Original Article

The Impact of Breast Reconstruction on the Delivery of Chemotherapy

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BACKGROUND: The purpose of this study was to evaluate the impact of postmastectomy breast reconstruction on the timing of chemotherapy. **METHODS:** The authors included stage I-III breast cancer patients from 8 National Comprehensive Cancer Network institutions for whom guidelines recommended chemotherapy. Surgery type was categorized as breast-conserving surgery (BCS), mastectomy alone, mastectomy with immediate reconstruction (M + IR), or mastectomy with delayed reconstruction (M + DR). A Cox regression analysis was used to assess the association between surgery type and timing of chemotherapy initiation. **RESULTS:** Of the 3643 patients, only 5.1% received it ≥8 weeks from surgery. In the multivariate analysis, higher stage, Caucasian and Hispanic race/ethnicity, lower body mass index, and absence of comorbid conditions were all significantly associated with earlier time to chemotherapy. There was also significant interaction among age, surgery, and chemotherapy delivery. Among women <60, time to chemotherapy was shorter for all surgery types compared with M + IR (statistical significant for all surgery types in the youngest age group and for BCS in women 40 to <50 years old). In contrast, among women ≥60, time to chemotherapy was shorter among women receiving M + IR or M + DR compared with those undergoing BCS or mastectomy alone, a difference that was statistically significant for the M + IR versus BCS comparison. **CONCLUSIONS:** Immediate postmastectomy breast reconstruction does not appear to lead to omission of chemotherapy, but it is associated with a modest, but statistically significant, delay in initiating treatment. For most, it is unlikely that this delay has any clinical significance. ***Cancer*** **2010;116:1791–800.** © *2010 American Cancer Society.*

KEYWORDS: breast reconstruction, breast cancer, chemotherapy, NCCN.

Postmastectomy breast reconstruction is an integral part of breast cancer care. Breast reconstruction, especially when performed at the time of the mastectomy, has been associated with improved psychosocial well-being and high levels of patient satisfaction.[1-5] In particular, reconstruction can have a positive influence on women's body image, sexuality, and social well-being, thus having a long-term impact in the cancer survivorship period.[6] However, less than 20% of women receive reconstruction at the time of the mastectomy.[7] There is also wide geographic variation in the use of reconstruction, raising the concern that there may be unmet need and access barriers to reconstructive surgery.[7,8]

One barrier to the use of immediate breast reconstruction—that is reconstruction performed at the time of mastectomy—is the concern that complications of reconstruction may unduly delay the initiation of systemic chemotherapy or lead to its omission altogether.[9] Adjuvant chemotherapy in appropriately selected breast cancer patients is a life-saving intervention. Delay in initiating adjuvant treatment may compromise its effectiveness, and omitting it will have even more serious consequences.[10]

Little is known about the impact of immediate breast reconstruction on the administration of adjuvant chemotherapy. Immediate breast reconstruction offers better esthetic results, cushions the psychological impact of the breast amputation, and decreases healthcare costs by decreasing the number of operations the patient requires.[3,9,11,12] However, immediate reconstruction is associated with higher surgical complication rates compared with those performed after the

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mastectomy,[13] which could delay the timing of chemotherapy delivery, and might lead some patients to forego chemotherapy altogether. Previous studies have not found an association between immediate breast reconstruction and delayed chemotherapy[14-21]; however, these have been small, single-center studies with limited ability to generalize to other healthcare settings because of the high variability of surgical techniques and patient-level factors across medical centers. Furthermore, these studies have looked exclusively at the timing of chemotherapy among treated patients, so they could not determine whether reconstruction had an effect on the use of adjuvant therapy.

We sought to examine the impact of breast reconstruction on the delivery of chemotherapy using a large, multicenter cohort of patients. Specifically, we wanted to 1) describe the effect of the primary surgery type on the use and timing of adjuvant therapy, controlling for patient factors, and 2) identify factors associated with a significant delay or omission of adjuvant chemotherapy.

