BRÖSTCANCER FÖRBUNDET

Forskningsrapport

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Frågeställning:

Vilka är riskfaktorerna för implantatförlust vid primär implantatbaserad bröst-rekonstruktion? Kommer patientrapporterad livskvalitet att ändras huruvida patienter har erhållit strålning efter primär implantatbaserad bröstrekonstruktion jämfört med icke strålade?

Tre frågor till Jana:

Hur kan resultatet av er forskning hjälpa patienterna, rent konkret?

Studien visade att patienter som har erhållit strålning oftare opererade bort implantatet och att sannolikheten för implantatförlust pga kirurgisk komplikation var störst inom de två första åren postoperativt. Trots detta höll sig den egenrapporterade hälsorelaterade livskvaliteten på en stabil nivå efter en medianuppföljning på 10 år. Riskfaktorer för implantatförlust visade sig vara strålbehandling, att vara över 50 år gammal vid det primära rekonstruktionstillfället, BMI över 25 och att ha haft en kirurgisk komplikation i anslutning till rekonstruktionen.

Hur viktigt har stödet från Bröstcancerförbundet varit för er forskning?

Stödet från Bröstcancerförbundet har inneburit att forskarna kunnat få tid avsatt för forskningen, vilket därmed drivit detta projektet till sitt mål. Finansiering har möjliggjort en djupgående analys av den hälsorelaterade livskvaliteten hos bröstcancerpatienter då de själva i lugn och ro, i hemmamiljö, fått utvärdera sina upplevelser av sin kropp och psyke via validerade enkäter.

Vad vill du hälsa alla Bröstcancerförbundets givare?

Tack vare ditt bidrag har vi kunnat nå ut till patienterna själva och efterfråga om egna upplevelser av kroppen, psyket och erfarenheterna efter en bröstrekonstruktion. Detta tror vi i sin tur har egenvärde i att patienterna upplever sig hörda och stärker känslan av att patienten bidrar till forskningen för att förbättra vården för andra kvinnor som i framtiden hamnar i samma sits.

Janas populärvetenskapliga rapport finns att läsa på efterföljande sidor.

Direkt bröstrekonstruktion med implantat hos bröstcancerpatienter: komplikationer, onkologisk säkerhet, negativa effekter av strålbehandling, och livskvalitet

Det har blivit allt vanligare att bröstet återskapas (rekonstrueras) ifall hela bröstet behöver opereras bort (mastektomi) vid bröstcancer: i Stockholm valde 31 % av alla kvinnor som genomgick en mastektomi under 2019 att samtidigt rekonstruera bröstet (så kallad direkt rekonstruktion). Direkt rekonstruktion görs oftast med implantat, försämrar inte prognosen och försvårar inte upptäckten av återfall. Bröstrekonstruktion kan även ske senare, och då kan man använda implantatmetoden eller också en rekonstruktion med förflyttning av kroppsegen vävnad från t ex mage eller rygg.

Större kirurgi, men även svåra sjukdomar, infektioner och trauman frisätter ämnen ur vävnaden som misstänks kunna främja tillväxten av tumörceller. Detta borde kunna betyda att patienter som råkar ut för större komplikationer efter rekonstruktiv kirurgi kan löpa större risk för senare bröstcanceråterfall. Hittills finns bara små studier som dels bekräftar den misstanken, dels förkastar den, och inga stadiga konklusioner har kunnat dras. Det är viktigt att analysera sambandet mellan komplikationer och återfallsrisk i en större grupp kvinnor för att kunna dra säkra slutsatser och därmed eventuellt förstärka förebyggande åtgärder och se över selektionsprocessen inför en direkt bröstrekonstruktion.

