Optimizing breast reconstructive surgery in the Netherlands using clinical audit data

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CHAPTER 4

Large hospital variation in immediate breast reconstruction rates after mastectomy for breast cancer in the Netherlands

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ABSTRACT

Background: The present study aimed to describe the use of immediate breast reconstruction (IBR) after mastectomy for invasive breast cancer and ductal carcinoma in situ (DCIS) in hospitals in the Netherlands and determine whether patient and tumor factors account for the variation.

Methods: Patients undergoing mastectomy for primary invasive breast cancer or DCIS diagnosed between January 1, 2011 and December 31, 2013 were selected from the NABON Breast Cancer Audit. All the 92 hospitals in the Netherlands were included. The use of IBR in all hospitals was compared using unadjusted and adjusted analyses. Patient and tumor factors were evaluated by univariate and multivariate analyses.

Results: In total, 16,953 patients underwent mastectomy: 15,072 for invasive breast cancer and 1,881 for DCIS. Unadjusted analyses revealed considerable variation between hospitals in postmastectomy IBR rates for invasive breast cancer (mean 17%; range 0–64%) and DCIS (mean 42%; range 0–83%). For DCIS, younger age and multifocal disease were factors that significantly increased IBR rates. For patients diagnosed with invasive breast cancer, IBR was more often used in younger patients, multifocal tumors, smaller tumors, tumors with a lower grade, absence of lymph node involvement, ductal carcinomas, or hormone-receptor positive/HER2-positive tumors. After case-mix adjustments for these factors, the variation in the use of IBR between hospitals remained large (0–43% for invasive breast cancer and 0–74% for DCIS).

Conclusions: A large variation between hospitals was found in postmastectomy IBR rates in the Netherlands for both invasive breast cancer and DCIS even after adjustment for patient and tumor factors.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer in women in the Netherlands. Curative surgical treatment for breast cancer consists of breast conserving therapy or mastectomy. Mastectomy is performed in approximately 40% of patients with invasive breast cancer[1,2] and in 33% of patients with ductal carcinoma in situ (DCIS).[3]

To restore the breast contour following mastectomy, a breast reconstruction can be performed. Breast reconstruction during initial breast cancer surgery is known as immediate breast reconstruction (IBR); delayed breast reconstruction is reconstruction at a later time.[4] Reasons to offer patients IBR are of both esthetic and psychosocial nature. IBR generally leads to higher patient satisfaction, improved body image, and increased self-esteem compared to delayed reconstruction.[5] Therefore, guidelines suggest considering IBR in all patients who undergo mastectomy.[6,7] However, the percentage of patients actually undergoing IBR or delayed reconstruction after mastectomy is generally low and varies significantly from 5% to 30% in population-based studies.[8] Several factors such as patient factors, tumor-related factors, hospital factors, and demographic factors may contribute to the final decision to perform IBR.[8]

Current practice patterns of postmastectomy IBR in the Netherlands are unknown. Evaluating hospital performances using case-mix-adjusted data can identify true variation between hospitals and ultimately help to reduce undesirable variation in clinical practice and improve the quality of care for breast cancer patients. Therefore, the present study aimed to investigate the variation in the use of IBR after mastectomy for invasive breast cancer and DCIS between all hospitals in the Netherlands and identify whether the variation could be attributed to patient and tumor factors influencing the use of IBR.

MATERIALS AND METHODS

Data source

Data were derived from the NABON (National Breast Cancer Consultation Netherlands) Breast Cancer Audit (NBCA),[9] a continuous national multidisciplinary quality improvement project in which a wide range of variables concerning patient, diagnostics, and treatments are prospectively collected by the hospitals themselves or the Netherlands Cancer Registry. The NBCA contains data registered in all 92 hospitals performing breast cancer surgery in the Netherlands.[10] The information concerning individual patients and hospitals is de-identified for this study, allowing comparisons without identification.

Study population

Data from all female patients who underwent a mastectomy for either primary DCIS or nonmetastatic invasive breast cancer diagnosed between January 1, 2011 and December 31, 2013 were selected. Information available in the NBCA on patient characteristics (age) and tumor characteristics (TNM classification, histological subtype, grade, and receptor status) were extracted. Four types of IBR were defined: implant breast reconstruction (including tissue expander), autologous breast reconstruction, a combination of both, and reconstruction not otherwise specified.