MATERIALS AND METHODS

Study Population

Our study population comprised 3643 women with stage I-III unilateral breast cancer who were treated at 1 of the 8 participating National Comprehensive Cancer Network (NCCN) institutions between July 1, 1997 and December 31, 2003 for whom NCCN guidelines recommended adjuvant chemotherapy. Patients were eligible for this analysis if they received their definitive surgery at the NCCN institution and continued to receive their care there for at least 1 year after first presentation. The database includes information on receipt of chemotherapy regardless of the administering institution for patients who continue to be seen in the NCCN center. We limited the sample to patients for whom the version of the NCCN guidelines in effect at the time of their diagnosis recommended adjuvant chemotherapy.[22,23] This was done for 2 reasons. First, we were not interested in capturing information on whether type of surgery resulted in delayed initiation of a treatment that was not indicated. Second, defining our cohort by clinical indication rather than chemotherapy administration allowed us to examine the effect of surgery type not just on the timing but also on the use of adjuvant chemotherapy. Patients who received 1) neoadjuvant systemic or radiation therapy (N = 635), 2) radiation therapy before initiation of adjuvant therapy (N = 34), or 3) breast reconstruction more than a day after completion of their primary surgery but before the initiation of adjuvant chemotherapy (N = 8) were not eligible for this analysis, because these patterns of care would confound an analysis of the relationship between primary surgery type and time to initiation of adjuvant treatment. Institutional Review Board approval was obtained from each institution.

Measures

All variables used in the analysis were obtained from the NCCN Breast Cancer Outcomes Project Database. Definitive surgery was assigned after considering all breast-directed surgical procedures and was classified as breast-conserving surgery (BCS), mastectomy only, mastectomy with immediate breast reconstruction (M + IR), or mastectomy with delayed breast reconstruction (M + DR). Reconstruction was considered "immediate" if it was either started or completed on the same day as the mastectomy, and "delayed" otherwise.

Other variables in the analysis are as follows: type of reconstructive surgery (implant, pedicle transverse rectus abdominus myocutaneous flap [TRAM], free TRAM requiring microvascular surgery, other rotational flap, and other free flap); NCCN institution; race/ethnicity (Caucasian, Hispanic, African American, other); median household income (<$35,426, $35,426-<$44,639, $44,639-<$58,844, $58,844-$159,538, unknown); age at diagnosis; body mass index (BMI; <25 kg/m^2, 25-35 kg/m^2, >35 kg/m^2, unknown); American Joint Committee on Cancer stage at diagnosis (I, II, III); tumor size ($\leq$2 cm, >2-5 cm, >5 cm, unknown); number of positive lymph nodes (0, 1-3, 4-9, $\geq$10, unknown); Charlson comorbidity score (0,1, $\geq$2); NCCN breast cancer guideline that the patient was eligible for based on clinical characteristics; and participation in an adjuvant therapy clinical trial.

Adjuvant chemotherapy was defined as systemic cancer-directed therapy given after completion of definitive surgery and before any recurrence. Time to adjuvant chemotherapy was the interval from the last definitive surgical procedure to the first dose of adjuvant chemotherapy. For the descriptive analyses, time to chemotherapy was reported as a categorical variable (<8 weeks, $\geq$8 weeks, and no chemotherapy). In the logistic model, the outcome variable was defined as adjuvant chemotherapy initiated before recurrence. In the time to event multivariable analysis, time to chemotherapy from definitive surgery was analyzed as a continuous variable.

Statistical Analysis

Descriptive analyses were conducted with time to treatment as a categorical variable. For the time to event analysis, we first assessed the association of other variables with the continuous time to chemotherapy variable in univariate Cox regression. On the basis of variables with $P < .20$, we then constructed a multivariable Cox proportional hazards model to assess the impact of type of definitive surgery on chemotherapy administration, controlling for other factors. In the results of this analysis, a hazard ratio (HR) >1 for a particular group indicates that chemotherapy was initiated earlier in that group compared with the reference category group, whereas a HR <1 indicates that treatment was delayed compared with the reference category. The final multivariable model included only those terms significant at $P < .05$, including significant interactions terms. All analyses were conducted using SAS V9.1.3 software (Cary, NC). All modeling reports 95% confidence intervals (CI) and 2-sided *P*-values. The assumption of the proportional hazards was tested and met.

RESULTS

Table 1 displays the study sample characteristics by receipt of chemotherapy grouped as: early (<8 weeks), late (≥8 weeks), or no chemotherapy. The majority of patients (59.2%) had BCS, 21.7% had mastectomy only, 16.4% had M + IR, and 2.7% had M + DR. Of the 696 patients who had mastectomy with either immediate or delayed reconstruction, 49.7% had an implant, 22.1% had a free TRAM flap, and 18.5% had a pedicle TRAM flap. Of the 3643 breast cancer patients for whom NCCN guidelines recommended adjuvant chemotherapy, 67.4% received it early (within 8 weeks), 5.1% received it late (≥8 weeks), and 27.5% did not receive adjuvant chemotherapy at any time point. Overall, 98% of patients who received chemotherapy started the treatment within 12 weeks postoperatively.

