A comprehensive approach for quality assessment of breast cancer care

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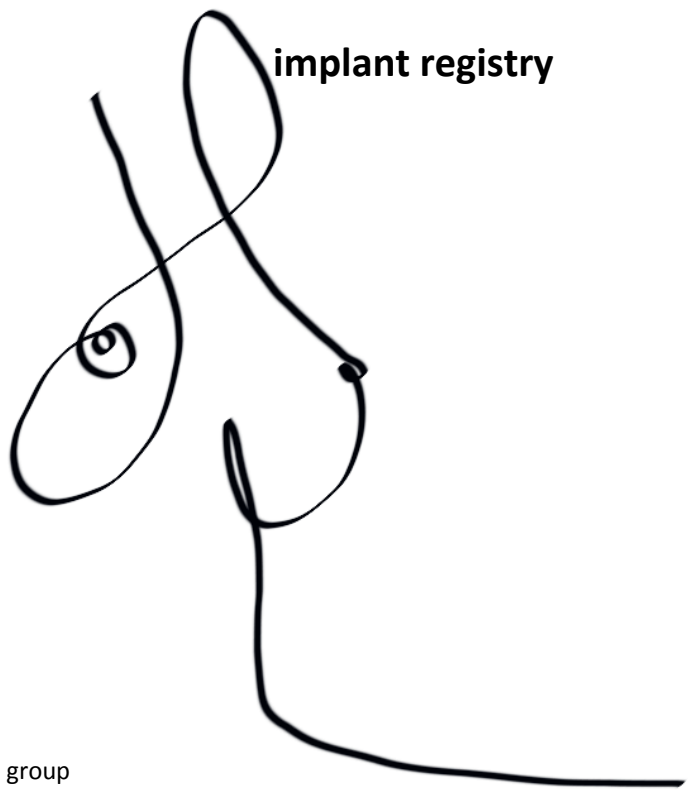
Part III

Quality assessment of breast reconstruction strategies

Chapter 6

Revision incidence after immediate direct-to-implant versus two-stage implant-based breast reconstruction: results from a nationwide breast implant registry



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Abstract

Background

In immediate implant-based breast reconstruction (IBBR), large variation is observed in current practices between a direct-to-implant or two-stage approach. This population-based study aimed to compare unplanned short- and long-term revision incidence between direct-to-implant and two-stage IBBR in the Netherlands.

Methods

All patients with immediate IBBR following a mastectomy between 2015 and 2019 were selected from the nationwide Dutch Breast Implant Registry (DBIR). Short- and long-term unplanned revision incidence was studied per immediate IBBR, including revision indications, and total number of additional operations. Confounding by indication was limited using propensity score matching.

Results

A total of 4,938 breast implants (4,321 women) were included, of which 2,350 (48%) for direct-to-implant IBBR and 2,588 (52%) for two-stage IBBR. Median (i.q.r) follow-up was 30 (15-45) months and 32 (20-47) months, respectively. Short-term revision incidence was 4.2% and 11.7%, respectively (conditional OR 0.32, 95%-CI 0.25-0.43). Long-term revision incidence was 10.8% (95%-CI 9.4-12.1) and 16.3% (95%-CI 14.8-17.7), respectively. In the propensity score matched cohort, similar results were found. In the direct-to-implant group, more breasts were reconstructed within the planned number of operations than in the two-stage group.

Conclusion

Unplanned revision surgery occurred less often after direct-to-implant IBBR, and more breasts were reconstructed within the planned number of operations compared to two-stage IBBR. These results, based on real-world data, are important for improving patient counselling and shared decision-making.

Introduction

Immediate postmastectomy breast reconstruction is becoming increasingly popular, with up to 50% of mastectomy patients undergoing this type of reconstruction in current practice.[1,2] Although autologous techniques are increasingly being used, immediate implant-based breast reconstruction (IBBR) is still most often performed (70-90%).[1-5] Immediate IBBR can be achieved either using a one-stage direct-to-implant approach or a two-stage technique with a tissue expander (TE), which is replaced by a definite breast implant during a second surgery.

There is an ongoing debate about the differences in complications and cosmetic outcomes between direct-to-implant and two-stage breast reconstruction, as direct comparisons in randomized controlled trials (RCTs) have not been performed.[6-9] Possible advantages of direct-to-implant IBBR include fewer outpatient clinic visits and fewer surgeries, expected lower overall costs, and a quicker return to the patient's social and working life.[10,11] Possible disadvantages are difficulties in using implant sizes larger than the original breast(s), higher probability of asymmetry, and the potentially higher risk of adverse events, especially if ADMs or meshes are used.[12,13]

The latest evidence-based Dutch guideline for breast reconstruction from 2015 states that it is difficult to make evidence-based recommendations due to a lack of high-quality evidence.[14] This lack of high-quality evidence may contribute to unwanted variation in current practices among healthcare providers. These arguments emphasize the need for a better understanding of the differences in risks and outcomes to improve patient counselling and quality of care. Therefore, this study aimed to compare revision incidence, revision indications, and the additional number of operations per breast between direct-to-implant and two-stage IBBR in a nationwide, population-based cohort using the Dutch Breast Implant registry (DBIR).

Methods

Design and study population

This observational cohort study included all women who had been prospectively registered in the DBIR after undergoing a direct-to-implant or two-stage immediate IBBR between January 1, 2015, and December 31, 2019. Indications for an immediate IBBR were mastectomy for breast cancer or prophylactic mastectomy.

Patients who had undergone reconstruction for a benign condition, who had received any previous breast implant surgery, and in whom additional surgical techniques (fat

grafting or mastopexy) had been used during implant insertion, were excluded from analysis.
Of the women with a two-stage IBBR, information on both the first stage (tissue expander insertion) and second stage (tissue expander exchange for permanent breast implant) was necessary for inclusion.