De negativa effekterna av strålbehandling på direkt rekonstruktion – i form av komplikationer, sämre kosmetiska resultat och nedsatt livskvalitet – är väl dokumenterade. Åt andra sidan ger direkt rekonstruktion många fördelar och den sammanvägda bedömningen är att en kvinna som planeras för mastektomi ska få information om direkt bröstrekonstruktion även om strålbehandling kan behöva ges. Trots att detta är en del av Sveriges nationella riktlinjer anser flera regioner att strålning är ett hinder mot rekonstruktion, och det finns kirurger som hävdar att det vore oetiskt att erbjuda direkt rekonstruktion om strålbehandling kan bli aktuellt. Detta är en ganska stark kontrast mot andra länder, där direkt rekonstruktion erbjuds i mycket större utsträckning än i Sverige, och det är av stor vikt att undersöka kvinnors egna upplevelser efter rekonstruktion med eller utan strålning. På så sätt ska vi kunna inhämta kunskap om kvinnors erfarenheter som kan vara viktig beslutsgrundande information till nya bröstcancerpatienter och deras behandlande läkare, och sätta dessa erfarenheter i ett samband där vi tittar på hur ofta kvinnor genomgått nya operationer efter sin rekonstruktion, hur vanligt komplikationer är och hur kvinnorna upplever sitt kosmetiska resultat och sin livskvalitet.

För att besvara ovanstående frågor samlas omfattande uppgifter om operationer, behandlingar och resultat i en stor elektronisk databas i Stockholm. Data från alla kvinnor som har genomgått direkt bröstrekonstruktion på grund av bröstcancer i Stockholm mellan 1990 och 2015 registreras, och uppgifter inhämtas genom noggrann granskning av individuella journaler. En del av dessa kvinnor har redan år 2012 besvarat en enkät om sin livskvalitet efter bröstrekonstruktionen, vilket ledde till en viktig publikation om kvinnors syn på detta ingrepp, både med och utan strålbehandling. Resultaten används idag som bas för patientinformation och rekommendationer. Aktuellt samlar vi in enkätsvar från samma kvinnor igen, för att kunna undersöka på vilket sätt livskvalitet och resultat efter rekonstruktionen förändrar sig över tid: målet är att kunna sammanställa kvinnornas egna perspektiv i en vetenskaplig analys för att sedan kunna kommunicera detta både till kvinnor som drabbas av bröstcancer och står inför beslut gällande operation och rekonstruktion, och till vårdpersonal som fungerar som beslutsstöd i denna situation.

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Original Article

Effect of radiotherapy on expanders and permanent implants in immediate breast reconstruction: long-term surgical and patient-reported outcomes in a large multicentre cohort

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Abstract

Background: Current evidence for the effects of radiotherapy (RT) on implant-based immediate breast reconstruction (IBR) is limited by short follow-up and lack of patient-reported outcomes (PROs). It is central to integrate long-term comprehensive outcome data into the preoperative decision-making process. The aim of the present study was to determine long-term surgical outcomes and PROs in relation to RT after implant-based IBR.

Methods: This was a longitudinal cohort study of PRO data obtained in surveys conducted in 2012 and 2020 using the BREAST-Q questionnaire. All women undergoing therapeutic mastectomy and implant-based IBR between 1 January 2007 and 31 December 2011 at four breast centres in Stockholm, Sweden, were identified. The endpoint was implant removal owing to surgical complications or patient preference.

Results: Median follow-up was 120 (range 1–171) months. After 754 IBRs in 729 women, implant removal occurred in 128 (17 per cent): 34 of 386 (8.8 per cent) in the no-RT group, 20 of 64 (31.3 per cent) in the group with previous RT, and 74 of 304 (24.3 per cent) in the postoperative RT group ($P < 0.001$). Implant removal was because of surgical complications in 60 instances (7.9 per cent), and patient preference in 68 (9.0 per cent). The BREAST-Q response rate was 72.2 per cent. Women with previous RT scored lower than those without RT on all scales, apart from psychosocial well-being. Women with postoperative RT scored lower only on physical well-being. No scores in the two RT groups had deteriorated between the survey time points, whereas satisfaction with breasts and overall outcome had decreased in the no-RT group.

Conclusion: Although RT was significantly associated with higher implant removal rates, PROs remained stable over 8 years despite irradiation.

