



## Exploring the Effect of Post-mastectomy complications on 5-year survival



Jacob B. Hammond <sup>a</sup>, Ga-ram Han <sup>a</sup>, Patricia A. Cronin <sup>b</sup>, Heide E. Kosiorek <sup>c</sup>,  
Alanna M. Rebecca <sup>d</sup>, William J. Casey III <sup>d</sup>, Erwin A. Kruger <sup>d</sup>, Chad M. Teven <sup>d</sup>,  
Barbara A. Pockaj <sup>b,\*</sup>

<sup>a</sup> Department of Surgery, Mayo Clinic, Phoenix, AZ, USA

<sup>b</sup> Division of Surgical Oncology & Endocrine Surgery, Mayo Clinic, Phoenix, AZ, USA

<sup>c</sup> Department of Health Sciences Research, Section of Biostatistics, Mayo Clinic, Scottsdale, AZ, USA

<sup>d</sup> Division of Plastic & Reconstructive Surgery, Mayo Clinic, Phoenix, AZ, USA

### ARTICLE INFO

#### Article history:

Received 20 March 2020

Received in revised form

24 July 2020

Accepted 3 September 2020

#### Keywords:

Mastectomy  
Reconstruction  
Complications  
Overall survival  
Disease-free survival

### ABSTRACT

**Background:** Ramifications of postoperative complications on long-term survival after mastectomy are uncertain.

**Methods:** Overall complications (Clavien-Dindo Grades I-IIIb) and wound complications were analyzed using the Kaplan-Meier method for impact on 5-year overall (OS) and disease-free survival (DFS).

**Results:** A total of 378 patients underwent mastectomy alone (157, 41%) or mastectomy with reconstruction (221, 59%) for Stage I-III disease with a median follow-up of 5 years. Postoperative complications occurred in 186 patients (49%), requiring non-surgical (I/II = 83, 22%) or surgical (IIIa/IIIb = 103, 27%) management. Wound complications occurred in 140 patients (37%). Reconstruction was associated with a higher rate of complication ( $P < 0.001$ ). Postoperative complications after mastectomy (with or without reconstruction) did not significantly affect OS or DFS. Wound complications also showed no significant effect on OS or DFS following mastectomy alone, or mastectomy with reconstruction.

**Conclusions:** Postoperative complications after mastectomy, with or without reconstruction, bear no significant impact on 5-year survival.

© 2020 Published by Elsevier Inc.

### Table of contents summary

A retrospective cohort study analyzing the effect of postoperative complications on 5-year survival after mastectomy with and without reconstruction.

### Introduction

According to the World Health Organization, breast cancer is diagnosed in 2.1 million women each year.<sup>1</sup> Patients diagnosed today with early stage disease in the United States have an estimated 5-year overall survival >90%.<sup>2</sup> Since 1995, the implementation of evidence-based multidisciplinary treatment among surgeons, oncologists, pathologists, radiologists, and nursing has led to significant improvements in overall and breast cancer

specific survival.<sup>3,4</sup> Multidisciplinary advances across treatment modalities, including the individualized and timely administration of chemotherapy and radiotherapy based on tumor biology, contribute to the favorable outcomes present in this modern era of breast cancer care.<sup>5–9</sup>

The surgical modalities of multidisciplinary breast cancer treatment have also progressed, and surgical techniques and trends continue to evolve. Young breast cancer patients with more aggressive tumor biology, who reluctant to undergo radiation therapy, are more likely to pursue mastectomy over breast-conserving therapy (BCT) despite evidence of no survival advantage.<sup>10,11</sup> Along with current increasing rates of contralateral prophylactic mastectomy, more patients today are pursuing concurrent breast reconstruction after mastectomy; this is especially true among young patients with early stage cancers.<sup>12–14</sup> Compared to mastectomy alone or BCT, patients undergoing breast reconstruction are reported to experience better physical and sexual well-being.<sup>15,16</sup> Despite these benefits, immediate breast reconstruction is also associated with a higher risk for postoperative

\* Corresponding author. should be addressed to 5777 E. Mayo Blvd, Phoenix, AZ, 85054

E-mail address: [Pockaj.Barbara@mayo.edu](mailto:Pockaj.Barbara@mayo.edu) (B.A. Pockaj).

complications.<sup>17,18</sup> While an association between postoperative complications and worse survival has been demonstrated in some studies, associations with complications and outcomes for breast cancer patients have not been thoroughly studied.<sup>19,20</sup> More data are needed to better elucidate if the potential benefits of breast reconstruction are outweighed by a higher risk for complications that could negatively impact survival.

The purpose of this study is to explore the potential influence of postoperative complications on 5-year overall survival (OS) and disease-free survival (DFS) after mastectomy with and without concurrent breast reconstruction.

## Materials and methods

After institutional review board approval, a retrospective review of a prospectively-maintained database was conducted for patients undergoing mastectomy with and without reconstruction from 2010 to 14 for invasive carcinoma. Patients undergoing BCT, as well as those with in-situ carcinoma, Stage IV, or recurrent disease were excluded from analysis.

Postoperative complications were graded based on the Clavien-Dindo (CD) classification system.<sup>21</sup> Patient characteristics, comorbidities, cancer stage, tumor characteristics, surgical techniques, and oncologic therapies underwent univariate analysis for associations with postoperative complications requiring non-surgical (CD Grades I/II) or surgical (CD Grades IIIa/IIIb) management; wound complications (infection, ischemia, breakdown) were also reviewed and included in an additional, separate analysis.