In a logistic model controlling for age, stage, race and ethnicity, income, comorbidity, BMI, NCCN institution, and NCCN guideline, there was no effect of surgery type on use of adjuvant chemotherapy ($P = .33$). On the basis of an a priori hypothesis that the effect might differ by patient age, we also did an analysis to assess for an interaction between age and surgery type and found no association.

As shown in Figure 1, the relationship between surgery type and time to initiation of adjuvant chemotherapy varied by patient age. For patients younger than 50, the proportion of patients initiating chemotherapy within 8 weeks was lower for M + IR than for any of the other treatment approaches. In contrast, among patients over age 60, patients who opted for mastectomy with either immediate or delayed reconstruction were more likely to receive chemotherapy within 8 weeks.

Because of the marked difference in the relationship between surgery type and chemotherapy by patient age, the results of univariate analyses are difficult to interpret. Therefore, in Table 2, we present the multivariable results of the time to chemotherapy analysis, including interactions between age and surgery type. In this analysis, a hazard ratio >1 indicates that patients in that category were more likely to receive chemotherapy early than patients in the reference category. As shown in the table, higher stage, Caucasian and Hispanic race versus African American, lower BMI, and absence of comorbid conditions were all associated with earlier time to chemotherapy. The effect of surgery type depended on age. Controlling for all other factors, among women under age 60, time to chemotherapy was shorter for all surgery types compared with M + IR. These differences reached statistical significance for all surgery types in the youngest age group, and for BCS in women 40-<50 years of age. In contrast, among women 60 years old or older, time to chemotherapy was shorter among women receiving reconstruction (immediate or delayed) compared with those undergoing BCS or mastectomy alone, a difference that was statistically significant for the M_IR versus BCS comparison.

Figure 2 shows the time to treatment for the entire patient sample by surgery type among women younger than 60 years of age (Fig. 2A) and age 60 or older (Fig. 2B). Because of the similarity in the multivariable results across age strata younger than age 60, we aggregated those patients for this analysis. Among women younger than age 60, the median time to initiation of treatment was 5.29 weeks for BCS, 5.14 weeks for mastectomy alone, 4.86 weeks for M + DR, and 6.00 weeks for M + IR. Among women 60 and older, fewer than half the women who received BCS or mastectomy alone received chemotherapy, so there was no median time to treatment initiation for those groups. Median time to treatment for women who received M + DR was 7.14 weeks compared with 8.14 weeks among women treated with M + IR. Among the subset of patients who received chemotherapy, the median time to chemotherapy for those <60 years and ≥60 was as follows: 4.86 weeks and 5.43 weeks for BCS; 5.00 weeks and 5.86 weeks for mastectomy alone;

Table 1. Study Sample Characteristics (N=3643)[a]