Lay summary

Current evidence for the effects of radiotherapy (RT) on implant-based immediate breast reconstruction (IBR) is limited by short follow-up. The aim was to determine surgical outcomes and patient-reported outcomes (PROs) in relation to RT up to 13 years after implant-based IBR. After 754 implant-based breast reconstructions in 729 women in Stockholm, Sweden, implant removal was more common in irradiated than non-irradiated patients ($P < 0.001$). The response rate to the BREAST-Q questionnaire was 72.2 per cent. Women with previous RT scored lower than those without RT on all scales apart from psychosocial well-being. Women who had postoperative RT scored lower only on physical well-being. Although RT was significantly associated with higher implant removal rates, PROs remained stable despite irradiation.

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Introduction

Breast surgery is an integral part of breast cancer treatment and consists of either breast-conserving surgery or mastectomy. In the case of mastectomy, immediate breast reconstruction (IBR) can be offered. In IBR, implant-based reconstruction using either permanent implants or tissue expanders is the most common method[1–4]. National IBR rates increased from 10 to 23 per cent in the UK between 2010 and 2014, and from 21.7 to 26.6 per cent in the USA between 2010 and 2013[5,6]. In Sweden, the national IBR rate increased from 6 to 15 per cent between 2010 and 2019, with the Stockholm area reporting a 31 per cent rate[7]. Breast reconstruction improves various aspects of health-related quality of life (HRQoL), and patients having mastectomy should be offered reconstructive alternatives according to national and international guidelines[7–13].

Radiotherapy (RT) is one of the most important factors negatively affecting the outcome of IBR. There is a higher risk of postoperative complications after RT, such as infection, wound dehiscence, seroma formation, and skin flap necrosis, potentially leading to implant loss. Moreover, long-term consequences such as tissue fibrosis and capsular contracture increase the need for surgical revisions and have a negative impact on HRQoL[14–29]. Postmastectomy radiotherapy (PMRT) reduces the 5-year local recurrence risk of patients with node-positive disease by 17 per cent and improves overall survival by 4.4 per cent[24–28], and the proportion of patients receiving RT after IBR has increased over time. PMRT is also associated with a significantly higher risk of surgical complications in direct-to-implant prepectoral breast reconstruction. BREAST-Q scores did not differ significantly in recent studies[30,31] comparing prepectoral and subpectoral implant placement.

HRQoL is an important parameter to investigate in patients with breast cancer to assess adjustment problems and decisional regret after surgery[29]. The BREAST-Q questionnaire is a validated, condition-specific instrument measuring patient-reported outcomes (PROs) after breast surgery, and includes a specific module for implant-based breast reconstruction[32]. RT has been associated with significantly lower scores on all five BREAST-Q scales and an increased risk of implant failure after a median follow-up of 3 years[25].

The aim of the present study was to provide long-term data on the effect of RT on implant removal, differentiating between those removed owing to surgical complications and implants removed based on patient preference. A further aim was to provide data on the longitudinal development of PROs over time.

Methods

The study population has been reported in an earlier publication and included all prospectively registered consecutive patients with breast cancer who underwent mastectomy and implant-based IBR between 1 January 2007 and 31 December 2011 at Stockholm's four main hospitals (Capio St Göran's Hospital, Karolinska University Hospital, Southern General Hospital, and Danderyd Hospital)[25]. The study was approved by the ethical review board at Karolinska Institutet (2015/1183-31/4).

Surgical methods and outcomes

All patients were discussed at preoperative and postoperative multidisciplinary team conferences. The choice of skin- or nipple-sparing mastectomy techniques and the type of implant was made by the surgeons. During the study interval, breast implants were always placed in a subpectoral pocket with the aim of achieving full muscle coverage, using the pectoralis major muscle and parts of the anterior serrate and abdominal external oblique muscles. No meshes or acellular dermal matrices were used. Implants were categorized into temporary expanders, permanent expanders, and permanent implants. Importantly, only reconstructions using temporary expanders were preplanned as two-stage procedures. Any exchange of permanent expander to another implant was not preplanned but based on surgeon and patient judgement several months after operation. If the result was satisfactory, the filling device of the permanent expander was removed after adjustment of the final volume. No patient was preplanned for an exchange from an expander or implant to an autologous reconstruction (immediate-delayed reconstruction). Further reconstruction by autologous methods was decided on during the postoperative period, and depended on the reconstructive results and aims. Autologous flap reconstruction was either based on pedicled flaps, such as latissimus dorsi flaps with or without implant, or free autologous flaps, for example deep inferior epigastric perforator flaps.