Data collection: the Dutch Breast Implant Registry

The DBIR is a nationwide, population-based registry. Since 2015, patient, surgery, and implant characteristics are prospectively collected of all patients undergoing breast implant surgery in the Netherlands for breast reconstruction or breast augmentation. More details about the registry have been described previously.[1,15,16] Currently, 100% (n=74) of the hospitals and 95% (n=37) of the private clinics where breast implant surgery is being performed are included in DBIR. For the current study, the last data update was on May 8th, 2020.

Definitions

Direct-to-implant IBBR was defined as the insertion of a permanent breast implant during the same operation as the mastectomy. Two-stage IBBR was defined as the insertion of a tissue expander (TE) during the same operation as the mastectomy, followed by a second operation in which a permanent breast implant replaced the TE.
Completion of each reconstruction trajectory was defined as the moment a permanent breast implant was inserted. The reconstruction trajectory of a two-stage IBBR was defined as the time between mastectomy with immediate TE insertion and TE replacement with a permanent breast implant. Revision surgery was defined as the first unplanned reoperation after insertion, in which the breast implant or TE was repositioned, explanted or replaced. Indications for an unplanned revision were mastectomy skin flap necrosis, skin scarring problems, autologous flap problems, deep wound infections, seroma or hematoma, capsular contracture, newly diagnosed breast cancer, BIA-ALCL, breast pain, asymmetry, dissatisfaction with volume, patient-requested implant removal due to nonspecific health symptoms, device malposition, and device rupture or deflation.
Exact definitions of all patient, surgery, revision, and implant variables used for analysis can be found in the DBIR Data Dictionary (Appendix S6.1, supporting information).

Outcome measures

The primary outcome was the short-term revision incidence of both IBBR techniques during the time from mastectomy until 60 days after the last planned surgery in each reconstruction trajectory (Figure 6.1). A time interval of 60 days was chosen because a substantial amount of complications in breast implant surgery occur after 30 days.[17,18] Subsequently, the long-term cumulative revision incidence within two years after mastectomy, revision indications, and the total number of additional operations per breast were evaluated for both IBBR techniques. Potential confounding factors were identified based on existing literature and clinical rationale. A Directed Acyclic Graph (DAG) was used to visualize this process before performing analyses.[19]

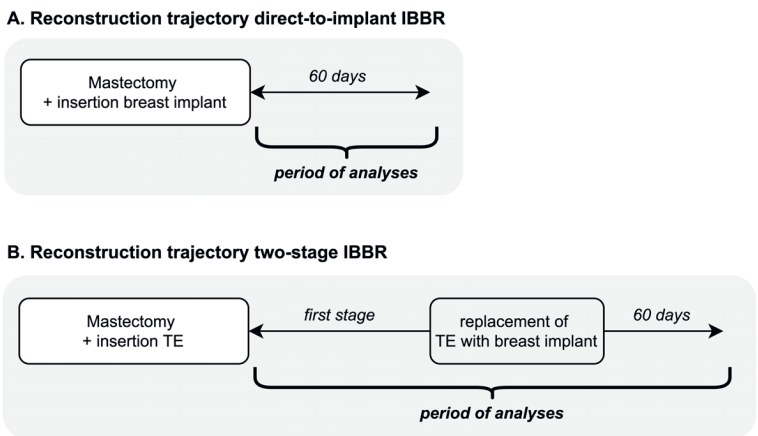

Figure 6.1. Schematic view of the two analyzed reconstruction trajectories: from mastectomy and immediate IBBR until 60 days after completion of the reconstruction

Statistical analysis

All analyses were performed with the implant as the unit of analysis, using R software, version 1·2·5019-©2009-2019, RStudio, Inc. Missing data patterns were evaluated, resulting in the assumption of data being missing at random. Multiple imputation by chained equations was performed ('mice' package, version 3.6.0).[20,21] The outcome variable itself was not imputed. Statistical models were fitted and results were pooled following Rubin's rules.[22] See Table S6.1 in the supporting information for non-imputed data.

Baseline characteristics were compared between groups using Student's t-tests, Mann Whitney U tests, χ^2 tests or Fisher's exact tests accordingly. Two-sided $p<0.050$ was considered statistically significant.

To assess the likelihood of short-term revision, multivariable logistic regression analyses were performed ('stats' package, version 3.6.1). Subsequently, to account for clustering of patients and implants within healthcare institutions which were likely to be correlated with practices performed, a conditional OR with 95%-CI was calculated using a mixed-effects logistic regression model ('lme4' package, version 1·1-21). In this mixed-effects model, confounding factors that were distributed differently between the revision and no-revision groups were entered as fixed effects and healthcare institutions were included as random intercepts.

The crude, long-term cumulative revision incidence was calculated using Nelson-Aalen estimates. Implants without any revision at closure of the dataset on May 8, 2020, were censored. After reassuring the proportional hazard assumption was met, a hazard ratio (HR) was calculated using a Cox proportional hazards model. The total number of additional surgeries was calculated per reconstruction trajectory per breast.

Sensitivity analysis

Two sensitivity analyses were performed. First, the E-value was calculated ('EValue' package, version 2.0.0). An E-value assesses the minimum strength an unmeasured confounding factor must have, to negate the observed treatment-outcome association.[23] Second, propensity score matching (PSM) was used to assess the likelihood of short- and long-term revision while limiting potential confounding by indication.[24,25] A logistic regression model was used to calculate the propensity score for undergoing direct-to-implant IBBR using all preoperative covariates: age, ASA classification, BMI, smoking status, previous radiotherapy, postoperative radiotherapy planned, year of surgery, healthcare institution, healthcare institution volume, reconstruction indication, and laterality. In the PSM analyses, records with any missing preoperative characteristic were excluded. Matching was performed using a 1:1 ratio with a calliper width of 0·2 times the standard deviation of the logit ('MatchIt' package, version 3.0.2). Potential imbalances before and after matching were assessed using standardized mean differences (s.m.d.).[26] A baseline characteristic with an s.m.d. of 10% or more indicates an imbalance between the direct-to-implant and two-stage group.