Statistical analyses

Invasive breast cancer and DCIS patients were analyzed separately. Differences in the use of IBR between hospitals were compared using a funnel plot. Patient and tumor- specific factors potentially affecting the use of IBR were compared between women with and without IBR. Subsequently, to investigate which factors were related to the use of IBR, univariate regression analyses were performed. Next, factors with p-values of <0.10 were included into multivariate regression analyses using an enter model. These multivariate regression analyses were used to identify independent factors determining the use of IBR, corrected for the other factors that were included into the model.

A second analysis was performed to identify variation in the use of IBR between hospitals using the adjusted data based on observed/expected calculations (i.e., case-mix adjustment for predicting factors of IBR). All statistical analyses were performed using SPSS (SPSS for MAC Version 20.0; SPSS Inc., Chicago, IL).

RESULTS

Patient characteristics

In total, 16,953 patients underwent a mastectomy for invasive M0 breast cancer (n=15,072) or DCIS (n=1881) in one of the 92 hospitals in the Netherlands. Results are separately presented for invasive breast cancer and DCIS. Patient and tumor characteristics by reconstruction status are shown in **Table 1** for invasive breast cancer and **Table 2** for DCIS.

Table 1. Baseline characteristics of 15,072 invasive breast cancer patients treated with a mastectomy by reconstruction status between 2011 and 2013 in the Netherlands.

		Immediate reconstruction			
		No		Yes	
		n	%	n	%
Age	Below 50	2471	68%	1170	32%
	50 to 65	4222	79%	1153	22%
	65 or above	5836	97%	211	4%
Clinical tumor stadium	cTx / Unknown	752	72%	288	28%
	cT1	4596	79%	1248	21%
	cT2	5228	86%	864	14%
	cT3	1365	92%	125	8%
	cT4	595	98%	11	2%
Clinical lymph node stadium	cNx / Unknown	487	82%	108	18%
	cN0	8614	80%	2098	20%
	cN1	3141	91%	307	9%
	cN2	113	93%	9	7%
	cN3	181	93%	14	7%
Multifocal	No	9164	85%	1681	16%
	Yes	3372	80%	855	20%
Histology	Ductal	9444	82%	2025	18%
	Lobular	2027	88%	265	12%
	Combination	400	80%	103	21%
	Unknown	665	82%	143	18%
Grade	1	1944	79%	513	21%
	2	5445	84%	1065	16%
	3	3779	85%	685	15%
	Unknown	1368	83%	273	17%
Receptor groups	HR positive, Her2 negative	8140	84%	1608	17%
	HR positive, Her2 positive	1140	80%	294	21%
	HR negative, Her2 positive	682	84%	135	17%
	Triple negative	1455	83%	292	17%
	Unknown	1119	84%	207	16%

HR,Hormone Receptor.
Percentages are rounded off, which in some cases leads to a total of above 100%.

Table 2. Baseline characteristics of 1,881 patients with ductal carcinoma in situ treated with a mastectomy by reconstruction status between 2011 and 2013 in the Netherlands.

		Immediate reconstruction			
		No		Yes	
		n	%	n	%
Age	Below 50	128	33%	265	67%
	50 to 65	500	53%	452	48%
	65 or above	466	87%	69	13%
Multifocal	No	942	60%	627	40%
	Yes	153	49%	159	51%
Grade	1	93	54%	80	46%
	2	354	57%	271	43%
	3	596	60%	398	40%
	Unknown	52	58%	37	42%

Percentages are rounded off, which in some cases leads to a total of above 100%.