	Time From Definitive Surgery to Chemotherapy					
	Early[b] (N=2454)		Late[c] (N=186)		No Chemotherapy (N=1003)	
	No.	(%)	No.	(%)	No.	(%)
Type of surgery						
Mastectomy with immediate reconstruction	446	(74.8)	53	(8.9)	97	(16.3)
Breast conserving surgery	1387	(64.4)	91	(4.2)	677	(31.4)
Mastectomy alone	534	(67.4)	39	(4.9)	219	(27.7)
Mastectomy with delayed reconstruction	87	(87.0)	3	(3.0)	10	(10.0)
Patient age at diagnosis, y						
<40	402	(89.7)	22	(4.9)	24	(5.4)
40-49	901	(83.3)	58	(5.4)	123	(11.4)
50-59	725	(74.4)	53	(5.4)	197	(20.2)
≥60	426	(37.4)	53	(4.7)	659	(57.9)
Stage at diagnosis						
Stage I	659	(49.1)	53	(3.9)	630	(46.9)
Stage II	1730	(77.9)	127	(5.7)	365	(16.4)
Stage III	65	(82.3)	6	(7.6)	8	(10.1)
Path tumor size						
≤2 cm	1348	(60.6)	103	(4.6)	773	(34.8)
>2-5 cm	981	(78.4)	72	(5.8)	198	(15.8)
>5 cm	84	(80.0)	7	(6.7)	14	(13.3)
Unknown/missing	41	(65.1)	4	(6.3)	18	(28.6)
No. of positive nodes						
0	1106	(57.4)	88	(4.6)	734	(38.1)
1-3	1019	(78.6)	70	(5.4)	208	(16.0)
4-9	226	(83.4)	21	(7.7)	24	(8.9)
10 or more	99	(86.1)	7	(6.1)	9	(7.8)
N/A	4	(12.5)	0	(0.0)	28	(87.5)
Race/ethnicity						
Caucasian	2052	(67.0)	155	(5.1)	854	(27.9)
Hispanic	138	(71.1)	13	(6.7)	43	(22.2)
African-American	176	(66.7)	13	(4.9)	75	(28.4)
Other	88	(71.0)	5	(4.0)	31	(25.0)
Median household income, quartiles						
Q1: $0-<$35,426	562	(63.9)	50	(5.7)	267	(30.4)
Q2: $35,426 to <$44,639	582	(66.2)	58	(6.6)	239	(27.2)
Q3: $44,639 to <$58,844	588	(66.9)	47	(5.3)	244	(27.8)
Q4: $58,844-$159,538	632	(71.8)	27	(3.1)	221	(25.1)
Foreigner	26	(81.3)	2	(6.3)	4	(12.5)
Unknown	64	(68.1)	2	(2.1)	28	(29.8)
Comorbidity score						
0	2091	(71.1)	148	(5.0)	701	(23.8)
1	265	(54.9)	28	(5.8)	190	(39.3)
≥2	98	(44.5)	10	(4.5)	112	(50.9)
Body mass index						
<25 kg/m^2	1050	(72.6)	49	(3.4)	348	(24.0)
25-35 kg/m^2	1036	(64.4)	90	(5.6)	483	(30.0)
>35 kg/m^2	252	(63.2)	36	(9.0)	111	(27.8)
Unknown	116	(61.7)	11	(5.9)	61	(32.4)
Type of reconstruction						
No reconstruction	1921	(65.2)	130	(4.4)	896	(30.4)
Implant	264	(76.3)	20	(5.8)	62	(17.9)
Pedicle TRAM flap	105	(81.4)	17	(13.2)	7	(5.4)
Free TRAM flap	115	(74.7)	12	(7.8)	27	(17.5)
Other rotational flap	37	(72.5)	5	(9.8)	9	(17.6)
Other free flap	12	(75.0)	2	(12.5)	2	(12.5)

(Continued)

Table 1. (Continued)

	Time From Definitive Surgery to Chemotherapy					
	Early[b] (N=2454)		Late[c] (N=186)		No Chemotherapy (N=1003)	
	No.	(%)	No.	(%)	No.	(%)
Institution						
A	111	(66.5)	11	(6.6)	45	(26.9)
B	443	(73.2)	24	(4.0)	138	(22.8)
C	259	(65.6)	40	(10.1)	96	(24.3)
D	415	(62.5)	30	(4.5)	219	(33.0)
E	263	(63.2)	18	(4.3)	135	(32.5)
F	168	(76.7)	3	(1.4)	48	(21.9)
G	386	(70.1)	32	(5.8)	133	(24.1)
H	409	(65.3)	28	(4.5)	189	(30.2)
Guideline						
Stage I/II node-negative, tubular/colloid, tumor size ≥3 cm	3	(33.3)	0	(0.0)	6	(66.7)
Stage I/II node-negative, HR-negative, tumor size >1 cm	427	(78.3)	38	(7.0)	80	(14.7)
Stage I/II node-negative, HR-positive, tumor size >1-3 cm	602	(46.7)	41	(3.2)	645	(50.1)
Stage I/II node-negative, HR-positive, tumor size gt;3 cm	78	(67.2)	9	(7.8)	29	(25.0)
Stage I/II node-positive, HR-negative	335	(85.7)	28	(7.2)	28	(7.2)
Stage I/II node-positive, HR-positive	944	(77.7)	64	(5.3)	207	(17.0)
Stage IIIA with T3N1	65	(82.3)	6	(7.6)	8	(10.1)

[a]Newly diagnosed stages I, II, and III breast cancer patients who presented at National Comprehensive Cancer Network (NCCN) institution from July 30, 1997 to December 31, 2003, received definitive surgery, and were recommended to receive adjuvant chemotherapy based on NCCN guidelines (v. 1997 – v. 2003).
[b]Early delivery of chemotherapy is receipt less than 8 weeks from definitive surgery.
[c]Late delivery of chemotherapy is receipt 8 weeks or more from definitive surgery.