Results

A total of 4,321 patients and 4,938 breast implants met the inclusion criteria (Figure S6.1, supporting information), of whom 4,064 patients (94.1%) underwent immediate IBBR after mastectomy for breast cancer and 257 (5.9%) after prophylactic mastectomy. These reconstructions were performed in 76 healthcare institutions with a mean volume per institution of 110 (range 13-546) breast implant surgeries per year.
A total of 2,350 (47.6%) breast implants were inserted for a direct-to-implant IBBR, and 2,588 (52.4%) TE's were inserted for a two-stage IBBR. Direct-to-implant IBBR was more frequently performed in younger, non-smoking patients, if postoperative radiotherapy was planned, in case of nipple-sparing surgery, the use of ADM/mesh, and autologous flap cover. Furthermore, direct-to-implant IBBR was more frequently registered in more recent years, and in healthcare institutions with a volume of >200 implant surgeries per year (Table S6.2, supporting information).

Short-term revision incidence

Of 2,350 breast implants inserted during direct-to-implant IBBR, 99 (4.2%) underwent unplanned revision surgery within 60 days after completion of the reconstruction trajectory. Of 2588 breasts that underwent two-stage IBBR, 302 (11.7%) had an unplanned revision within 60 days after completion of the entire reconstruction trajectory. The majority of these unplanned revisions occurred during the first stage of two-stage reconstruction (n=279) (Figure 6.2).
Revision surgery was more frequently observed after two-stage IBBR, in patients with higher age, ASA classification, and BMI, in patients who smoked, in middle-volume healthcare institutions (50-200 implant surgeries per year), and after non-nipple sparing surgery (Table 6.1). Compared with a two-stage procedure, implants inserted during a direct-to-implant procedure had a lower likelihood of short-term revision surgery (unadjusted OR 0.33, 95%-CI 0.26-0.42; adjusted OR 0.28, 95%-CI 0.22-0.36; conditional OR 0.32, 95%-CI 0.25-0.43) (Table 6.2).

Long-term revision incidence

The median (i.q.r.) follow-up time was 30 (15-45) months in the direct-to-implant group and 32 (20-47) months in the two-stage group. After direct-to-implant IBBR, the crude cumulative unplanned revision incidence within two years was 10.8% (n=251, 95%-CI 9.4-12.1). Within the two-stage group, this was 16.3% (n=443, 95%-ci 14.8-17.7) (Figure 6.3A). A hazard ratio could not be calculated, because the proportional hazard assumption was not met. Differences in baseline characteristics between the groups

with and without long-term revision surgery were the same differences as seen between the groups with and without short-term revision surgery.

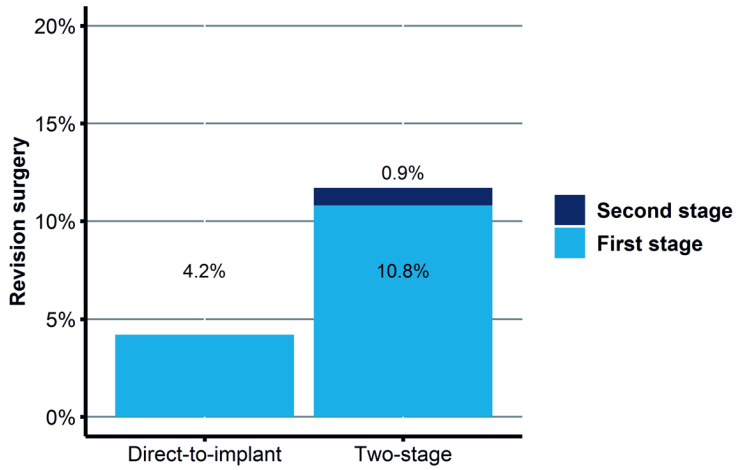

Figure 6.2. Short-term (≤60 days) revision incidence per breast reconstruction trajectory.

Revision indications

Within 60 days after direct-to-implant IBBR, most frequently registered revision indications were mastectomy skin flap necrosis, deep wound infections, and autologous flap problems (Table 6.3). After 60 days, asymmetry, dissatisfaction with volume, and breast pain were most frequently observed.

During the complete first stage of a two-stage IBBR, revision surgery was mostly performed for deep wound infections, seroma or hematoma, mastectomy skin flap necrosis, and device rupture or deflation. Within 60 days of the second stage of two-stage IBBR, the majority of revisions was for seroma or hematoma, deep wound infections, and skin scarring problems. Over the longer term, asymmetry, breast pain, capsular contracture, and dissatisfaction with volume were mostly observed.

Very few implants were removed on patients' request due to nonspecific health symptoms. No implant removals for BIA-ALCL were registered.

Table 6.1. Patient and surgery factors at time of mastectomy and immediate IBBR, per group with and without short-term (≤60 days) revision surgery after completion of the reconstruction trajectory