For oncologic therapies, standard institutional practice involved the use of neoadjuvant chemotherapy for patients presenting with human epidermal growth-factor receptor 2 positive (HER2+) or triple negative (ER-PR-HER2-) pathology. Following surgical convalescence, recommendation to pursue adjuvant endocrine and/or chemotherapy was made by the treating oncologist based on tumor biology. The initiation and timing of these adjuvant therapies were examined in accordance to National Quality Forum (NQF) breast cancer treatment recommendations: initiation of chemotherapy within 120 days of diagnosis (NQF #0559), and endocrine therapy within 1 year of diagnosis (NQF #0220).<sup>22</sup> Timing of adjuvant chemotherapy was further evaluated to assess the potential impact of postoperative complications. Recommendation to pursue adjuvant radiation therapy was made by the treating radiation oncologist; a timing threshold of 1 year from diagnosis to initiation of radiation therapy was used to assess patient adherence to recommended adjuvant radiation.

CD Grade I-IIIb complications and wound complications were then analyzed using the Kaplan-Meier method for their effect on 5-year OS and DFS. Stratified log-rank testing was used to account for differences in OS and DFS depending on cancer stage (I-III). Analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). Two-tailed tests were used. An alpha level of 0.05 defined statistical significance.

## Results

A total of 378 patients with a mean age of 58 years (range 22–90) were identified. Simple mastectomy without reconstruction was performed in 157 patients (41%), while 221 patients (59%) underwent mastectomy with concurrent breast reconstruction. Mastectomy techniques included nipple-sparing (54%), skin-sparing (41%), or simple (5%) mastectomy. Types of breast reconstruction included tissue expander (41%), direct-to-implant (39%), or use of autologous tissue (20%). The majority of patients had bilateral procedures (52%) utilizing contralateral prophylactic mastectomy. Regarding race/ethnicity, patients reported they were

White/Caucasian (323, 86%), Hispanic (25, 6.7%), Asian/Pacific Islander (19, 5.1%), African American (6, 1.6%), or they did not specify (5, 0.6%). This cohort had 76 patients (27%) who reported a pertinent comorbidity: 18 patients (4.8%) with diabetes, 17 (4.5%) active smokers, and 14 patients (3.7%) with cardiopulmonary disease. Stage at diagnosis was Stage I (43%), II (37%), and III (20%). The majority of patients (71%) were ER+/HER2-, 16% were HER2+, and 13% were triple negative. Median follow-up for all patients was 5 years, with 9 patients (2%) lost to follow-up.

Overall, 186 patients (49%) experienced a postoperative complication requiring non-surgical (CD Grade I/II = 83, 22%) or surgical (CD Grade IIIa/IIIb = 103, 27%) management; no CD Grade IV/V complications occurred. Wound complications occurred in 140 patients (37%). On univariate analysis, factors associated with postoperative complication included young age ( $P < 0.001$ ), active smoking ( $P=0.008$ ), reconstruction ( $P < 0.001$ ), and bilateral procedure ( $P < 0.001$ ). With the exception of active smoking ( $P=0.072$ ), these factors were also associated with a higher frequency of wound complications. Patient characteristics and their associations with postoperative complications are summarized in Table 1.

Regarding oncologic therapies, 84 patients (22%) underwent neoadjuvant chemotherapy, while 110 patients (29%) had adjuvant chemotherapy, and 78 patients (21%) had adjuvant radiation therapy. Rates of adherence to NQF treatment measures for both adjuvant endocrine therapy and adjuvant chemotherapy were 90% and 96% respectively. Among patients undergoing adjuvant chemotherapy, the average timing of treatment initiation did not significantly differ between patients experiencing a postoperative complication and those without complication (76 days vs. 75 days respectively, Wilcoxon rank-sum  $P$ -value = 0.638). Among all patients pursuing adjuvant radiation therapy, initiation of treatment within 1 year of diagnosis occurred in 98% of patients.

On Kaplan-Meier analysis, the only patient factor associated with worse survival was triple negative cancer (5-year OS = HR 4.4, 95% CI 1.6–11.9,  $p=0.003$ ; 5-year DFS = HR 5.1, 95% CI 1.5–17.1,  $P=0.008$ ). Among the 157 patients undergoing mastectomy alone (Fig. 1), postoperative complications exhibited no significant impact on 5-year OS (Grade I/II HR = 1.66, 95% CI 0.82–3.36, Grade IIIa/IIIb HR = 1.00, 95% CI 0.30–3.35,  $P=0.354$ ), or 5-year DFS (Grade I/II HR = 1.45, 95% CI 0.50–4.19, Grade IIIa/IIIb HR = 0.76, 95% CI 0.10–5.93,  $P=0.737$ ). Postoperative complications were also found to not significantly impact survival among patients undergoing mastectomy with reconstruction (Fig. 2): 5-year OS = Grade I/II HR = 0.00, Grade IIIa/IIIb HR = 0.78, 95% CI 0.27–2.27 ( $P=0.129$ ); 5-year DFS = Grade I/II HR = 1.10, 95% CI 0.33–3.69, Grade IIIa/IIIb HR = 1.00, 95% CI 0.35–2.85 ( $P=0.986$ ).

