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Consensus Statement

Socioeconomic status significantly contributes to the likelihood of immediate postmastectomy breast reconstruction in the Netherlands: A nationwide study

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ABSTRACT

Background: Previous studies have shown that breast cancer patients with a low socioeconomic status (SES) are less likely to undergo postmastectomy immediate breast reconstruction (IBR). However, these studies were performed in countries with unequal access to healthcare. Therefore, the aim of this study was to investigate whether SES also contributes to the likelihood of receiving IBR in a country with equal access to healthcare.

Materials and methods: Patients with stage I or II breast cancer diagnosed between 2011 and 2018 who underwent mastectomy were selected from the Netherlands Cancer Registry. SES was calculated from the average incomes of each postal code which were divided into 10-deciles. Primary outcome was the effect of SES on the likelihood of receiving IBR, controlled for patient, tumour and hospital characteristics expressed as Odds Ratio (OR) with 95% confidence interval (CI).

Results: Higher SES significantly increased the probability of undergoing postmastectomy IBR (OR 1.05 per 10% SES stratum), just as larger hospital volume (average volume OR 1.89 and large volume 2.58), oestrogen positive tumours (OR 1.19) and neo-adjuvant therapy (OR 1.42). In contrast, factors significantly reducing the likelihood of receiving IBR were older age (OR 0.92 per year), stage II (OR 0.61 compared to stage I) and adjuvant therapy (OR 0.56).

Conclusion: Women with lower SES undergoing mastectomy were less likely to receive postmastectomy IBR. More research is warranted to study whether lifestyle factors associated with lower SES such as smoking and higher BMI, language barrier, illiteracy and less access to internet explain these differences.

Introduction

Breast cancer is the most common cancer in women and the second most common cause of death due to cancer in women worldwide [1]. There are approximately 17.000 new cases of breast cancer in the Netherlands every year and over 3.000 women of the Dutch population annually die due to breast cancer [2,3].

Approximately 40% of patients with invasive breast cancer and 30% of patients with ductal carcinoma in situ (DCIS) undergo mastectomy in the Netherlands [4]. To restore the breast contour, breast reconstruction may be performed either at the time of initial breast cancer surgery (immediate breast reconstruction, IBR) or as a delayed procedure some time later. IBR has positive effects on body image and psychosocial well-being and current guidelines recommend to offer the possibility of IBR to every patient with an indication for mastectomy [5]. Nonetheless, a rather low mean IBR rate of 18% in patients undergoing mastectomy for invasive breast cancer was observed in The Netherlands with a substantial

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variation between Dutch hospitals [6]. In previous studies, case-mix variation [6], hospital organizational factors [7], attitudes of clinicians towards IBR also taking risk factors for complications after IBR such as smoking and body mass index (BMI) into account [8], and information provision about IBR were identified as possible causes of this hospital variation [9].

Previous studies from Denmark and the USA have found that women with lower socioeconomic status (SES) are less likely to undergo IBR after mastectomy [10,11]. However, the Danish study is over 20 years old and in the USA there is no universal healthcare system, which means the insurance and financial reimbursement system of the USA leads to unequal insurance coverage of patients, related to their income and SES, which in turn heavily influences therapeutic choices [12–15].

SES is a multi-layered system to stratify economic and social factors such as income, prestige and social status [16]. SES has been shown to be of influence in a wide array of diseases. For example, low SES has been associated with higher rates of diabetes, cardiovascular disease and many types of cancer in the western world and also psychiatric disorders are more often seen in patients with low SES [17–20]. Moreover, high-risk behaviour (such as drugs, tobacco and alcohol abuse, high BMI) occurs more often in people with low SES and therefore contributes to an increased risk of the aforementioned diseases [21]. Since SES plays an important role in the previously mentioned points, it is important to determine whether SES also relates to medical decisions such as the choice of IBR in countries with equal access to healthcare. Therefore, the aim of this study was to investigate whether SES contributes to the likelihood of receiving postmastectomy IBR in patients with stage I or II breast cancer in a country with equal access to healthcare, controlled for other patient, tumour and hospital characteristics which have been shown to affect the use of IBR.