	Total group (n=4938)	No short-term revision (n=4537)	Short-term revision (n=401)	p-value
Intervention of interest				
Type of IBBR				<0·001
Direct-to-implant	2350 (47·6)	2251 (49·6)	99 (24·7)	
Two-stage	2588 (52·4)	2286 (50·4)	302 (75·3)	
Patient characteristics				
Age (years, s.d.)	49·3 (11·4)	49·1 (11·4)	51·1 (10·6)	0·001
ASA classification				<0·001
I	3092 (62·6)	2896 (63·8)	196 (48·9)	
II	1695 (34·3)	1510 (33·3)	185 (46·1)	
III+	151 (3·1)	131 (2·9)	20 (5·0)	
Body Mass Index (kg/m^2, i.q.r.)	23·0 (20·7-26·1)	22·9 (20·7-25·9)	24·5 (22·2-28·2)	<0·001
Smoking status				<0·001
Not smoking	4293 (86·9)	3970 (87·5)	323 (80·5)	
Smoking	645 (13·1)	567 (12·5)	78 (19·5)	
Previous radiotherapy				0·354
No	4605 (93·3)	4236 (93·4)	369 (92·0)	
Yes	333 (6·7)	301 (6·6)	32 (8·0)	
Surgery characteristics				
Healthcare institution volume (per year)				0·001
<50 implant surgeries	569 (11·5)	523 (11·5)	46 (11·5)	
50-99 implant surgeries	900 (18·2)	804 (17·7)	96 (23·9)	
100-200 implant surgeries	1989 (40·3)	1819 (40·1)	170 (42·4)	
>200 implant surgeries	1480 (30·0)	1391 (30·7)	89 (22·2)	
Reconstruction indication				1·000
Breast cancer	4488 (90·9)	4124 (90·9)	364 (90·8)	
Prophylactic mastectomy	450 (9·1)	413 (9·1)	37 (9·2)	
Laterality				0·220
Unilateral	3230 (65·4)	2956 (65·2)	274 (68·3)	
Bilateral	1708 (34·6)	1581 (34·8)	127 (31·7)	
Incision site				0·040
Nipple sparing	1132 (22·9)	1058 (23·3)	74 (18·5)	
Non-nipple sparing	3470 (70·3)	3166 (69·8)	304 (75·8)	
Other	336 (6·8)	313 (6·9)	23 (5·7)	
Plane				0·003
Sub flap	234 (4·7)	220 (4·8)	14 (3·5)	
Completely covered with PM muscle	2598 (52·6)	2408 (53·1)	190 (47·4)	
Partially covered with PM muscle	1931 (39·2)	1759 (38·8)	172 (42·9)	
Other	175 (3·5)	150 (3·3)	25 (6·2)	
Number of applied ICMs during implant insertion				0·050
<4	947 (19·2)	879 (19·4)	68 (17·0)	
4	1742 (35·3)	1615 (35·6)	127 (31·7)	
>4	2249 (45·5)	2034 (45·0)	206 (51·3)	
ADM/Mesh				0·105
No	4448 (90·1)	4077 (89·9)	371 (92·5)	
Yes	490 (9·9)	460 (10·1)	30 (7·5)	
Autologous flap cover				0·291
No	43659 (88·3)	3998 (88·1)	361 (90·0)	
Yes	579 (11·7)	539 (11·9)	40 (10·0)	

Values in parentheses are percentages, unless indicated otherwise. IBBR, implant-based breast reconstruction; s.d., standard deviation; ASA, American society of anesthesiologists; i.q.r, interquartile range; PM, pectoralis major; ICMs, infection control measures; ADM, acellular dermal matrix.

Table 2. Likelihood of short-term revision surgery after completion of the reconstruction trajectory

Direct-to-implant IBBR (n=2,350 implants) Two-stage IBBR (n=2,588 implants)	**OR**
Unadjusted (univariable logistic regression model)	
Two-stage	1 (reference)
Direct-to-implant	0·33 (0·26-0·42)
Adjusted (multivariable logistic regression model)	
Age	0·34 (0·27-0·43)
Age & ASA	0·33 (0·26-0·42)
Age, ASA, & BMI	0·33 (0·26-0·42)
Age, ASA, BMI & smoking	0·34 (0·27-0·43)
Age, ASA, BMI, smoking & institution volume	0·34 (0·27-0·44)
Age, ASA, BMI, smoking, institution volume & incision site	0·34 (0·27-0·43)
Age, ASA, BMI, smoking, institution volume, incision site & plane	0·28 (0·22-0·37)
Age, ASA, BMI, smoking, institution volume, incision site, plane & number of applied ICMs	0·28 (0·22-0·36)
Conditional (mixed-effects logistic regression model)	
Age, ASA, BMI, smoking, institution volume, incision site, plane, number of applied ICMs & healthcare institution*	0·32 (0·25-0·43)

Values in parentheses are 95%-CI. *The conditional OR was obtained by entering age, ASA classification, BMI, smoking, institution volume, incision site, plane, and number of applied ICMs as fixed effects into the model, and healthcare institution as random effect. IBBR, implant-based breast reconstruction; ASA, American society of anesthesiologists' classification; BMI, body mass index; ICMs, infection control measures.

Additional operations

During the follow-up period, 2,099 of 2,350 breasts (89.3%) in the direct-to-implant IBBR cohort were reconstructed within one operation. Eighty-three breasts (3.5%) needed one, 125 (5.3%) two, and 43 (1.8%) three or more additional operations.
In the two-stage IBBR group, 2,155 of 2,588 breasts (83.3%) were reconstructed within the planned two procedures. Hundred eighty-one breasts (7.0%) needed one, 82 (3.2%) two, and 82 (3.2%) three or more additional operations. Eighty-eight breasts (3.4%) needed revision surgery right after TE insertion and did not reach the second stage within the median follow-up.

Sensitivity analysis

For the conditional OR of short-term revision surgery, the E-value was 5.7. This indicates that residual confounding could explain the observed association if an unidentified confounding factor exists with a relative risk association of at least 5·7. The E-value for the adjusted HR of long-term revision surgery could not be calculated because the proportional hazard assumption was not met.
After limiting confounding by indication using propensity score matching, 381 (50.0%) direct-to-implant records were matched to 381 (50.0%) two-stage IBBRs. While before matching, an imbalance in preoperative baseline characteristics was observed, no imbalances were observed after matching (Table S6.3, supporting information). In the

matched cohort (n=762), implants inserted during direct-to-implant IBBR had a lower conditional likelihood of short-term revision compared to a two-stage procedure (conditional OR 0.33, 95%-CI 0.20-0.53). For the long-term, the crude cumulative revision incidence was 14.3% (95%-CI 10.3-18.1) after direct-to-implant IBBR and 22.7% (95%-CI 17.8-27.2) after a two-stage procedure (non-proportional hazards) (Figure 6.3B).