Revisional surgery comprised ipsilateral IBR-associated procedures such as capsulectomy, implant exchange, abdominal advancement flaps, nipple reconstruction, liposuction, lipofilling, and scar revision. Contralateral symmetrizing procedures included mastopexy, breast reduction, and implant-based augmentation.

Major postoperative surgical complications included reoperations owing to infection, wound dehiscence, skin flap necrosis or bleeding, but also intravenously administered antibiotic treatment, thus necessitating readmission or prolonged hospital stay. Minor surgical complications were defined as those not necessitating readmission to hospital, and included any degree of clinical suspicion of infection, seroma, delayed wound healing or haematoma. Infection was categorized in three levels: clinical signs of infection without confirmatory tests; laboratory-confirmed infection (raised levels of C-reactive protein or positive bacterial cultures); and infection treated with intravenous antibiotics.

Data on tumour stage, oncological treatment including RT, IBR, complications and reoperations, revisional surgery, conversion to autologous reconstruction, recurrence, death, and cause of death were obtained by individual medical chart review and registered in the Stockholm Breast Reconstruction Database. RT data included irradiation field, number of fractions, cumulative dose, and date of administration of last fraction. The standard cumulative dose of radiation was 50 Gy in 25 fractions.

Patient-reported outcomes

The BREAST-Q questionnaire has been validated for the assessment of HRQoL in European women[33,34]. The reconstruction module includes scales for satisfaction with breasts, satisfaction with overall outcome, and for psychosocial, sexual, and physical well-being. Each scale produces an independent score from 0 to 100, transformed via the Qscore™ software (RUMM Laboratory Pty Ltd, Duncraig, Australia), where lower values indicate lower satisfaction or well-being. To enable comparison with the 2012 scores from the same cohort, version 1.0 of the BREAST-Q was used.

A survey was done first in 2012 and repeated 8 years later in February 2020. Patients who had died and those who had had the implant removed according to the medical chart review were not sent the questionnaire. Questionnaires were sent by mail, and one reminder was issued after 2 months. In bilateral breast

cancer, one questionnaire was sent per patient as the BREAST-Q questions are designed to account for both breasts.

Statistical analyses

The primary endpoint was implant removal either due to surgical complication or patient preference, with or without a simultaneous or subsequent autologous reconstruction. The number of unplanned reoperations was also reported. Patients not reaching the primary endpoint were censored at the date of last follow-up, set as the date of medical chart review or date of death.

Categorical variables are reported as numbers and percentages, and continuous variables as mean(s.d.) or median (range). The normality of distribution of all continuous variables was tested by the Shapiro–Wilk test. Pearson's χ^2 test and Fisher's exact test were used to analyse the distribution of categorical variables between the groups, and the Kruskal–Wallis test for continuous variables.

Between-group comparisons for each BREAST-Q scale were done by simple linear regression. For within-group differences between the two surveys, mean questionnaire scores for each scale were compared using repeated-measures analysis through paired-samples *t* test. The Shapiro–Wilk test and visual inspection of histograms, normal Q-Q plots, and box plots showed normally distributed differences between the BREAST-Q-scores at the two time points. Non-responder analysis was undertaken using Pearson's χ^2 test.

Risk factors for overall implant removal were tested by means of univariable and multivariable Cox proportional hazards regression. The proportional hazards assumption was checked using statistical testing and graphical diagnostics based on the global test of Schoenfeld's residuals. Results are presented as hazard ratios (HRs) with 95 per cent confidence intervals.

All reported *P* values are two-tailed, and $P < 0.050$ was considered statistically significant. Statistical analyses were performed using SPSS® version 26 (IBM, Armonk, NY, USA) and Stata® version 16 (StataCorp, College Station, TX, USA). The established database is registered and managed in accordance with the European General Data Protection Regulation.