Materials and methods

Study design and population

In this nationwide population-based study, we selected breast cancer patients of the Netherlands Cancer Registry (NKR). The present study focused on primary stage I and II breast cancer patients who had undergone a mastectomy between January 1st, 2011 and December 31st, 2018. Only patients diagnosed with breast cancer for the first time were included in this study. If patients developed contralateral breast cancer, only the first diagnosis was included in this study.

Definitions

The NKR contains patient-, tumour- and treatment characteristics. Tumours are categorized according to the tumour, node and metastasis (TNM) classification system [22]. Due to changes in the N1 category from the 5th to the 6th editions of the International Classification of Diseases for Oncology, we classified the number of positive lymph into N categories. Patients without lymph node involvement were classified as N0 and patients with 1–3 positive lymph nodes were classified as N1. TNM was converted to tumour stage (stage I or stage II). Histological subtype consisted in lobular, ductal, mucinous, medullary tubular, not specified or no special type [23]. Tumour grade was divided into low, intermediate and high grade cancers [24].

Only the use of IBR was registered and for the analyses the different types of breast reconstruction (implant-based with or without ADM/mesh, latissimus dorsi with implant, autologous) were also grouped together. In addition, the hospital where patients had received surgery was also recorded since some hospitals may favour IBR while other hospitals may not. Therefore, we stratified hospitals based on breast cancer patients operated per year; low (<100), medium (100–149) and high volume (>150), as described in previous studies [9]. Furthermore, radiotherapy, hormone therapy, immune therapy and chemotherapy were grouped into adjuvant or neo-adjuvant therapy.

SES was determined using the average income of a household according to the four-digit postal code in the Netherlands at time of diagnosis and surgical procedure, and was defined according to the Dutch Bureau of Statistics (CBS) [25]. Furthermore, the average incomes of each postal code were divided into 10-deciles.

Outcomes

Primary outcome was the effect of SES on the likelihood of receiving IBR after mastectomy. The primary outcome was controlled for other patient, tumour and hospital characteristics which have been shown to affect the use of IBR expressed as Odds Ratio (OR).

Statistics

Descriptive statistics were used to describe patient, tumour and treatment characteristics. Continuous data are described with mean along with standard deviation (SD), or with median and interquartile range (IQR), depending on whether or not the data were normally distributed. Mann-Whitney-U tests or Student's t tests were used to test differences between groups of not normally and normally distributed continuous data, respectively. Differences between categorical data were analysed with Chi-Square or Fisher's exact tests.

Since some data was missing during the study period, multiple imputation by chained equations (MICE) were performed using the *MICE* package in R. After comparing and correlating the missing to

Table 1
Baseline characteristics of all new onset breast cancer patients diagnosed in the Netherlands between 2011 and 2018 who underwent mastectomy (N = 32,559 patients).

Age in years, mean (SD)	60.8 (14.7)
Age groups	
Under 40 years, N (%)	2321 (7.1%)
40 – 50 years, N (%)	6028 (18.5%)
50 – 75 years, N (%)	17,620 (54.1%)
Over 75 years, N (%)	6590 (20.2%)
Affected side	
Left, N (%)	16,543 (50.8%)
Right, N (%)	16,013 (49.2%)
Medical history	
No medical history, N (%)	29,291 (91.5%)
Positive non-oncological medical history, N (%)	2471 (7.7%)
Positive oncological medical history, N (%)	241 (0.8%)
Detected by national screening program, N (%)	7726 (23.9%)
Tumour stage	
Stage I, N (%)	12,697 (39.0%)
Stage II, N (%)	19,862 (61.0%)
Immediate beast reconstruction, N (%)	6096 (18.7%)
Socioeconomic status	
0-9%, N (%)	3398 (10.4%)
10-20%, N (%)	3410 (10.5%)
20-30%, N (%)	3318 (10.2%)
30-40%, N (%)	3214 (9.9%)
40-50%, N (%)	3223 (9.9%)
50-60%, N (%)	3121 (9.6%)
60-70%, N (%)	3130 (9.6%)
70-80%, N (%)	3216 (9.9%)
80-90%, N (%)	3124 (9.6%)
90-100%, N (%)	3404 (10.5%)