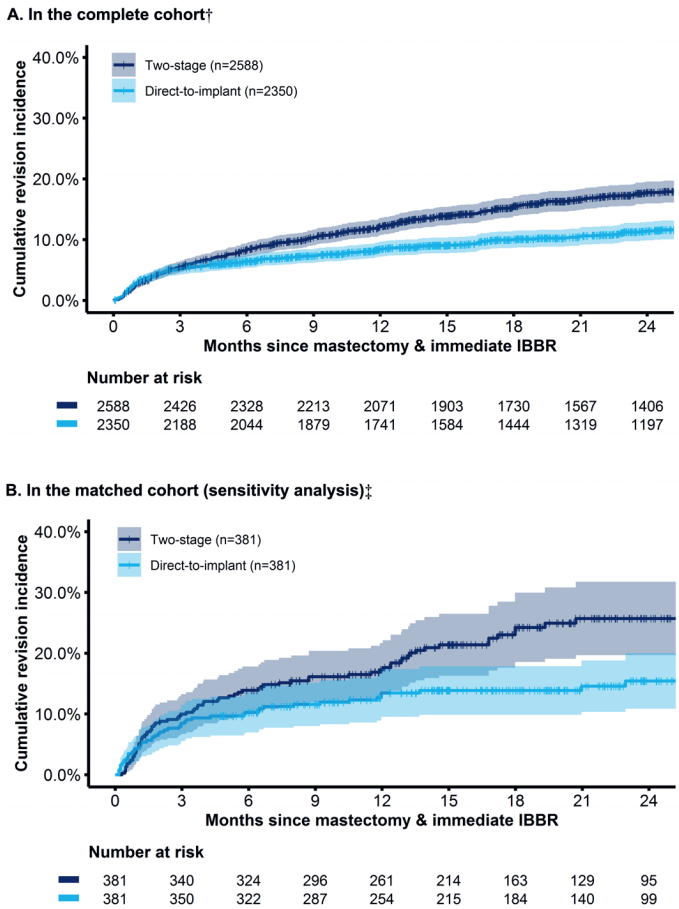

Figure 6.3. Crude, long-term cumulative revision incidence after mastectomy and immediate direct-to-implant IBBR or immediate two-stage IBBR*
*Curve includes revisions during the first and second stage of the reconstruction trajectory. †Direct-to-implant: within 1 month 2.8% (2.1 to 3.4), 6 months 6.2% (5.2 to 7.2), 12 months 8.1% (7.0 to 9.2), 24 months 10.8% (9.4 to 12.1). Two-stage: within 1 month 2.4% (1.8 to 3.0), 6 months 8.0% (6.9 to 9.0), 12 months 11.4% (10.2 to 12.7), 24 months 16.3% (14.8 to 17.7). ‡Direct-to-implant: within 1 month 4.2% (2.2 to 6.2), 6 months 9.7% (6.7 to 12.7), 12 months 12.6% (9.1 to 15.9), 24 months 14.3% (10.3 to 18.1). Two-stage: within 1 month 4.2% (2.2 to 6.2), 6 months 13.0% (9.5 to 16.3), 12 months 15.8% (12.0 to 19.5), 24 months 22.7% (17.8 to 27.2). Values in parentheses are 95%-CIs. IBBR, implant-based breast reconstruction.

Table 6.3. Indications* for short- and long-term revision surgery per reconstruction trajectory.

	Direct-to-implant IBBR		Two-stage IBBR		
	Short-term ≤60 days (n=99)	Long-term >60 days (n=152)	Short-term during first stage (n=279)	Short-term ≤60 days second stage (n=23)	Long-term >60 days second stage (n=131)
Deep wound infection	42 (42)	19 (13)	117 (42)	6 (26)	7 (5)
Seroma or hematoma	15 (15)	17 (12)	64 (23)	10 (44)	10 (8)
Mastectomy skin flap necrosis	52 (53)	14 (10)	48 (17)	1 (4)	4 (3)
Asymmetry	2 (2)	57 (39)	18 (7)	2 (9)	48 (37)
Breast pain	7 (7)	33 (23)	36 (13)	2 (9)	40 (31)
Capsular contracture	1 (1)	28 (19)	35 (13)	0 (0)	35 (27)
Skin scarring problems	11 (11)	7 (5)	32 (12)	5 (22)	12 (9)
Dissatisfaction with volume	2 (2)	34 (23)	9 (3)	1 (4)	30 (23)
Device malposition	2 (2)	28 (19)	18 (7)	1 (4)	25 (19)
Autologous flap problems	29 (29)	6 (4)	16 (6)	1 (4)	3 (2)
Device rupture or deflation	2 (2)	9 (6)	43 (15)	1 (4)	6 (5)
Newly diagnosed breast cancer	7 (7)	12 (8)	11 (4)	1 (4)	1 (1)
Patient-requested implant removal due to nonspecific health symptoms	1 (1)	3 (2)	1 (<1)	0 (0)	1 (1)
BIA-ALCL	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Values in parentheses are percentages. *Multiple indications could be reported per revision procedure. IBBR, implant-based breast reconstruction; BIA-ALCL, Breast Implant - Associated Anaplastic Large Cell Lymphoma.

After limiting confounding by indication using propensity score matching, 381 (50.0%) direct-to-implant records were matched to 381 (50.0%) two-stage IBBRs. While before matching, an imbalance in preoperative baseline characteristics was observed, no imbalances were observed after matching (Table S6.3, supporting information). In the matched cohort (n=762), implants inserted during direct-to-implant IBBR had a lower conditional likelihood of short-term revision compared to a two-stage procedure (conditional OR 0.33, 95%-CI 0.20-0.53). For the long-term, the crude cumulative revision incidence was 14.3% (95%-CI 10.3-18.1) after direct-to-implant IBBR and 22.7% (95%-CI 17.8-27.2) after a two-stage procedure (non-proportional hazards) (Figure 6.3B).