Results

Overall, 729 women with 754 implant-based IBRs were included. Three groups of women were identified, those who had not received any radiotherapy (no-RT group; 386 IBRs), those who had received RT to the breast and/or chest wall before IBR, that is after previous breast-conserving surgery or for other malignancies (previous RT group; 64), and those who had postoperative RT to the chest wall with or without additional regional RT (postoperative RT group; 304). Median follow-up was 120 (range 1–171) months and did not differ between groups (124, 123, and 119 months respectively; $P = 0.111$). The total number of breast cancer recurrences was 109; there were 22 local, 24 regional, and 58 distant recurrences, and five patients were diagnosed with multiple recurrences. Patient and tumour characteristics are shown in *Table 1*. Among those who had received RT previously, 57 had been irradiated for a previous ipsilateral breast cancer and one for lung cancer. The indication for previous RT in the remaining six patients was unknown. One previously irradiated patient (whole-breast irradiation) received postoperative regional RT.

Implant removal and reoperations

There were 128 instances of implant removal (17.0 per cent), after which 72 breasts were reconstructed using autologous tissue in the same session (54) or at a later stage (18). Implant removal was undertaken after 46 reconstructions with temporary expanders (18.0 per cent), 62 (19.3 per cent) with permanent expanders, and 20 (11.3 per cent) with permanent implants ($P = 0.066$). Implant removal was due to surgical complications in 60 breasts (7.9 per cent), 18 (30.0 per cent) of which underwent further reconstruction with autologous tissue at a later stage. Implant removal was because of patient preference in 68 breasts (9.0 per cent), 54 (79.4 per cent) of which underwent autologous breast reconstruction in the same session. Overall, implant removal was significantly more common in irradiated IBRs: 31.3 per cent in the previous RT group, 24.3 per cent in the postoperative RT group, and 8.8 per cent in the no-RT group ($P < 0.001$). The likelihood of implant removal owing to surgical complications was higher within the first 2 years after IBR, whereas the likelihood of implant removal because of patient preference increased after about 7 years after IBR (*Fig. 1*). The median interval from IBR to implant removal was 11 (range 0–144) months if due to surgical complications, but 116 (11–157) months if the reason was patient preference ($P < 0.001$). There was a trend towards shorter implant removal time in the previous RT group for both categories (2 and 97 months respectively). Independent risk factors associated with implant removal for any reason were previous RT (HR 4.65, 95 per cent c.i. 2.55 to 8.45) or postoperative RT (HR 3.42, 2.24 to 5.23), age above 50 years at the time of IBR, BMI of at least 25 kg/m^2, and any (minor or major) surgical complication after IBR (*Table 2*). Having a permanent implant was negatively associated with implant removal, whereas no association was found with implant volume.

Apart from preplanned revision in patients who had initially received a temporary tissue expander, any other ipsilateral revisional surgery was defined as an unplanned reoperation. The main difference was seen for three or more unplanned reoperations, which occurred in 98 of 751 IBRs: 30 of 384 (7.8 per cent) in the no-RT group, 5 of 64 (7.8 per cent) in the previous RT group, and 63 of 303 (20.8 per cent) in the postoperative RT group ($P < 0.001$). Although all RT groups had a median of one unplanned operation, the range varied (0–6, 0–5, and 0–8, respectively; $P = 0.001$). The median time between completion of RT and the first unplanned reoperation was 12 (1–128) months. The median interval between all IBRs and the first unplanned reoperation was 11 (2–124) months in the no-RT group, 11 (2–138) in the previous RT group, and 16 (2–132) in the postoperative RT group ($P < 0.001$).