SD = Standard deviation, N = Number, BIRADS = Breast Imaging Reporting and Data System.

the non-missing data, it was concluded that the values were missing at random. The imputation was repeated 20 times, followed by application of Rubin's rule to combine parameter estimates and standard errors [26,27]. Imputed data was later compared to the complete cases to determine validity of the imputation model. Subsequently, the imputed data was used for analyses.

Univariate and multivariate logistic regression analyses were performed to study the association between SES and the likelihood (quantified in odds ratio [OR] and 95% confidence interval [CI]) of receiving IBR in patients with stage 1 or 2 breast cancer. Possible confounding factors and effect modifiers to be considered are age at diagnosis, stage (1 or 2) and co-morbidities. Two-sided *P*-values below 0.05 were considered statistically significant.

All calculations were performed using RStudio 1.2.5001 (with R version: ×64 3.6.3). Visualization of plots was performed using the *ggplot 2* package.

Results

Between 2011 and 2018, 105,423 patients were diagnosed with breast cancer in the NKR with new onset stage I or II breast cancer, of whom 32,559 patients had undergone mastectomy (Table 1). Mean age was 60.8 years (range, 18−101 years) and most patients (17,620 patients, 54.1%) were between 50 and 75 years at diagnosis. The national screening program detected breast cancer in 7726 (23.9%) patients and 241 (7.5%) patients had a positive oncological history other than breast cancer. A total of 12,697 (39.0%) patients were diagnosed with new onset stage I breast cancer and 6096 (18.7%) of all patients had received IBR after mastectomy. Finally, the incidence of breast cancer was evenly spread among the different strata of SES (Table 1).

Compared to patients without IBR, patients with IBR after mastectomy were significantly older (63.3 years vs 49.7 years, respectively) and significantly more often had a stage I tumour (47.4% vs 37.1%, respectively; Table 2). Tumour grade did not differ significantly between the groups but tumour histology did vary significantly between patients who had received reconstruction

Table 2
Differences between patients with and without immediate breast reconstruction.