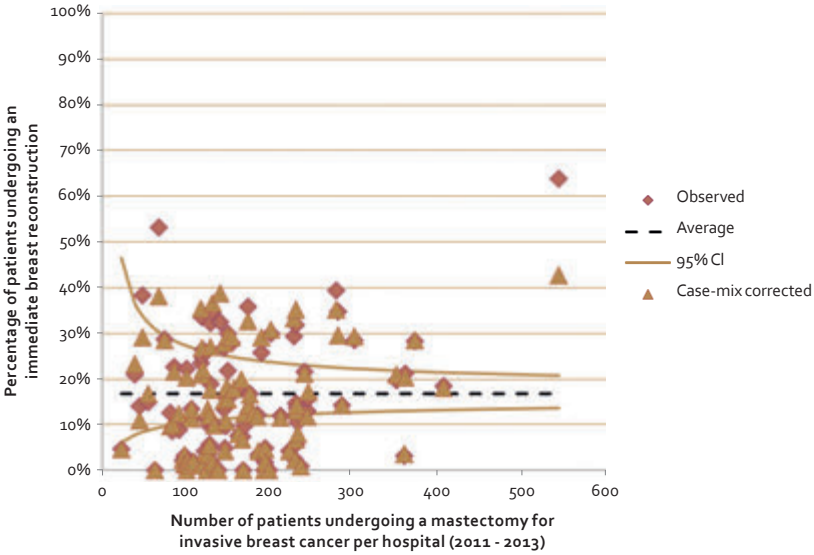
Invasive breast cancer

Variation in use of immediate breast reconstruction

On average, 16.8% (n=2536) of all patients with a mastectomy for invasive breast cancer underwent IBR. An increase in the mean use and range of IBR was seen over the years from 14.6% (range 0–54%) in 2011 to 19.3% (range 0–74%) in 2013. There was a decrease in the number of hospitals not performing IBR from 23 in 2011 to 11 in 2013. Unadjusted IBR rates for all hospitals combining 3 years together varied from 0% to 64% (**Figure 1**).

Immediate implant-based breast reconstructions were performed most frequently (89%). Immediate autologous reconstructions and a combination of autologous and implant reconstructions were both used in less than 5% of the patients who underwent IBR, and in 1.9% the reconstruction was not otherwise specified.

Figure 1. Funnel plot showing hospital differences in percentage of patient with invasive Mo breast cancer treated with mastectomy and immediate breast reconstruction, unadjusted (terra squares) and adjusted for age, clinical tumor stage, clinical nodal stage, multifocality, histology, grade and receptor status (ocher triangles) (2011 – 2013).



Predictive factors for immediate breast reconstruction

The percentage of patients receiving IBR significantly decreased with increasing age. Younger patients (<50 years) had more frequent IBR [Odds Ratio (OR) 1.73; 95% Confidence Interval (95% CI) 1.58–1.91] compared to older patients (50–65 years). IBR was less often used in patients with larger tumors and patients with involved lymph nodes. Patients who were treated for a clinical T3 tumor had a three times lower chance of receiving IBR than those treated for a clinical T1 tumor (OR 0.34; 95% CI 0.28–0.41). For lymph node-positive tumors, a similar lower chance of receiving IBR was observed; a patient with a clinical N2 tumor had a three times lower chance of receiving IBR than those with lymph node-negative tumors (95% CI 0.17–0.65).

Patients with multifocal tumors had a higher chance of receiving IBR. Being diagnosed with a ductal carcinoma increased the chance of undergoing IBR compared to lobular carcinoma diagnosis. IBR was more frequently used in lower tumor grades. Hormone Receptor positive (HR+)/ HER2-positive tumors were associated with a

higher likelihood of IBR than the reference category of HR+/HER2-negative tumors (OR 1.31; 95% CI 1.14–1.50). Compared to the reference category, patients with triple-negative tumors had a similar chance of receiving IBR. All predictive factors (age, TNM classification, multifocality, histology, tumor grade, and receptor groups) remained statistically significant in multivariate analyses (**Table 3**).

Table 3. Univariate and multivariate analyses of factors determining the use of immediate breast reconstruction after mastectomy in 15,072 invasive breast cancer patients operated between 2011 and 2013 in the Netherlands.