Surgical complications

Minor surgical complications occurred after 223 IBRs (29.6 per cent): 110 (28.6 per cent) in the no-RT group, 27 (42.2 per cent) in the previous RT group, and 86 (28.4 per cent) in the postoperative RT group ($P = 0.055$). Major surgical complications occurred after 40 IBRs (5.3 per cent): 21 (5.5 per cent) in the no-RT group, four (6.3 per cent) in the previous RT group, and 15 (5.0 per cent) in the postoperative RT group ($P = 0.703$). Thirty-two patients had reoperations for postoperative complications within 30 days: 18 (4.7 per cent) in the no-RT group, four (6.3 per cent) in the previous RT group, and 10 (3.3 per cent) in the postoperative RT group ($P = 0.477$). Of the patients with major surgical complications, 17 had undergone axillary clearance, 18 sentinel node biopsy only, and five did not have surgery to the axilla ($P = 0.158$). The distribution was similar for minor surgical complications.

Table 1 Patient and tumour characteristics by radiotherapy group

	No RT ($n = 386$)	Previous RT ($n = 64$)	Postoperative RT ($n = 304$)	P‡
Age (years)*	50 (24–77)	55 (28–75)	46 (21–74)	<0.001§
Invasiveness				<0.001
Invasive	259 (44.7)	45 (7.8)	275 (47.5)	
In situ only	124 (72.5)	18 (10.5)	29 (17.0)	
Tumour size (mm)*†	23 (1–125)	14 (2–120)	35 (1–190)	<0.001§
Hospital				<0.001
A	159 (43.7)	26 (7.1)	179 (49.2)	
B	82 (62.6)	8 (6.1)	41 (31.3)	
C	67 (63.8)	10 (9.5)	28 (26.7)	
D	78 (50.6)	20 (13.0)	56 (36.4)	
Smoker				0.490
Yes	61 (55.0)	9 (8.1)	41 (36.9)	
No	298 (49.3)	47 (7.8)	259 (42.9)	
BMI (kg/m^2)*	23.8 (3.6)	23.7 (3.0)	24.3 (3.8)	0.401§
Lymph node status				<0.001
Positive	51 (23.6)	1 (0.5)	164 (75.9)	
Negative	304 (64.8)	28 (6.0)	137 (29.2)	
Type of implant				0.005
Temporary expander	133 (52.0)	16 (6.3)	107 (41.8)	
Permanent expander	152 (47.6)	21 (6.6)	146 (45.8)	
Permanent implant	98 (56.3)	26 (14.9)	50 (28.7)	
Preoperative chemotherapy				<0.001
Yes	7 (9.1)	1 (1.3)	69 (89.6)	
No	379 (56.1)	62 (9.2)	235 (34.8)	
Plastic surgeon present at IBR				0.285
Yes	184 (54.3)	26 (7.7)	129 (38.1)	
No	202 (48.7)	38 (9.2)	175 (42.2)	
Adjuvant chemotherapy				<0.001
Yes	138 (41)	20 (6)	175 (53)	
No	248 (59)	42 (10)	128 (31)	
Adjuvant endocrine therapy				0.135
Yes	228 (49)	37 (8)	204 (43)	
No	151 (55)	26 (10)	96 (35)	
Implant volume (ml)*	350 (100–650)	305 (110–550)	350 (54–660)	0.369§

Data represent immediate breast reconstruction (IBR) procedures. Values in parentheses are percentages unless indicated otherwise. *Values are median (range). # Values are mean(s.d.). †Invasive tumour size if invasiveness was diagnosed, leaving associated *in situ* disease unacknowledged; extension reported for pure *in situ* disease; preoperative clinical tumour size for patients who had preoperative chemotherapy. RT, radiotherapy. ‡Pearson's χ^2 test or Fisher's exact test. §except Kruskal–Wallis test. Most of this table was published previously[25].

Patient-reported outcomes

Questionnaires were sent out to 575 patients, 390 of whom responded (*Fig. S1*). Two patients who returned the questionnaire declined to participate in the study and were counted as non-responders. Even though most implant removals had been identified by scrutiny of medical records, 35 patients returned the questionnaire stating that they had undergone implant removal or autologous reconstruction and could not answer the questions. These patients were not included in the PROs analysis. The resulting response rate was 72.2 per cent. A total of 382 women responded to the surveys both in 2012 and in 2020. A responder analysis showed no differences in demographics and tumour characteristics between responders and non-responders, except for a higher proportion of smokers (12.3 *versus* 19.3 per cent; $P = 0.045$) and of women with breast cancer recurrence (5.6 *versus* 12.7 per cent; $P = 0.006$) among non-responders.