Discussion

This nationwide population-based study included close to 100% of all healthcare institutions performing breast reconstruction in the Netherlands. After adjusting for confounders and variation among centers, direct-to-implant IBBR was associated with a lower short-term and long-term unplanned revision incidence compared to two-stage IBBR. After limiting confounding by indication, comparable results were found. In the

direct-to-implant group, more breasts were reconstructed within the planned number of operations than in the two-stage group.

Interestingly, both Basta et al. and Lee et al. reported in their meta-analysis that direct-to-implant procedures were associated with a 1.24 (95%-CI 1.02-1.53) and 1.25 (95%-CI 0.40-3.89) higher risk of revision surgery, respectively, although the latter result was not statistically significant.[8,9] However, both meta-analyses included mainly single-centre studies, with low numbers of reconstructions, high heterogeneity in follow-up time, and without adjusting for confounders or indication bias. Additionally, the second stage of a two-stage IBBR was not always included, and often comparison of direct-to-implant versus two-stage IBBR was not the study aim.

Bennett et al. compared different types of IBBR during a two-year follow-up, using data from the Mastectomy Reconstruction Outcomes Consortium Study.[27] After adjusting for confounders and variation among centers, re-operative complication rates were 19% after direct-to-implant IBBR and 16% after two-stage IBBR (OR 1.06, 95%-CI 0.56-1.99). However, these results were statistically not significant and not adjusted for confounding by indication. Other smaller studies reported comparable proportions of long-term revision surgery between both IBBR groups (range 20-28%).[28,29] Nevertheless, comparing the results of the current study to previous studies remains difficult, because many different outcome definitions are used, such as reconstructive failure, reoperation, or re-operative complications.[7,18,27,30]

There are two likely explanations for the lower risk of short- and long-term revision surgery in the direct-to-implant IBBR group compared to the two-stage group. First, the reconstruction trajectory of a two-stage IBBR is longer by definition with two potentially hazardous events instead of one. Second, patient selection may have affected the probability of revision surgery. Direct-to-implant IBBR was more often performed in younger, non-smoking patients. Additionally, fewer infection control measures were used compared to two-stage IBBR, suggesting that direct-to-implant IBBR was more frequently performed in low-risk patients. However, after limiting confounding by indication using propensity score matching, comparable results were found.

To decrease the risk of short-term revision surgery after direct-to-implant IBBR, current findings suggest that one should focus specifically on mastectomy skin flap quality and prevention of deep wound infections. After two-stage IBBR, most short-term revisions were due to deep wound infections and seroma or hematoma formation. As most of these revision indications were related, different preventive strategies may be useful. For example, prophylactic intravenous tranexamic acid administration and a more aggressive surgical dead space management to prevent hematoma and seroma formation, respectively, and consequently deep wound infections.[31,32] Another specific

complication after two-stage procedures was TE deflation during the expansion period. Innovations that would obviate the need to puncture a TE for expanding, such as carbon dioxide-inflated TEs, could, therefore, be interesting, also to further reduce infections.[33] Long-term outcomes of both IBBR techniques could be improved by focusing on patient selection and counselling, especially regarding the risk of asymmetry, pain and capsular contracture, dissatisfaction with volume and device malposition.

Strengths and limitations

One of the strengths of this study is that real-world data was used from a nationwide population-based registry, including implants that were followed over time within different healthcare institutions. Consequently, the findings reflect daily clinical practice in the Netherlands. Randomized Controlled Trials are still the golden standard for comparative studies. However, RCTs are not always feasible if the outcome has a low event rate. As the next best alternative, selection and indication bias was limited using imputation techniques for missing data and propensity score matching to mimic pseudo-randomization. Also, clustering of patients and implants within healthcare institutions were taken into account. Finally, the DBIR uses definitions similar for all breast implant registries affiliated with the International Collaboration of Breast Registry Activities (ICOBRA), thereby improving comparability to future studies and meta-analyses using data from breast implant registries.[34]

There are several limitations. First, revision surgeries might have been underreported. Registration of inserted medical devices is mandatory by law in the Netherlands, but explantations are not. However, it is unlikely that revisions were less frequently registered for only one of the IBBR techniques. Thus, the presented revision incidences need to be interpreted as minimum incidences. Second, there may be residual confounding, due to missing potential confounders such as mastectomy skin flap quality, breast volume or mastectomy weight, and detailed information on (neo)adjuvant therapy.[3,18,35,36] However, the sensitivity analysis indicated that residual confounding could explain the observed association if an unidentified confounding factor with an OR of at least 5·7 would exist. The majority of the measured confounders had an OR below 2. Therefore, it is unlikely that unidentified confounders would alter our conclusions.

Future research

In daily practice, healthcare institutions tend to prefer one technique over the other. Future studies should focus on nationwide variation in the use of both IBBR techniques

and the underlying reasons. Insight into variation, patient selection, and outcomes helps to further improve guidelines and the quality of care provided.

Conclusions

Unplanned revision surgery occurred less often after direct-to-implant IBBR, and a higher proportion of breasts were reconstructed within the planned number of operations compared to two-stage IBBR. These population-based results are important to improve patient counselling and shared decision-making. Besides, they may help to start the discussion about whether a direct-to-implant approach should be considered more often.