			Univariate Analysis		Multivariate Analyses	
		n	OR	95% CI	OR	95% CI
Age	Below 50	1170	1.73	1.58 - 1.91	2.09	1.89 - 2.32
	50 to 65	1153	ref		ref	
	65 or above	211	0.13	0.11 - 0.15	0.13	0.11 - 0.15
Clinical tumor stadium	cTx / Unknown	288	1.41	1.22 - 1.64	1.24	1.05 - 1.47
	cT1	1248	ref		ref	
	cT2	864	0.61	0.55 - 0.67	0.68	0.61 - 0.76
	cT3	125	0.34	0.28 - 0.41	0.34	0.28 - 0.43
	cT4	11	0.07	0.04 - 0.12	0.10	0.06 - 0.19
Clinical lymph node stadium	cNx / Unknown	108	0.91	0.74 - 1.13	0.72	0.57 - 0.92
	cNo	2098	ref		ref	
	cN1	307	0.40	0.35 - 0.46	0.37	0.32 - 0.43
	cN2	9	0.33	0.17 - 0.65	0.36	0.18 - 0.72
	cN3	14	0.32	0.18 - 0.55	0.33	0.18 - 0.58
Multifocal	No	1681	ref		ref	
	Yes	855	1.38	1.26 - 1.51	1.14	1.03 - 1.26
Histology	Ductal	2025	ref			
	Lobular	265	0.61	0.53 - 0.70	0.71	0.61 - 0.83
	Combination	103	1.20	0.96 - 1.50	1.19	0.93 - 1.52
	Other	143	1.00	0.83 - 1.21	1.12	0.91 - 1.39
Grade	1	513	ref		ref	
	2	1065	0.74	0.66 - 0.83	0.84	0.73 - 0.96
	3	685	0.69	0.61 - 0.78	0.64	0.55 - 0.75
	Unknown	273	0.76	0.64 - 0.89	0.98	0.81 - 1.19
Receptor groups	HR positive, Her2 negative	1608	ref		ref	
	HR positive, Her2 positive	294	1.31	1.14 - 1.50	1.22	1.04 - 1.42
	HR negative, Her2 positive	135	1.00	0.83 - 1.21	1.06	0.85 - 1.31
	Triple negative	292	1.02	0.89 - 1.17	1.15	0.98 - 1.36
	Unknown	207	0.94	0.80 - 1.10	0.92	0.77 - 1.09

CI, Confidence interval; OR, Odds Ratio; HR, Hormone Receptor.

Effect of case-mix adjustment on variation in IBR rates between hospitals

After case-mix correction for tumor and patient factors (age, clinical tumor status, clinical nodal status, multifocality, histology, grade, and receptor status), a slightly narrower but statistically significant variation in the use of IBR between hospitals was observed, ranging from 0% to 43% (**Figure 1**), compared to the initially observed variation.

Ductal carcinoma in situ

Variation in use of immediate breast reconstruction

With an average rate of 42% (786/1881), IBR was more often performed after mastectomy for DCIS than for invasive breast cancer. Nineteen hospitals in 2011 and 17 hospitals in 2013 did not perform IBR for DCIS. IBR rates after mastectomy for DCIS varied largely between hospitals (range 0–83%). The use of IBR slightly increased in 3 years; 41% of the patients received IBR in 2011 (range 0–100%) compared to 45% in 2013 (range 0–83%) using unadjusted data. Most patients diagnosed with DCIS received an implant-based reconstruction (86.1%). Autologous reconstruction and a combination of autologous and implant reconstruction were both performed in 5% of the patients undergoing IBR. The type of reconstruction was unknown in 3.3% of the patients.

Predictive factors for immediate breast reconstruction

Factors potentially affecting the use of IBR following mastectomy for DCIS were age, multifocality, and DCIS grade. Older patients (≥65 years) had an OR of 0.16 compared to patients aged between 50 and 65 years. Patients with multifocal disease had a 1.56-fold higher chance of undergoing IBR than patients with unifocal tumors (95% CI 1.22–1.99). DCIS grade did not have a statistically significant relationship with receiving IBR, and therefore was not included in multivariate analyses. Patient age and multifocality remained statistically significant predictive factors in multivariate analyses. **Table 4** shows univariate and multivariate analyses of factors predicting the use of IBR after mastectomy for DCIS.