	No IBR n = 26463	IBR n = 6096	p-value
Age in years, mean (SD)	63.3 (14.4)	49.7 (10.6)	<0.001[a]
Age groups			<0.001[b]
Under 40 years, N (%)	1287 (55.5%)	1034 (44.5%)	
40 − 50 years, N (%)	4019 (66.7%)	2009 (33.3%)	
50 − 75 years, N (%)	14,605 (82.9%)	3015 (17.1%)	
Over 75 years, N (%)	6552 (99.4%)	38 (0.6%)	
Detected during screening, N (%)	6461 (24.4%)	1329 (21.8%)	<0.001[b]
Socioeconomic status			<0.001[b]
0-9%, N (%)	2913 (85.7%)	486 (14.3%)	
10-19%, N (%)	2871 (84.2%)	539 (15.8%)	
20-29%, N (%)	2761 (83.2%)	557 (16.8%)	
30-39%, N (%)	2685 (83.5%)	529 (16.5%)	
40-49%, N (%)	2669 (82.8%)	554 (17.2%)	
50-59%, N (%)	2566 (82.2%)	555 (17.8%)	
60-69%, N (%)	2491 (79.6%)	639 (20.4%)	
70-79%, N (%)	2555 (79.4%)	661 (20.6%)	
80-89%, N (%)	2423 (77.6%)	701 (22.4%)	
90-100%, N (%)	2529 (74.3%)	875 (25.7%)	
Received neo-adjuvant therapy, N (%)	3194 (12.1%)	1699 (27.9%)	<0.001[b]
Received adjuvant therapy, N (%)	12,708 (48.0%)	2894 (47.5%)	0.448[b]
Tumour stage			<0.001[b]
Stage I, N (%)	9809 (37.1%)	2888 (47.4%)	
Stage II, N (%)	16,654 (62.9%)	3208 (52.6%)	
Medical history			<0.001[b]
No medical history, N (%)	24,385 (92.1%)	5402 (88.6%)	
Positive non-oncological medical history, N (%)	1865 (7.0%)	663 (10.9%)	
Positive oncological medical history, N (%)	213 (0.8%)	31 (0.5%)	
Tumour receptor status			
Her 2 positive, N (%)	22,766 (86.0%)	5132 (84.2%)	<0.001[b]
Progesterone positive, N (%)	17,033 (64.4%)	4132 (67.8%)	<0.001[b]
Oestrogen positive, N (%)	21,083 (79.7%)	4883 (80.1%)	0.460[b]
Tumour grade			0.088[b]
Low grade, N (%)	4843 (18.3%)	1131 (18.6%)	
Intermediate grade, N (%)	13,382 (50.6%)	3129 (51.3%)	
High grade, N (%)	8238 (31.1%)	1836 (30.1%)	
Histological tumour type			<0.001[b]
No special type (ductal), N (%)	19,560 (73.9%)	4800 (78.7%)	
Lobular (ILC), N (%)	4545 (17.2%)	799 (13.1%)	
Both, N (%)	1199 (4.5%)	282 (4.6%)	
Mucinous, N (%)	484 (1.8%)	72 (1.2%)	
Medullary, N (%)	147 (0.6%)	48 (0.8%)	
Tubular, N (%)	112 (0.4%)	36 (0.6%)	
Other, N (%)	416 (1.6%)	59 (1.0%)	

BCT = breast conserving therapy, N = Number, SD = Standard deviation, BIRADS = Breast Imaging Reporting and Data System, ILS = Invasive lobular carcinoma, IBR = Immediate breast reconstruction.
[a] Two Sample *t*-test.
[b] Chi-square test.

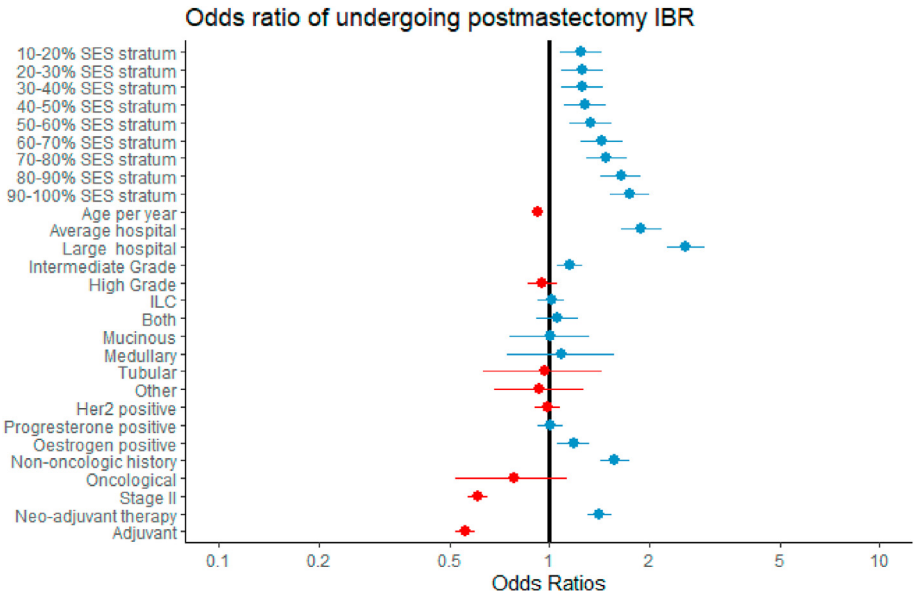

Fig. 1. Multivariate analysis of factors affecting the probability whether or not patients had undergone postmastectomy immediate breast reconstruction (IBR). SES = socioeconomic status, ILC = invasive lobular carcinoma.

and those who had not. Finally and most importantly, 486 (14.3%) of the patients with the lowest SES had received IBR after mastectomy which was significantly less than the 875 (25.7%) of the patients with the highest SES (Table 2).

