progesterone and estrogen receptors (ER-alpha and ER-beta) gene expression in breast cancer patients. *Breast Cancer (Auckl)* 2011; 5:227-37.
14. Sparano JA, Wang M, Zhao F, et al. Obesity at diagnosis is associated with inferior outcomes in hormone receptor-positive operable breast cancer. *Cancer* 2012; 118: 5937-46.
15. Matthews SB, Thompson HJ. The obesity-breast cancer conundrum: an analysis of the issues. *Int J Mol Sci* 2016; 17.
16. Heyler LK, Varnic M, Le LW, Leong W, McCready D. Obesity is a risk factor for developing postoperative lymphedema in breast cancer patients. *Breast J* 2010; 16: 48-54.
17. Vitug AF, Newman LA. Complications in breast surgery. *Surg Clin N Am* 2007; 87:431-51.
18. Griggs JJ, Mangu PB, Anderson H, et al, American Society of Clinical Oncology. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology clinical practice guidelines. *J Clin Oncol* 2012; 30: 1553-61.
19. Jiralerspong S, Goodwin PJ. Obesity and breast cancer prognosis: evidence, challenges, and opportunities. *J Clin Oncol* 2016; 34:4203-16.
20. The Breast International Group (BIG) 1-98 Collaborative Group, Thürlimann B, Keshaviah A, Coates AS, et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. *N Engl J Med* 2005; 353:2747-57.
21. Walston JD. Sarcopenia in older adults. *Curr Opin Rheumatol* 2012; 24: 623-7.
22. Feliciano E, Caan BJ, Prado C, et al. Prevalence of sarcopenia and predictors of body composition among women with early-stage breast cancer. *J Clin Oncol* 2017; 35(5 Suppl):160.