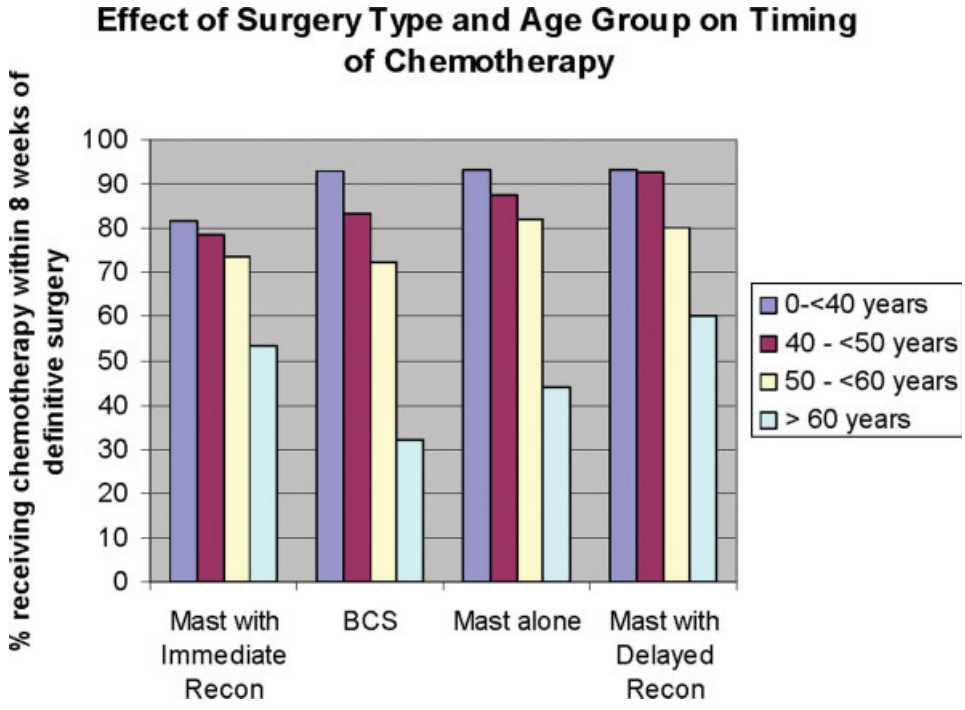

Figure 1. Proportion of patients who received chemotherapy within 8 weeks of definitive surgery, by patient age and type of surgery is depicted.

Table 2. Multivariate Results of Patient and Clinical Factors Significantly Associated With the Timing of Postoperative Adjuvant Chemotherapy (N = 3643)

	HR	95% CI	P
Main Effects Terms			
Stage at diagnosis			<.0001
Stage I	Ref		
Stage II	1.76	1.55-2.01	
Stage III	1.98	1.50-2.63	
Race/Ethnicity			.0347
Caucasian	Ref		
Hispanic	1.02 0	85-1.21	
African-American	0.80	0.68-0.93	
Other	0.98	0.79-1.21	
Median household income (quartiles)		0.0110	
Q1: $0 to <$35,426		Ref	
Q2: $35,426 to <$44,639	1.03	0.92-1.15	
Q3: $44,639 to <$58,844	1.03	0.91-1.16	
Q4: $58,844 to $159,538	1.11	0.98-1.25	
Foreigner	2.02	1.36-3.01	
Unknown	1.15	0.88-1.48	
Comorbidity score			<.0001
0	Ref		
1	0.94	0.83-1.06	
>2 0.	59 0	48-0.72	
Body mass index			.0119
<25 kg/m^2	Ref		
25-35 kg/m^2	0.90	0.83-0.98	
>35 kg/m^2	0.83	0.72-0.94	
Unknown	0.85	0.71-1.04	
NCCN institution			<.0001
E	Ref		
A	0.95	0.76-1.19	
B	1.10	0.94-1.29	
C	0.95	0.80-1.13	
D	1.01	0.86-1.17	
F	1.10	0.94-1.28	
G	1.18	1.01-1.38	
H	1.79	1.46-2.19	
Guideline			<.0001
Stage I/II node-positive, HR-positive	Ref		
Stage I/II node-negative, tubular/colloid, tumor size ≥3 cm	0.34	0.11-1.06	
Stage I/II node-negative, HR-negative, tumor size >1 cm	1.20	1.05-1.36	
Stage I/II node-negative, HR-positive, tumor size >1-3 cm	0.64	0.56-0.74	
Stage I/II node-negative, HR-positive, tumor size >3 cm	0.76	0.61-0.95	
Stage I/II node-positive, HR-negative	1.18	1.04-1.33	
Stage IIIA with T3N1	LC[a]	LC[a]	
Interaction Terms			
Type of definitive surgery by age at diagnosis			.0009
0 to <40 years of age			
Mastectomy with immediate reconstruction	Ref		
Breast-conserving surgery	1.79	1.43-2.25	
Mastectomy alone	1.53	1.13-2.06	
Mastectomy with delayed reconstruction	2.27	1.49-3.46	
40 to <50 years of age			
Mastectomy with immediate reconstruction	Ref		
Breast-conserving surgery	1.38	1.18-1.63	
Mastectomy alone	1.18	0.96-1.45	
Mastectomy with delayed reconstruction	1.38	0.98-1.96	