Multivariate analysis showed that histological subtype, her2 receptor positivity, and progesterone receptor positivity were not significant predictors (Fig. 1 and Supplementary Table 1). Factors significantly increasing the probability of undergoing post-mastectomy IBR were higher SES (OR 1.05 [1.04–1.06] per 10% SES stratum), larger hospital volume (average volume OR 1.89 [1.64–2.18] and large volume 2.58 [2.26–2.94]), oestrogen positive tumours (OR 1.19 [1.06–1.33]) and neo-adjuvant therapy (OR 1.42 [1.31–1.55]. In contrast, factors significantly reducing the likelihood of receiving postmastectomy IBR were older age (OR 0.92 [0.92–0.92] per year), stage II (OR 0.61 [0.57–0.65] compared to stage I) and adjuvant therapy (OR 0.56 [0.52–0.60]).

Most breast reconstructions were implant-based with or without ADM/mesh (80.3%) followed by autologous (6.9%) and combined techniques (latissimus dorsi and implant, 3.2%). In 9.6% the reconstruction type was unknown. There was no difference in breast reconstruction type distribution between the SES strata (Fig. 2).

In conclusion, SES remained a significant predictor for the likelihood of receiving IBR after multivariate logistic regression,

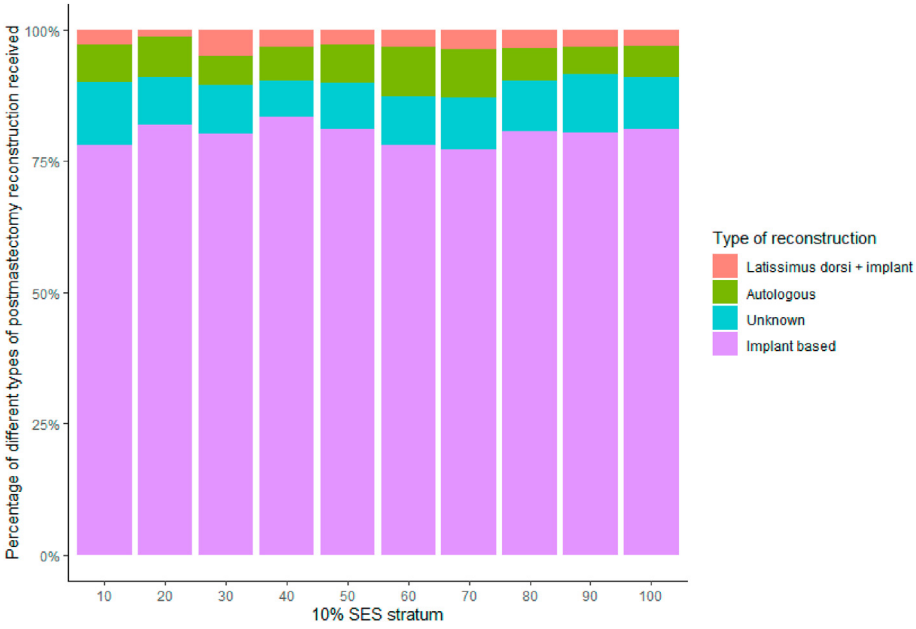

Fig. 2. Percentage of type of reconstruction per socioeconomic (SES) stratum.

controlling for age, tumour grade, tumour stage, (neo)adjuvant therapy, histological subtype, receptor status (oestrogen, progesterone and/or her2) and medical history.

Discussion

In this population-based study in a country where everyone has equal access to healthcare, patients with new onset stage I or II breast cancer undergoing mastectomy were more likely to undergo postmastectomy IBR with increasing SES. Other factors that increased the likelihood of undergoing IBR were larger hospital size in which the patient was treated, lower age and treatment with neo-adjuvant therapy and/or the absence of adjuvant therapy.