Wound complications after mastectomy alone (Fig. 3) showed no significant impact on 5-year OS (HR 0.68, 95% CI 0.26–1.77,  $P=0.421$ ) or 5-year DFS (HR 0.66, 95% CI 0.14–3.02,  $P=0.587$ ). For patients having mastectomy with reconstruction, wound complications were also found to have no significant impact on 5-year OS (HR 0.66, 95% CI 0.22–2.02,  $p=0.46$ ), or 5-year DFS (HR 1.24, 95% CI 0.48–3.19,  $P=0.66$ ); these results are summarized in Fig. 4.

## Discussion

Extensive research exists investigating the oncologic safety of breast reconstruction after mastectomy. Current literature shows that reconstruction does not negatively impact overall survival or breast cancer recurrence.<sup>23–26</sup> Some studies even suggest reconstruction is associated with better survival, however, the complex relationship between socioeconomic status and breast cancer survival have scrutinized the simplicity of this association.<sup>27–30</sup> While our data support the notion that concurrent breast reconstruction is associated with higher rates of postoperative complications, our

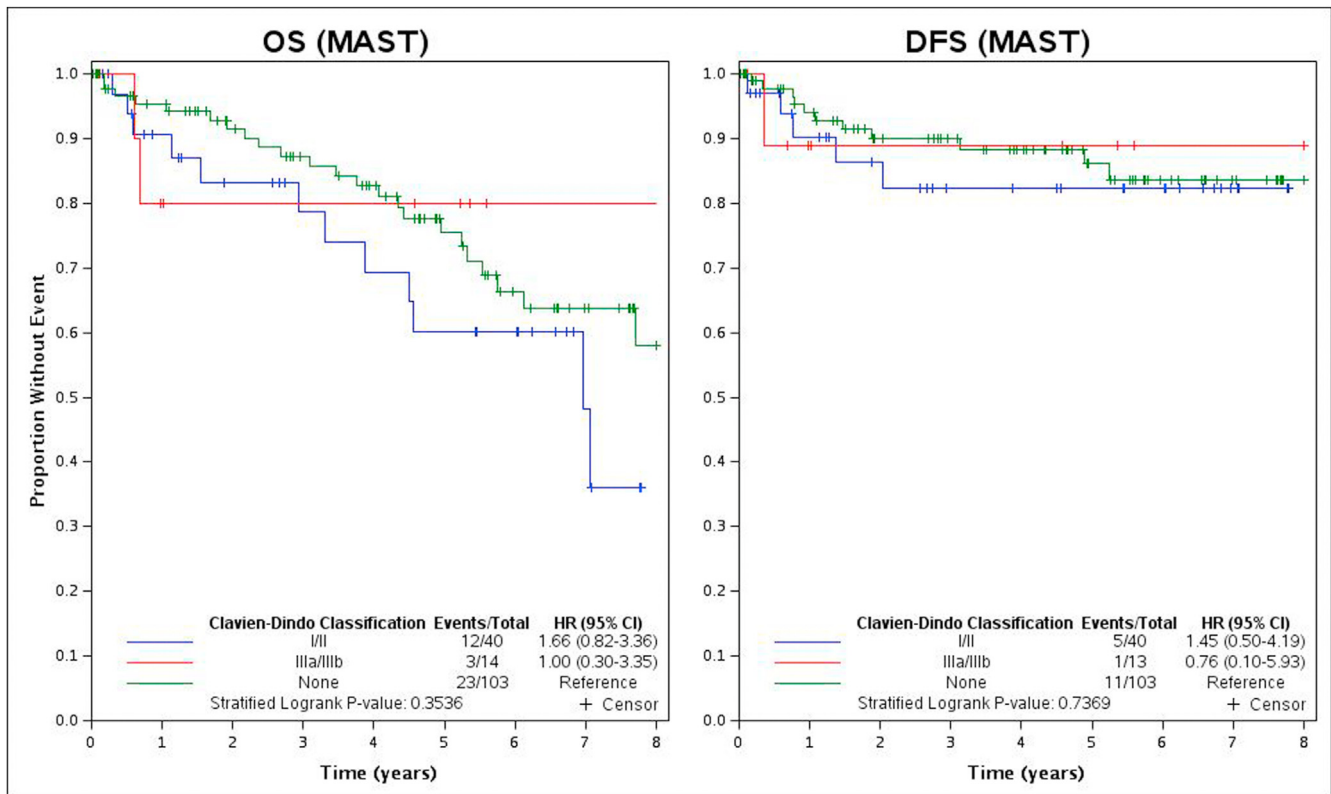
**Table 1**  
Patient Characteristics, Breast Cancer Stage, Surgeries, and Oncologic Therapies and their Associations with Postoperative Complications: <sup>1</sup>ANOVA F-test; <sup>2</sup>Unequal Variance Two Sample T-Test; <sup>3</sup>Chi-Square; <sup>4</sup>Fisher Exact Test.