Acknowledgement

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Supporting information

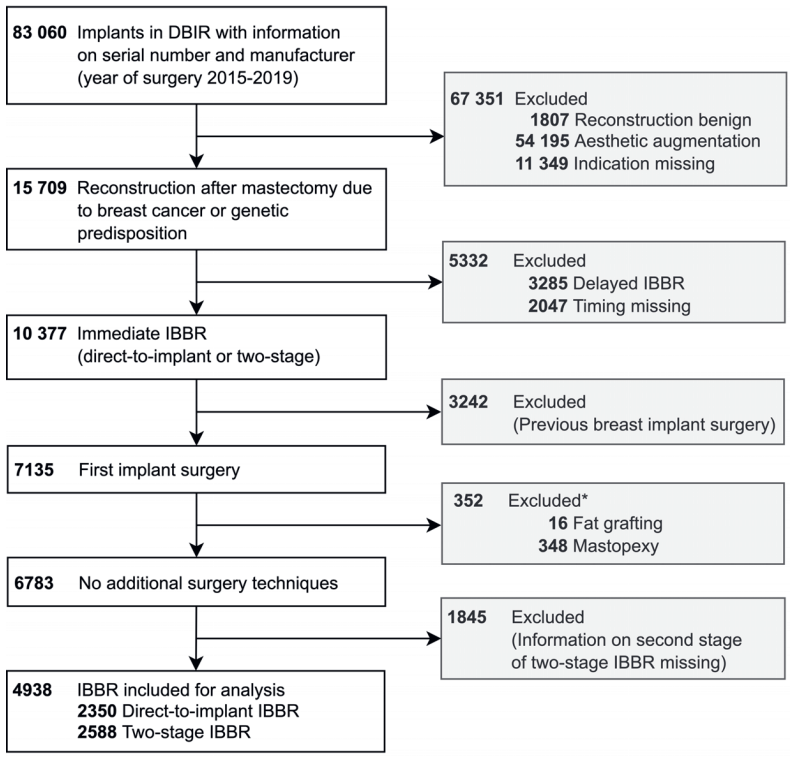

Figure S6.1. Flow chart of implant selection.
*More than one additional surgery technique could be registered per record. DBIR, Dutch Breast Implant Registry; IBBR, implant-based breast reconstruction; TE, tissue expander.

Table S6.1. Raw data of patient and surgery characteristics at time of mastectomy and immediate IBBR

	Total group (n=4,938)
Intervention of interest	
Type of IBBR	
Direct-to-implant	2,350 (47.6)
Two-stage	2,588 (52.4)
Patient characteristics	
Age (years, s.d.)	49.3 (11.4)
Missing	15 (0.3)
ASA classification	
I	3,056 (61.9)
II	1,673 (33.9)
III+	147 (3.0)
Missing	62 (1.2)
Body Mass Index* (kg/m^2, i.q.r.)	23.9 (21.6-26.8)
Missing	2494 (50.5)

Table S6.1. (continued)

	Total group (n=4,938)
Smoking status*	
Not smoking	1,808 (36.6)
Smoking	258 (5.2)
Missing	2,872 (58.2)
Previous radiotherapy	
No	3,994 (80.9)
Yes	254 (5.1)
Missing	690 (14.0)
Postoperative radiotherapy planned*	
No	2,188 (44.3)
Yes	155 (3.1)
Missing	2,595 (52.6)
Surgery characteristics	
Year of surgery	
2015	772 (15.6)
2016	987 (20.0)
2017	1,016 (20.6)
2018	1,185 (24.0)
2019	978 (19.8)
Healthcare institution volume (per year)	
<50 implant surgeries	569 (11.5)
50-99 implant surgeries	900 (18.2)
100-200 implant surgeries	1,989 (40.3)
>200 implant surgeries	1,480 (30.0)
Reconstruction indication	
Breast cancer	4,488 (90.9)
Prophylactic mastectomy	450 (9.1)
Laterality	
Unilateral	3,230 (65.4)
Bilateral	1,708 (34.6)
Incision site	
Nipple sparing	1,010 (20.5)
Non-nipple sparing	3,232 (65.5)
Other	256 (5.2)
Missing	440 (8.9)
Plane	
Sub flap	203 (4.1)
Completely covered with PM muscle	2,338 (47.3)
Partially covered with PM muscle	1,623 (32.9)
Other	154 (3.1)
Missing	620 (12.6)
Number of applied ICMs during implant insertion	
<4	947 (19·2)
4	1,735 (35·1)
>4	2,233 (45·2)
Missing	23 (0·5)
ADM/Mesh	
No	3,941 (79·8)
Yes	446 (9·0)
Missing	551 (11·2)
Autologous flap cover	
No	3,845 (77·9)
Yes	426 (8·6)
Missing	667 (13·5)

Values in parentheses are percentages, unless indicated otherwise. IBBR, implant-based breast reconstruction; s.d., standard deviation; ASA, American society of anesthesiologists; i.q.r, interquartile range; PM, pectoralis major; ICMs, infection control measures; ADM, acellular dermal matrix. *Registered since September 2017.

Table S6.2. Patient and surgery characteristics at time of mastectomy and immediate IBBR per reconstruction trajectory