(Continued)

Table 2. (Continued)

	HR	95% CI	*P*
50 to <60 years of age			
Mastectomy with immediate reconstruction	Ref		
Breast-conserving surgery	1.18	0.96-1.44	
Mastectomy alone	1.22	0.96-1.55	
Mastectomy with delayed reconstruction	1.44	0.88-2.34	
>60 years of age			
Mastectomy with immediate reconstruction	Ref		
Breast-conserving surgery	0.70	0.50-0.97	
Mastectomy alone	0.79	0.56-1.11	
Mastectomy with delayed reconstruction	1.50	0.64-3.54	

HR indicates hazard ratio; CI, confidence interval.
An HR >1 for a particular group indicates that chemotherapy was initiated earlier in that group compared with the reference category group, whereas an HR <1 indicates that treatment was delayed compared with the reference category.
[a]Linear combination of stage III did not fit in the multivariate model.

5.57 weeks and 5.93 weeks for M + IR; and 4.79 weeks and 5.79 weeks for M + DR, respectively.

DISCUSSION

In this large, multicenter cohort of breast cancer patients, we found that immediate reconstruction did not increase the chance that adjuvant chemotherapy would be omitted in women likely to benefit from it. Immediate reconstruction was associated with an increase in the time to chemotherapy initiation compared with all other treatment strategies among women younger than age 60, but the magnitude of the delay was quite modest. Among women younger than age 60, median time to chemotherapy after mastectomy with immediate reconstruction was 6.00 weeks compared with 5.29 weeks after BCS. In contrast, among women 60 years old or older, time to chemotherapy was shorter among women receiving reconstruction (immediate or delayed) compared with those undergoing BCS or mastectomy alone.

It is highly unlikely that a 1-week delay in the initiation of adjuvant chemotherapy that is otherwise administered within proven time frames impacts long-term survival. In all clinical trials demonstrating effectiveness of chemotherapy, treatment started within 8 weeks of the last surgery. There are no data to show improved outcomes when chemotherapy is initiated within shorter times. The Danish Breast Cancer Cooperative group and the British Columbia Cancer Agency have found no difference in survival between patients given chemotherapy early, such as 3 weeks, compared with those that received treatment up to 12 weeks postoperatively.[10,24] At the extreme of starting chemotherapy before surgery (neoadjuvant), available data show no advantage of this early therapy compared with postoperative therapy started within 8 weeks of surgery. However, delays older than 3 months have been associated with diminished relapse-free survival and overall survival.[10] In our series, 98% of breast cancer patients who received chemotherapy started the treatment within 12 weeks postoperatively across all medical centers and all surgical treatments.

Previous studies have not found immediate postmastectomy breast reconstruction to delay the delivery of adjuvant chemotherapy.[14-21] However, these studies have been limited by retrospective designs and small, single-center patient cohorts. More important, these studies defined their patient cohorts as those who received chemotherapy rather than whether chemotherapy was indicated. It is important to evaluate omission of treatment, along with delays in administration. By defining our study population by whether chemotherapy was indicated, rather than received, we were able to show that immediate breast reconstruction is not associated with any significant omission in chemotherapy treatment.