	Postoperative Complications (Clavien-Dindo Grade)			P-Value	Wound Complications		P-Value
	None	I/II	IIIa/IIIb		Yes	No	
	N (%)	N (%)	N (%)		N (%)	N (%)	
	192 (51)	83 (22)	103 (27)		140 (37)	238 (63)	
<b>Age, Years (Mean, SD) (Range)</b>	61 ± 14 29–90	59 ± 13 33–85	54 ± 12 22–82	<0.001 <sup>1</sup>	55 ± 12 22–82	61 ± 15 29.90	<0.001 <sup>2</sup>
<b>BMI (Mean, SD) (Range)</b>	26.5 ± 5.9 17.4–45.5	27.3 ± 5.6 16.6–48.8	26.2 ± 5.3 18.3–41.4	0.467 <sup>1</sup>	26.6 ± 5.4 18.3–41.4	26.6 ± 5.9 16.6–48.8	0.903 <sup>2</sup>
<b>Stage</b>				0.103 <sup>3</sup>			0.013 <sup>3</sup>
I	75 (39)	35 (42)	51 (50)		72 (51)	89 (37)	
II	72 (38)	30 (36)	41 (40)		49 (35)	94 (40)	
III	45 (23)	18 (22)	11 (10)		19 (14)	55 (23)	
<b>Active Smoking</b>	7 (4)	1 (1)	9 (9)	0.035 <sup>4</sup>	10 (7)	7 (3)	0.072 <sup>4</sup>
<b>Diabetes</b>	9 (5)	3 (4)	6 (6)	0.779 <sup>4</sup>	7 (5)	11 (5)	1.00 <sup>4</sup>
<b>Surgery</b>				<0.001 <sup>3</sup>			<0.001 <sup>3</sup>
Mastectomy Alone	103 (54)	40 (48)	14 (14)		30 (21)	127 (53)	
Mastectomy with Reconstruction	89 (46)	43 (52)	89 (86)		110 (79)	111 (47)	
<b>Bilateral Procedure</b>	76 (40)	47 (57)	74 (72)	<0.001 <sup>3</sup>	97 (69)	100 (43)	<0.001 <sup>3</sup>
<b>Neoadjuvant Chemotherapy</b>	43 (22)	19 (23)	22 (21)	0.966 <sup>3</sup>	24 (17)	43 (18)	0.292 <sup>3</sup>
<b>Adjuvant Chemotherapy</b>	55 (29)	25 (30)	30 (29)	0.970 <sup>3</sup>	39 (28)	71 (30)	0.683 <sup>3</sup>
<b>Adjuvant Radiation Therapy</b>	41 (21)	17 (21)	20 (19)	0.925 <sup>3</sup>	26 (19)	52 (22)	0.447 <sup>3</sup>

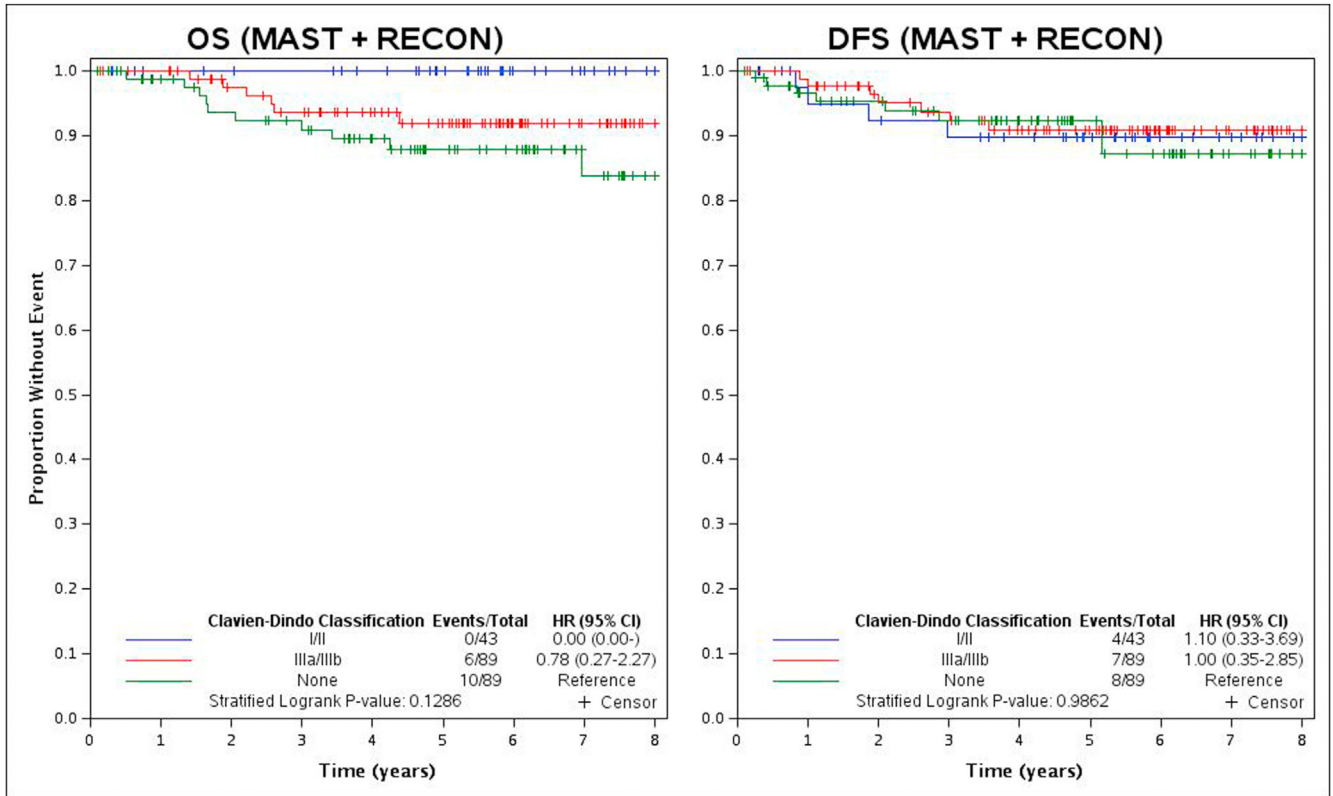
analyses fail to substantiate any negative impact on 5-year survival or oncologic outcomes with reconstruction after mastectomy.