The current study showed that 14.3% of the patients from the lowest SES decile underwent postmastectomy IBR compared to 25.7% of the patients from the highest SES decile. Even after controlling for patient and tumour characteristics and hospital size, there was an OR of 1.75 (95% CI of 1.53–2.01) of undergoing IBR in the highest SES decile compared to the lowest SES decile. This means that patients in the highest SES decile were 63.4% (95% CI; 60.4–66.8%) more likely to undergo IBR than patients in the lowest SES decile. This contributes to previous knowledge from studies which showed the effect of SES on the treatment of breast cancer [12,28,29]. The current study is also in line with a recent Swedish study which showed that age and SES contribute to the likelihood of receiving postmastectomy IBR [30]. In addition, the results of the current study confirm previously found results that SES affects the likelihood of undergoing postmastectomy IBR [10,11,31]. In the Netherlands this means that most medical interventions including postmastectomy IBR are covered by national insurance for all the patients even for those of lower SES.

It was also found that hospital size was an important independent predictor of postmastectomy IBR. This is in line with previous studies which reported that hospital volume affects different aspects of breast cancer treatment [6,7,32–34]. Compared to smaller hospitals in the Netherlands, larger hospitals often have plastic surgeons who are participating in the multidisciplinary y team discussions and involved in the decision making of IBR. Moreover, they are better aware of all reconstruction possibilities and also take lifestyle factors such as higher BMI and smoking into account as well as the possibility of (neo)adjuvant therapies when recommending IBR(7,8). The current study confirms that the higher volume breast cancer treatment hospitals are more likely to perform postmastectomy IBR.

Age also appeared to be an important predictor of IBR. 44.5% of younger patients (under 40 years old) received IBR compared to only 0.6% of older patients (over 75 years old). Patients with stage II breast cancer who had received adjuvant therapy were less likely to undergo postmastectomy IBR while patients who had received neo-adjuvant therapy were more likely to undergo IBR. This is also in line with the results of previous studies which used data from a different national registry [6,9], giving us confidence in the reliability of our findings.

The present study has some limitations. First, it showed that SES plays an important role whether or not patients received postmastectomy IBR. However, it is likely that other factors may also be important such as race, ethnicity and religious beliefs. However, these factors are known to be closely linked to SES [16,35,36]. Therefore, more research is warranted to study the possible effects of cultural background on whether patients are given the same choices regarding postmastectomy IBR possibilities when there is equal access to healthcare. A previous study from the UK showed that there was variation between hospitals and regions in information provision regarding postmastectomy reconstruction in breast cancer patients [37]. In the NKR we do not have information on cultural background, nor do we have information whether the possibility of IBR had been discussed with the patient. Therefore, it would be interesting to study whether there also exist differences in information provision to women undergoing mastectomy regarding IBR between hospitals and/or regions in the Netherlands and whether this is influenced by patients' SES. Moreover, maybe less access to patient information (due to e.g. language barrier, illiteracy, less access to internet) might contribute to the fact that patients with lower SES are less likely to undergo postmastectomy IBR. Therefore, it may be helpful to provide additional onco-psychological or social support to patients with lower SES.

In conclusion, the present study showed that, even in a country with equal access to healthcare, patients with lower SES were less likely to undergo postmastectomy IBR. More research is needed to determine why these differences exist.

CRediT authorship contribution statement

M.D. Filipe: Conceptualization, Methodology, Software, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Visualization, Project administration. **S. Siesling:** Conceptualization, Methodology, Software, Formal analysis, Resources, Writing - original draft, Writing - review & editing, Visualization. **M.R. Vriens:** Writing - review & editing. **P.J. van Diest:** Writing - review & editing, Supervision. **A.J. Witkamp:** Writing - review & editing, Supervision. **M.A.M. Mureau:** Conceptualization, Methodology, Validation, Writing - original draft, Writing - review & editing, Visualization, Data curation, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2020.09.016.

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