The esthetic, psychological and financial benefits of immediate breast reconstruction are clear. However, support for this approach among clinicians caring for women with breast cancer could depend on their perceptions about whether it compromises optimal chemotherapy and, thus, survival.[25] A recent survey of medical oncologists found that nearly 40% are concerned that immediate postmastectomy breast reconstruction interferes with adjuvant oncologic therapy.[26] Our results suggest that this concern is unwarranted regarding chemotherapy. Recommendations regarding immediate breast reconstruction may also be influenced by the likelihood that the patient

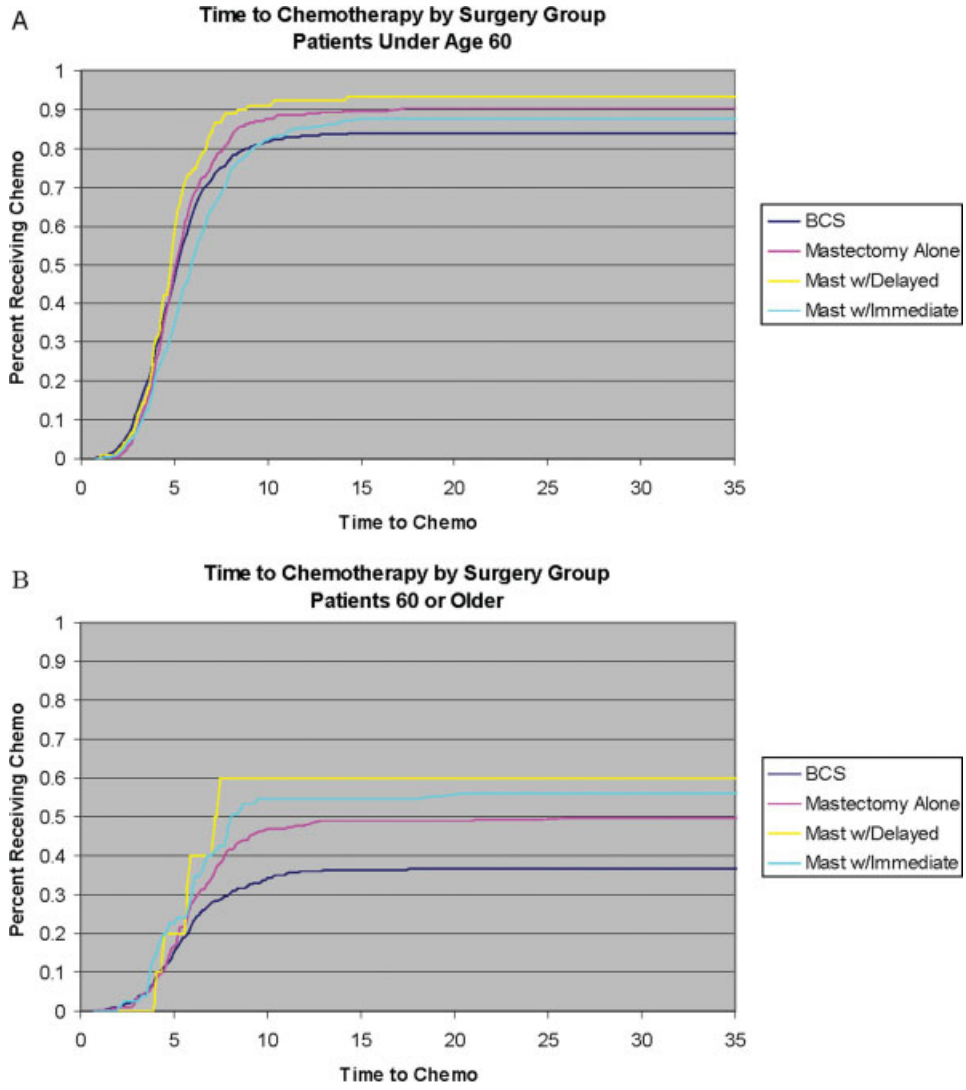

Figure 2. Time to chemotherapy percentages by surgery group for patients (A) younger than age 60 years and (B) age 60 years or older are depicted. The sample population for ages <60 years included 1454 breast-conserving surgery (BCS), 440 with mastectomy alone, 521 with mastectomy and immediate reconstruction, and 90 with mastectomy and delayed reconstruction. The sample population for ages >60 years included 701 BCSs, 352 with mastectomy alone, 75 with mastectomy and immediate reconstruction, and 10 with mastectomy and delayed reconstruction.