Current evidence evaluating the impact of post-mastectomy complications on timing of adjuvant therapies, and in turn oncologic outcomes, is less concrete. In regards to the NQF's recommended adjuvant chemotherapy treatment timeframe of <120 days from time of diagnosis, myriad literature evaluates the impact

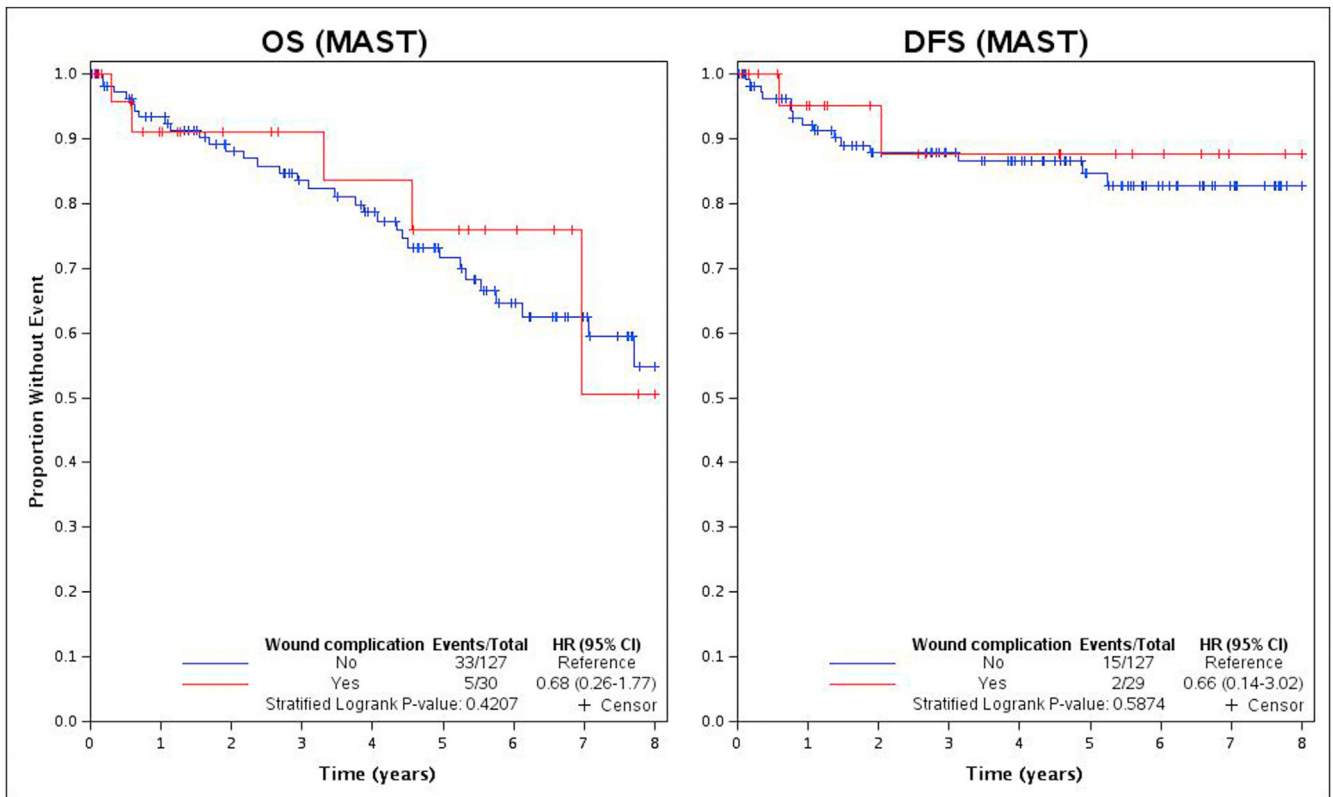
of delays in adjuvant chemotherapy on patient outcomes.<sup>31–34</sup> Recent evidence shows that delay of chemotherapy beyond 120 days from diagnosis is associated with worse 5-year OS.<sup>34</sup> Other studies assessing time from surgery to chemotherapy report mixed results, with some exhibiting declines in OS, DFS, and disease-specific survival.<sup>38</sup> Survival after chemotherapy delays can also vary by tumor subtype, with luminal-B, triple-negative, and