	Direct-to-implant IBBR (n=2,350, 47.6%)	Two-stage IBBR (n=2,588, 52.4%)	p-value
Patient characteristics			
Age (years, s.d.)	48.5 (11.5)	49.9 (11.2)	<0.001
ASA classification			0.197
I	1,487 (63.3)	1,606 (62.1)	
II	783 (33.3)	912 (35.2)	
III+	80 (3.4)	70 (2.7)	
Body Mass Index (kg/m^2, i.q.r.)	23·1 (20.8-26.0)	23.2 (20.7-26.3)	0.894
Smoking status			<0.001
Not smoking	2,109 (89.7)	2,181 (84.3)	
Smoking	241 (10.3)	407 (15.7)	
Previous radiotherapy			0.111
No	2,179 (92.7)	2,428 (93.8)	
Yes	171 (7.3)	160 (6.2)	
Postoperative radiotherapy planned			<0.001
No	2,096 (89.2)	2,476 (95.7)	
Yes	254 (10.8)	112 (4.3)	
Surgery characteristics			
Year of surgery			<0.001
2015	322 (13.7)	450 (17.4)	
2016	456 (19.4)	531 (20.5)	
2017	461 (19.6)	555 (21.4)	
2018	506 (21.5)	679 (26.2)	
2019	605 (25.7)	373 (14.4)	
Healthcare institution volume (per year)			<0.001
<50 implant surgeries	272 (11.6)	297 (11.5)	
50-99 implant surgeries	435 (18.5)	465 (18.0)	
100-200 implant surgeries	744 (31.7)	1,245 (48.1)	
>200 implant surgeries	899 (38.3)	581 (22.4)	
Reconstruction indication			0.306
Breast cancer	2,125 (90.4)	2,363 (91.3)	
Prophylactic mastectomy	225 (9.6)	225 (8.7)	
Laterality			0.175
Unilateral	1,514 (64.4)	1,716 (66.3)	
Bilateral	836 (35.6)	872 (33.7)	
Incision site			<0.001
Nipple sparing	674 (28.7)	460 (17.8)	
Non-nipple sparing	1,428 (60.8)	2,039 (78.8)	
Other	248 (10.6)	89 (3.4)	
Plane			<0.001
Sub flap	133 (5.7)	99 (3.8)	
Completely covered with PM muscle	919 (39.1)	1,686 (65.1)	
Partially covered with PM muscle	1,174 (50.0)	750 (29.0)	
Other	124 (5.3)	53 (2.0)	
Number of applied ICM's during implant insertion			<0.001
<4	621 (26.4)	326 (12.6)	
4	784 (33.4)	958 (37.0)	
>4	945 (40.2)	1,304 (50.4)	
ADM/Mesh			<0.001
No	1,961 (83.4)	2,486 (96.1)	
Yes	389 (16.6)	102 (3.9)	
Autologous flap cover			<0.001
No	1,958 (83.3)	2,402(92.8)	
Yes	392 (16.7)	186 (7.2)	

Values in parentheses are percentages, unless indicated otherwise. IBBR, implant-based breast reconstruction; s.d., standard deviation; ASA, American society of anesthesiologists; i.q.r., interquartile range; PM, pectoralis major; ICMs, infection control measures; ADM, acellular dermal matrix.

Table S6.3. Preoperative patient and surgery characteristics at time of mastectomy and immediate IBBR, per reconstruction trajectory, before and after propensity score matching*

	Before PSM			After PSM		
	Direct-to-implant IBBR n=800 (41.9)	Two-stage IBBR n=1,107 (58.1)	s.m.d.†	Direct-to-implant IBBR n=381 (50.0)	Two-stage IBBR n=381 (50.0)	s.m.d.†
Patient characteristics						
Age (years, s.d.)	48.7 (11.3)	48.8 (11.6)	0.01	48.6 (11.5)	48.7 (11.9)	0.01
ASA classification			0.15			0.04
I	(49.6)	631 (57.0)		194 (50.9)	194 (51.2)	
II	361 (45.2)	435 (39.3)		169 (44.4)	171 (44.9)	
III+	42 (5.2)	41 (3.7)		18 (4.7)	15 (3.9)	
Body Mass Index (kg/m^2, i.q.r.)	23.6 (21.5-26.4)	23.9 (21.5-26.8)	0.07	23.7 (22.0-26.8)	24.0 (21.8-27.0)	0.01
Smoking status			0.10			0.09
Not smoking	714 (89.2)	952 (86.0)		328 (86.1)	340 (89.2)	
Smoking	86 (10.8)	155 (14.0)		53 (13.9)	41 (10.8)	
Previous radiotherapy			0.06			0·01
No	751 (93.9)	1055 (95.3)		354 (92.9)	353 (92.7)	
Yes	49 (6.1)	52 (4.7)		27 (7.1)	28 (7.3)	
Postoperative radiotherapy planned			0.28			<0.01
No	715 (89.4)	1068 (96.5)		357 (93.7)	357 (93.7)	
Yes	85 (10.6)	39 (3.5)		24 (6.3)	24 (6.3)	
Surgery characteristics						
Year of surgery			0.23			0.03
2015	0 (0)	1 (0.1)		0 (0)	0 (0)	
2016	5 (0.6)	4 (0.4)		4(1.0)	4 (1.0)	
2017	131 (16.4)	194 (17.5)		57 (15.0)	60 (15.7)	
2018	348 (43.5)	585 (52.8)		187 (49.1)	181 (47.6)	
2019	316 (39.5)	323 (29.2)		133 (34.9)	136 (35.7)	
Healthcare institution volume (per year)			0.18			0.05
<50 implant surgeries	113 (14.1)	106 (9.6)		37 (9.7)	42 (11.0)	
50-99 implant surgeries	180 (22.5)	233 (21.1)		82 (21.5)	81 (21.3)	
100-200 implant surgeries	357 (44.6)	503 (45.4)		165 (43.3)	160 (42.0)	
>200 implant surgeries	150 (18.8)	265 (23.9)		97 (25.5)	98 (25.7)	
Reconstruction indication			0.05			0.01
Breast cancer	675 (84.4)	912 (82.4)		320 (84.0)	319 (83.7)	
Prophylactic mastectomy	125 (15.6)	195 (17.6)		61 (16.0)	62 (16.3)	
Laterality			0.02			0.01
Unilateral	476 (59.5)	647 (58.4)		215 (56.4)	217 (57.0)	
Bilateral	324 (40.5)	460 (41.6)		166 (43.6)	164 (43.0)	

Values in parentheses are percentages, unless indicated otherwise. *Sub-selection of original non-imputed data, records with any missing preoperative characteristic were excluded. †Standardized mean differences of ≥0·1 represent disbalances in characteristics between groups. PSM, propensity score matching; IBBR, implant-based breast reconstruction; s.m.d., standardized mean difference; s.d., standard deviation; ASA, American society of anesthesiologists; i.q.r., interquartile range

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