will also need adjuvant postmastectomy chest wall and nodal radiation. Radiation improves survival in certain subsets of women with positive nodes.[27] Reconstruction may affect the technical delivery of radiation,[28] and radiation may adversely affect the cosmetic result of reconstruction.[29] Although there is no uniform consensus, this concern leads some oncologists to recommend delayed reconstruction in women who are likely to receive radiation. The NCCN guidelines state that delayed reconstruction is preferred in this situation (a category 2B recommendation). This may account for the documented lower use of immediate breast reconstruction in NCCN centers in those women with more advanced cancer stage and larger tumors.[30]

We found an interesting interaction between patient age, type of surgical treatment, and delivery of chemotherapy. Our results are consistent with other studies showing that older patients are less likely to receive chemotherapy and also less likely to receive immediate breast reconstruction.[31] However, our data suggest that older women who undergo immediate breast reconstruction may be more likely to receive adjuvant chemotherapy. These results did

not reach statistical significance in multivariable modeling, perhaps because of small sample size. But if confirmed in larger studies, this would suggest that immediate breast reconstruction in those $\geq$60 years of age could be a marker for a more aggressive treatment philosophy by that patient, or overall more vigorous health as perceived by their providers. Our results offer additional support of the safety of breast reconstruction in well-selected older women.[13]

We found that in addition to age, other clinical and sociodemographic characteristics place patients at increased risk for delayed chemotherapy. From a clinical standpoint, postsurgical wounds and infections often are the primary reasons delaying chemotherapy. There has been well-established evidence linking patient obesity with postoperative complications.[13,32] Our data show a significant association between obesity and high comorbidity score with delayed chemotherapy delivery. Quality efforts should be aimed at improving patient selection for elective breast reconstructive surgery. Surgeons should be encouraged to delay breast reconstruction in these high risk populations, in particular, those with a BMI $>$35 kg/m^2 and a comorbidity score $\geq$2.

Patient race was also a significant predictor of delayed chemotherapy in our study. The reasons may be multifactorial. Compared with Caucasian women, African Americans experience the greatest delay in breast cancer diagnosis,[33] present with more aggressive disease,[34] have limited knowledge regarding their reconstructive options[35] and are significantly less likely to receive reconstruction at the time of the mastectomy.[7,8] We carefully controlled for clinical characteristics in our analysis by including not only stage, but also NCCN guideline, a more granular measure of factors relevant to clinical decision making, and used a standardized measure of comorbidity. Therefore, nonclinical factors may also be playing a role. A prior analysis of NCCN data found no effect of race on reconstruction after mastectomy,[36] suggesting that the factors that influence time to chemotherapy may differ from those that influence treatment choice.

Limitations

Ours is an observational study and not a controlled randomized trial, so we cannot rule out unaccounted for factors that could be associated with both treatment choice and timing of chemotherapy delivery. More important, our outcomes reflect the experience of high volume cancer centers and may not reflect practices in the community setting. Our database captures only information on margins from the definitive pathology report, so we cannot report on the frequency with which margins were thought to be negative intraoperatively but were reported as positive after definitive review. Although this is a theoretical disadvantage of immediate reconstruction, it would not be expected to increase the time to initiation of chemotherapy. We also do not have information on surgical complications, so we cannot comment on how those factors affected treatment timing. Last, we have not yet followed these patients long enough to assess the impact of delays in chemotherapy on long-term survival or recurrence.

Clinical Implications

Immediate postmastectomy breast reconstruction does not appear to lead to omission of adjuvant chemotherapy, but it is associated with a very modest, but statistically significant, delay in initiating treatment. For the typical patient, it is unlikely that this delay has any clinical significance. However, for patients who are at higher risk of delay on the basis of sociodemographic and clinical characteristics, the additional delay associated with immediate reconstruction should be considered. These higher risk groups would include patients with lower stage disease, morbid obesity, or serious comorbid conditions, as well as African Americans. Future efforts should be aimed at educating healthcare providers about these vulnerable populations and implementing strategies to either delay reconstruction in these groups or to facilitate the processes of care through 1) improved communication between physicians through multidisciplinary cancer clinics and 2) aggressive treatment of postoperative complications to expedite recovery.

CONFLICT OF INTEREST DISCLOSURES

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