Effect of case-mix adjustment on variation in IBR rates between hospitals

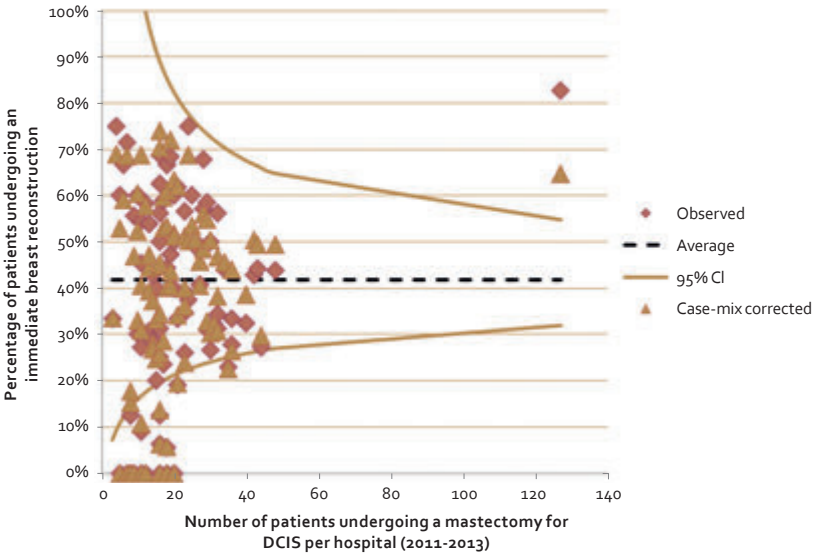
Case-mix adjustment of age and multifocality, enabling comparison between hospitals for IBR rates after mastectomy for DCIS, revealed a similar pattern as that of unadjusted data, with a variation between 0% and 74% (**Figure 2**).

Table 4. Univariate and multivariate analyses of factors determining the use of immediate breast reconstruction after mastectomy in 1,881 patients with ductal carcinoma in situ operated between 2011 and 2013 in the Netherlands.

			Univariate Analysis		Multivariate Analyses	
		n	OR	95% CI	OR	95% CI
Age	Below 50	265	2.29	1.79 - 2.93	2.29	1.79 - 2.94
	50 to 65	452	ref		ref	
	65 or above	69	0.16	0.12 - 0.22	0.17	0.13 - 0.22
Multifocal	No	627	ref		ref	
	Yes	159	1.56	1.22 - 1.99	1.40	1.07 - 1.82
Grade	1	80	ref		n.a.	
	2	271	0.89	0.64 - 1.25	n.a.	
	3	398	0.78	0.56 - 1.07	n.a.	
	Unknown	37	0.83	0.49 - 1.39	n.a.	

CI, Confidence interval; OR, Odds Ratio.

Figure 2. Funnel plot showing hospital differences in percentage of patient with ductal carcinoma in situ treated with mastectomy and immediate breast reconstruction, unadjusted (terra squares) and adjusted for age and multifocality (ocher triangles) (2011 – 2013).



DISCUSSION

This is the first nation-wide study investigating the variation in the use of IBR after mastectomy for invasive breast cancer and DCIS between hospitals in the Netherlands. A large variation was found; IBR was performed on average in 17% of patients with invasive breast cancer (range 0–64%) and in 42% of patients with DCIS (range 0–83%). Although various patient and tumor characteristics were found to have a significant effect, adjustment for these factors using multivariate analyses did not result in less variation between hospitals. Apparently, there are other yet unidentified factors, such as patient preferences, surgeons' beliefs, or hospital organizational factors, which probably affect the use of IBR to a larger extent.

Previous studies have reported on breast reconstruction rates after mastectomy[1,8,11]; however, the results of these studies cannot be compared with our results because immediate and delayed breast reconstructions and invasive breast cancer and DCIS were combined in other studies. Some studies reported mean postmastectomy IBR rates of 21% in the United Kingdom[1] and 24% in the United States[11] when combining invasive breast cancer and DCIS. In our study, we decided to analyze DCIS and invasive breast cancer separately because certain factors such as hormone receptor status are only available and relevant for patients diagnosed with invasive breast cancer. Moreover, the IBR rate for patients with DCIS was more than two-fold higher than that for patients with invasive breast cancer, which is consistent with literature.[2] Furthermore, previous studies often combined immediate and delayed breast reconstruction. A large meta-analysis (n=159,305 cases, 28 studies) showed an average of 16.9% of patients receiving immediate or delayed breast reconstruction. Comparison of the 10 largest population-based studies with a total of 10,000 mastectomy cases resulted in breast reconstruction rates (immediate and delayed) varying between 4.9% and 30.3%.[8] Combining immediate and delayed reconstruction for analysis is not preferred in our opinion because treatment approaches and patient populations may be different. Most importantly, the exact numerator to calculate the delayed breast reconstruction rate in a given time period is unknown because a delayed reconstruction may be performed many years after the initial surgery.