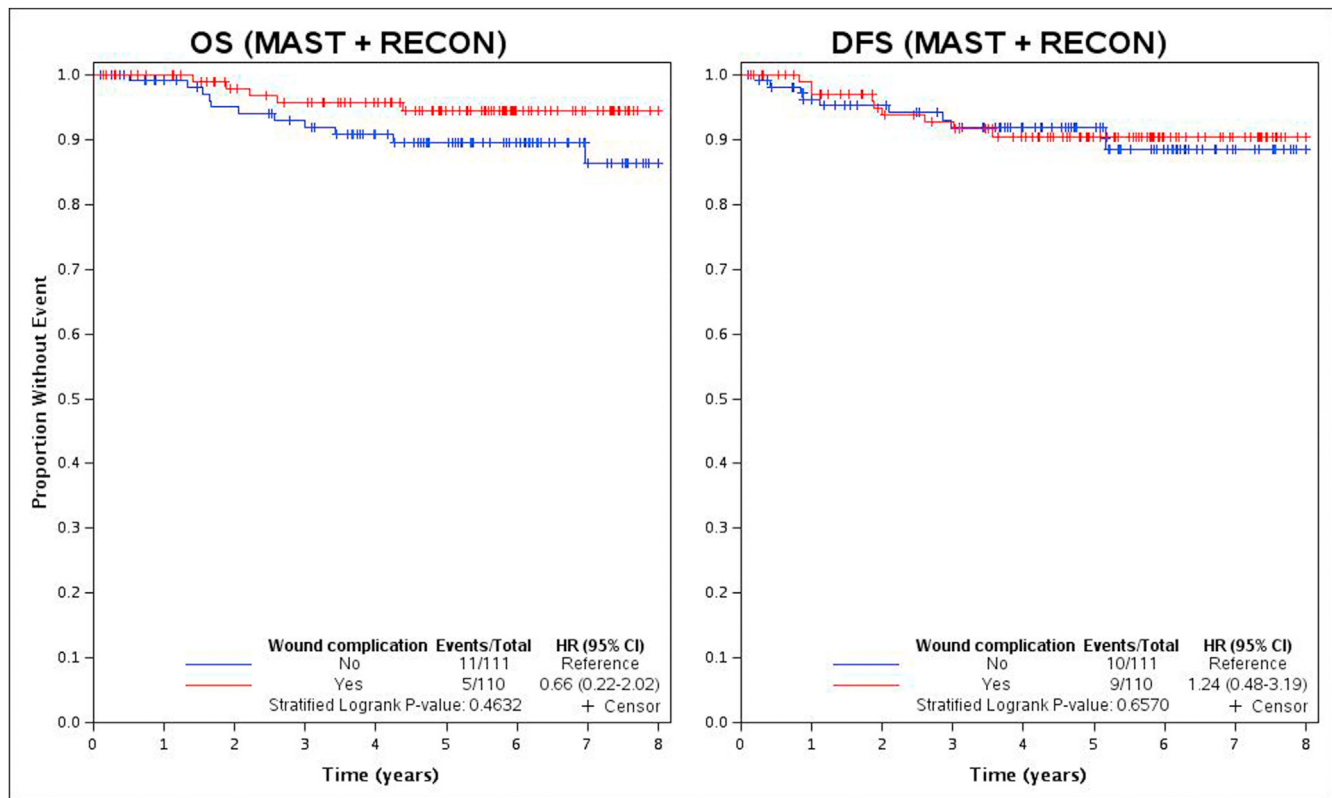
**Fig. 1.** Kaplan-Meier survival curves comparing the effect of postoperative complications (Clavien-Dindo Grades) on 5-year overall and disease-free survival following mastectomy.



**Fig. 2.** ) Kaplan-Meier survival curves comparing the effect of postoperative complications (Clavien-Dindo Grades) on 5-year overall and disease-free survival following mastectomy with reconstruction.



**Fig. 3.** ) Kaplan-Meier survival curves comparing the effect of postoperative wound-specific complications (ischemia, infection, and breakdown) on 5-year overall and disease-free survival following mastectomy.



**Fig. 4.** ) Kaplan-Meier survival curves comparing the effect of postoperative wound-specific complications (ischemia, infection, and breakdown) on 5-year overall and disease-free survival following mastectomy with reconstruction.

trastuzumab-untreated HER2+ patients experiencing worse DFS with treatment delay beyond 8 weeks from time of surgery.<sup>33</sup> These findings support current trends of increasing chemotherapy administration in the neoadjuvant setting, especially for patients with these more aggressive tumor phenotypes.<sup>7</sup> This approach is utilized for all patients presenting with HER2+ and triple-negative tumors at our institution, and obviates need to consider the impact of surgical complications on completion of systemic therapy.

In regards to the current NQF adjuvant radiation timeframe of <365 days from time of diagnosis, this recommendation only applies in the setting of BCT. Furthermore, despite current evidence that delay of radiation beyond this timeframe is associated an increased risk for local recurrence, substantial data evaluating the impact of such a delay in the setting of mastectomy are currently lacking.<sup>33</sup> Since all patients in our cohort underwent mastectomy, whereby 98% of radiation candidates were treated within 1 year, the impact of complications on delay to radiation, and the potential impact on oncologic outcomes, should be the topic of future studies.