In the present study, we investigated the possible effect of patient and tumor characteristics on the use of IBR. In accordance with other studies, we found that a younger age was significantly related with higher IBR rates.[2,8,12,13] This finding may be explained by both clinician beliefs and patient preferences. Younger patients may be more aware of and more interested in the possibility of IBR, and they may be more assertive to discuss reconstructive options. Clinicians in turn may consider younger patients to be more eligible to undergo a reconstruction. In addition, older patients are more likely to have significant comorbidities leading to the decision to not perform IBR, may more easily accept the loss of their breast(s), or may not want to undergo major surgery.

Patients with an early-stage tumor had a higher likelihood of receiving IBR, which was also consistent with literature.[2,8] Locoregionally advanced tumors require adjuvant therapies such as radiotherapy and chemotherapy more often, even after a mastectomy. Patients with an indication for adjuvant therapies, particularly radiotherapy, have a lower chance of being treated with IBR.[14] There is still much debate on the timing and type of reconstruction in case radiotherapy is needed.[15–17] Particularly in implant-based reconstructions, radiotherapy leads to a significantly higher reconstruction failure rate compared to patients without radiotherapy.[18] In cases where patients require radiotherapy, clinicians may decide not to perform IBR as most reconstructions are implant based. It is recommended to perform an autologous flap technique when radiotherapy is required because radiotherapy-related complications of the autologous flap are less frequent and less severe.[15] In case of adjuvant chemotherapy, it is not the fear of increased chance of IBR complications but the delay IBR may cause to initiate adjuvant chemotherapy. However, a recent review found that IBR does not necessarily delay the start of adjuvant chemotherapy to a clinically relevant extent.[19]

The presence of a multifocal cancer was associated with a higher rate of postmastectomy IBR. Although multifocality may explain the propensity to prefer ablative surgery in these patients because of the size of the involved breast area, the size of the individual lesions will rarely be a reason to abstain from IBR. The observation that IBR was more frequent in patients treated for DCIS than those

treated for invasive breast cancer supports this explanation because DCIS usually involves a larger area of the breast than invasive breast cancer. Similar findings were found in the study by Roder et al.[2]

The uptake and variation of IBR can be only partly explained by the identified patient and tumor factors, suggesting that other factors contributed to the variation to a larger extent. Patient preferences may vary between institutions or regions. For example, the reported percentages of patients deciding not to undergo IBR varied between 17% and 62% in different regions of the United Kingdom.[1] An even more important role could be attributed to the personal perception, preferences, and beliefs of physicians considering patients eligible for IBR.[6,7,13,20]

Hospital-related factors such as location in an urban environment or being a teaching hospital, high-volume breast cancer center, private hospital, or hospital with a plastic surgical department may all affect the rate of IBR.[8,14,21] Other organizational factors such as the length of the operation and availability of a plastic surgeon in the hospital may further challenge the frequency of IBR. Further research should focus on identifying these additional factors that may have contributed to the large variation found.

A strength of the present study is that a national audit with 100% participation of all hospitals in the Netherlands provides a unique insight into the quality of breast cancer care delivered and the areas for improvement. An audit includes patients who are usually not included in clinical trials and reflects practice patterns in daily practice. Moreover, the availability of data at a hospital level enables nationwide hospital comparisons. A limitation of the present study is in the nature of a national audit itself. Registration bias may be present as the data were collected for a national audit. However, high rate of case ascertainment was found when the data was compared with that in the National Cancer Registry. Second, although many case-mix variables were available, there may have been unknown confounding variables that were not available in the data set and may have influenced variation in IBR between hospitals.

CONCLUSION

In conclusion, we found large variation between hospitals in IBR after mastectomy for invasive breast cancer and DCIS. Several factors (e.g., age, tumor status, grade, and receptor status) could be identified as predictive factors but did not exclusively explain the variation between hospitals. Further research is needed to investigate other causes such as patient and surgeon's preferences and hospital-related factors and to increase the percentage of IBR in all eligible patients.

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