While postoperative complications may not lead to complete omission of treatments, current literature suggests they could potentially delay the initiation of adjuvant therapies.<sup>35,36</sup> Studies investigated the impact of wound complications on timing of adjuvant therapies show that treatment is not delayed, with patients only requiring an average of 3 additional weeks to recover.<sup>37,38</sup> In conjunction with this evidence, our data show that both wound-specific and CD Grade I-IIIb complications do not significantly impact the timing of adjuvant chemotherapy. Furthermore, analysis of overall and wound-specific complications within this cohort failed to demonstrate a significant impact on 5-year OS or DFS. It is worth noting that retrospective, single institution studies do demonstrate an association between wound

complications and increased rates of breast cancer recurrence, even when accounting for cancer prognosis factors and patient comorbidities.<sup>19,20</sup> This study is comparable in design and fails to demonstrate such an association.

Limitations to this study include its retrospective approach, use of data from a relatively healthy cohort, and patient follow-up. Our findings that active smoking and diabetes were not significantly associated with more wound complications are likely a result of the lack of these co-morbidities within this cohort. Regarding patient follow-up, specifically our median follow-up of 5 years with a loss to follow-up of 2%, our cohort size potentially minimizes the impact of expected bias within our results. In Okuyama et al., a recent study evaluating the impact of cohort size and loss to follow-up on cancer survival estimates, a breast cancer cohort of 100 patients with a 2% loss to follow-up is expected to generate an expected bias of only 0.26%; our inclusion of 378 patients likely minimizes variable bias in the current study.<sup>39</sup> Furthermore, the median time interval for locoregional recurrence after mastectomy is 2–3 years after treatment, well in advance of a 5-year follow-up.<sup>40</sup> Despite these potential limitations, our analysis was conducted in a reasonably sized cohort, whereby a significant proportion met NQF treatment recommendations, and abundant patient-to-provider communication services allowed for ample detection and documentation of postoperative complications.

## Conclusion

Despite the potential negative impact of postoperative complications on surgical outcomes, our data do not support the notion that postoperative complications delay initiation of adjuvant chemotherapy. Furthermore, this study presents compelling

evidence that postoperative complications bear no significant impact on 5-year OS or DFS after mastectomy, with or without reconstruction. Coupled with the heterogeneity of literature covering operative complications and breast cancer recurrence, these results exemplify the need for larger clinical trials investigating the true impact of mastectomy complications on cancer recurrence and long-term survival.

### Declaration of competing interest

The authors have no financial or commercial conflicts of interest to disclose.

### References

1. *Breast Cancer*; 2018. <https://www.who.int/cancer/prevention/diagnosis-screening/breast-cancer/en/>. Accessed February 24, 2020.
2. DeSantis CE, Ma J, Gaudet MM, et al. Breast cancer statistics, 2019. *CA A Cancer J Clin*. 2019;69(6):438–451.
3. Kesson EM, Allardice GM, George WD, et al. Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women. *BMJ*. 2012;344, e2718.
4. Tsai CH, Hsieh HF, Lai TW, et al. Effect of multidisciplinary team care on the risk of recurrence in breast cancer patients: a national matched cohort study. *Breast*. 2020.
5. Yu KD, Fan L, Qiu LX, et al. Influence of delayed initiation of adjuvant chemotherapy on breast cancer survival is subtype-dependent. *Oncotarget*. 2017;8(28), 46549.
6. Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;17(9503):2087–2106, 366.
7. Murphy BL, Day CN, Hoskin TL, et al. Neoadjuvant chemotherapy use in breast Cancer is greatest in excellent responders: triple-negative and HER2+ subtypes. *Ann Surg Oncol*. 2018;25(8):2241–2248.
8. Selz J, Stevens D, Jouanneau L, et al. Prognostic value of molecular subtypes, ki67 expression and impact of postmastectomy radiation therapy in breast cancer patients with negative lymph nodes after mastectomy. *Int J Radiat Oncol Biol Phys*. 2012;84(5):1123–1132.
9. Tseng YD, Uno H, Hughes ME, et al. Biological subtype predicts risk of locoregional recurrence after mastectomy and impact of postmastectomy radiation in a large national database. *Int J Radiat Oncol Biol Phys*. 2015;93(3):622–630.
10. Litière S, Werutsky G, Fentiman IS, et al. Breast conserving therapy versus mastectomy for stage I–II breast cancer: 20 year follow-up of the EORTC 10801 phase 3 randomised trial. *Lancet Oncol*. 2012;13(4):412–419.
11. McGuire KP, Santillan AA, Kaur P, et al. Are mastectomies on the rise? A 13-year trend analysis of the selection of mastectomy versus breast conservation therapy in 5865 patients. *Ann Surg Oncol*. 2009;16(10):2682–2690.
12. Ilonzo N, Tsang A, Tsantes S, et al. Breast reconstruction after mastectomy: a ten-year analysis of trends and immediate postoperative outcomes. *Breast*. 2017;32:7–12.
13. Kummerow KL, Du L, Penson DF, Shyr Y, Hooks MA. Nationwide trends in mastectomy for early-stage breast cancer. *JAMA Surgery*. 2015;150(1):9–16.
14. Iskandar ME, Dayan E, Lucido D, et al. Factors influencing incidence and type of postmastectomy breast reconstruction in an urban multidisciplinary cancer center. *Plast Reconstr Surg*. 2015;135(2), 270e–6e.
15. Howes BH, Watson DI, Xu C, et al. Quality of life following total mastectomy with and without reconstruction versus breast-conserving surgery for breast cancer: a case-controlled cohort study. *J Plast Reconstr Aesthetic Surg*. 2016;69(9):1184–1191.
16. Ueda S, Tamaki Y, Yano K, et al. Cosmetic outcome and patient satisfaction after skin-sparing mastectomy for breast cancer with immediate reconstruction of the breast. *Surgery*. 2008;143(3):414–425.
17. Garvey EM, Gray RJ, Wasif N, et al. Neoadjuvant therapy and breast cancer surgery: a closer look at postoperative complications. *Am J Surg*. 2013;206(6):894–899.
18. Hange PT, Jogerst K, Mohsen A, et al. Making an informed choice: which breast reconstruction type has the lowest complication rate? *Am J Surg*. 2019;218(6):1040–1045.
19. Murthy BL, Thomson CS, Dodwell D, et al. Postoperative wound complications and systemic recurrence in breast cancer. *Br J Canc*. 2007;97(9):1211–1217.
20. Beecher SM, O'Leary DP, McLaughlin R, et al. Influence of complications following immediate breast reconstruction on breast cancer recurrence rates. *Br J Surg*. 2016;103(4):391–398.
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240(2), 205.
22. National Quality Forum. Retrieved June 1, 2020, from <http://www.qualityforum.org/Home.aspx>.
23. Platt J, Baxter NN, McLaughlin J, Semple JL. Does breast reconstruction after mastectomy for breast cancer affect overall survival? Long-term follow-up of a retrospective population-based cohort. *Plast Reconstr Surg*. 2015;135(3), 468e–76e.
24. Siotos C, Naska A, Bello RJ, et al. Survival and disease recurrence rates among breast cancer patients following mastectomy with or without breast reconstruction. *Plast Reconstr Surg*. 2019;144(2), 169e–77e.
25. Eriksen C, Frisell J, Wickman M, et al. Immediate reconstruction with implants in women with invasive breast cancer does not affect oncological safety in a matched cohort study. *Breast Canc Res Treat*. 2011;127(2), 439.
26. Giemi M, Avram R, Dickson L, et al. Local breast cancer recurrence after mastectomy and immediate breast reconstruction for invasive cancer: a meta-analysis. *Breast*. 2012;21(3):230–236.
27. Zhong T, Fernandes KA, Saskin R, et al. Barriers to immediate breast reconstruction in the Canadian universal health care system. *J Clin Oncol*. 2014;32(20):2133–2141.
28. Sisco M, Du H, Warner JP, et al. Have we expanded the equitable delivery of postmastectomy breast reconstruction in the new millennium? Evidence from the national cancer data base. *J Am Coll Surg*. 2012;215(5):658–666.
29. Agarwal J, Agarwal S, Pappas L, Neumayer L. A population-based study of breast cancer-specific survival following mastectomy and immediate or early-delayed breast reconstruction. *Breast J*. 2012;18(3):226–232.
30. Bezuhly M, Temple C, Sigurdson LJ, et al. Immediate postmastectomy reconstruction is associated with improved breast cancer-specific survival: evidence and new challenges from the Surveillance, Epidemiology, and End Results database. *Cancer*. 2009;115(20):4648–4654.
31. Lohrisch C, Paltiel C, Gelmon K, et al. Impact on survival of time from definitive surgery to initiation of adjuvant chemotherapy for early-stage breast cancer. *J Clin Oncol*. 2006;24(30):4888–4894.
32. Cold S, Düring M, Ewertz M, et al. Does timing of adjuvant chemotherapy influence the prognosis after early breast cancer? Results of the Danish Breast Cancer Cooperative Group (DBCG). *Br J Canc*. 2005;93(6):627–632.
33. Bleicher RJ. Timing and delays in breast cancer evaluation and treatment. *Ann Surg Oncol*. 2018;25(10):2829–2838.
34. Kupstas AR, Hoskin TL, Day CN, et al. Effect of surgery type on time to adjuvant chemotherapy and impact of delay on breast cancer survival: a National Cancer Database analysis. *Ann Surg Oncol*. 2019;26(10):3240–3249.
35. Valente SA, Liu Y, Upadhyaya S, et al. The effect of wound complications following mastectomy with immediate reconstruction on breast cancer recurrence. *Am J Surg*. 2019;217(3):514–518.
36. Motwani SB, Strom EA, Schechter NR, et al. The impact of immediate breast reconstruction on the technical delivery of postmastectomy radiotherapy. *Int J Radiat Oncol Biol Phys*. 2006;66(1):76–82.
37. Mortenson MM, Schneider PD, Khatri VP, et al. Immediate breast reconstruction after mastectomy increases wound complications: however, initiation of adjuvant chemotherapy is not delayed. *Arch Surg*. 2004;139(9):988–991.
38. Lin KY, Johns FR, Gibson J, et al. An outcome study of breast reconstruction: presurgical identification of risk factors for complications. *Ann Surg Oncol*. 2001;8(7):586–591.
39. Okuyama A, Barclay M, Chen C, Higashi T. Impact of loss-to-follow-up on cancer survival estimates for small populations: a simulation study using Hospital-Based Cancer Registries in Japan. *BMJ open*. 2020;10(1).
40. Buchanan CL, Dorn PL, Fey J, et al. Locoregional recurrence after mastectomy: incidence and outcomes. *J Am Coll Surg*. 2006;203(4):469–474.