In the 2020 survey, the previous RT group scored significantly lower than the no-RT group in all scales with the exception of psychosocial well-being (*Table 3*). The postoperative RT group, however, only reported significantly lower scores than the no-RT group regarding physical well-being. Taking into account the survey from 2012, longitudinal within-group analyses showed a significant decrease over time in mean scores for satisfaction with breasts and with overall outcome in the no-RT group only ($P < 0.001$ and $P = 0.004$). A statistically significant increase in mean scores for psychosocial well-being was seen in women who underwent postoperative RT ($P = 0.011$) (*Table 4*).

Discussion

This large cohort study, with long-term longitudinal follow-up, confirmed the negative effect of irradiation on surgical outcomes and PROs after IBR. The surgical results were differentiated according to implant removal owing to surgical complications and that because of patient preference. Although the former was significantly more relevant in the early years following IBR, the latter became more common with longer follow-up. Even though irradiated individuals reported worse PROs than those who had not undergone RT, scores remained stable over 8 years.

The assessment of PROs by means of appropriate validated instruments is essential in order to gauge surgical results from the patients' perspective[35]. Only a few studies have reported longitudinal analyses of PROs reflecting the adverse effects of RT on implant-based IBR, often hampered by small and heterogeneous cohorts with a limited follow-up. In addition, most studies[8,23,36–40] had a single cross-sectional design with no longitudinal data for comparison. It has been suggested that aesthetic and functional results after implant-based IBR deteriorate

Table 2 Univariable and multivariable Cox regression analyses with implant removal for any reason as outcome variable, with or without a contemporary or subsequent autologous reconstruction. Numbers based on complete cases only.

	No. of IBRs	No. of events	Univariable analysis		Multivariable analysis	
	(*n* = 715)	(*n* = 125)	Hazard ratio	*P*	Hazard ratio	*P*
RT group						
No RT	362	34	1.00 (reference)		1.00 (reference)	
Previous RT	54	18	4.32 (2.44, 7.65)	<0.001	4.65 (2.55, 8.45)	<0.001
Postoperative RT	299	73	2.87 (1.91, 4.31)	<0.001	3.42 (2.24, 5.23)	<0.001
Smoker						
No	605	98	1.00 (reference)		1.00 (reference)	
Yes	110	27	1.59 (1.04, 2.44)	0.033	1.33 (0.86, 2.06)	0.199
BMI (kg/m^2)						
<25	460	63	1.00 (reference)		1.00 (reference)	
≥ 25	255	62	1.96 (1.38, 2.78)	<0.001	1.49 (1.03, 2.14)	0.034
Age at IBR (years)						
≤40	147	17	1.00 (reference)		1.00 (reference)	
41–50	271	41	1.35 (0.77, 2.38)	0.295	1.54 (0.86, 2.75)	0.146
51–65	240	53	2.05(1.19, 3.54)	0.010	2.59 (1.43, 4.67)	0.002
≥66	57	14	2.41 (1.19, 4.89)	0.015	2.63 (1.23, 5.61)	0.012
Type of implant						
Temporary expander	236	44	1.00 (reference)		1.00 (reference)	
Permanent expander	311	61	1.06 (0.72, 1.57)	0.754	0.92 (0.62, 1.38)	0.691
Permanent implant	168	20	0.59 (0.35, 0.99)	0.047	0.47 (0.27, 0.83)	0.009
Surgical complications						
None	464	48	1.00 (reference)		1.00 (reference)	
Minor	212	58	2.94 (2.00, 4.31)	<0.001	2.76 (1.87, 4.08)	<0.001
Major	39	19	7.21 (4.24, 12.28)	<0.001	8.84 (5.09, 15.36)	<0.001

Values in parentheses are 95 per cent confidence intervals. Analyses include only patients with no missing information on all co-variables in both models.
IBR, immediate breast reconstruction; RT, radiotherapy.

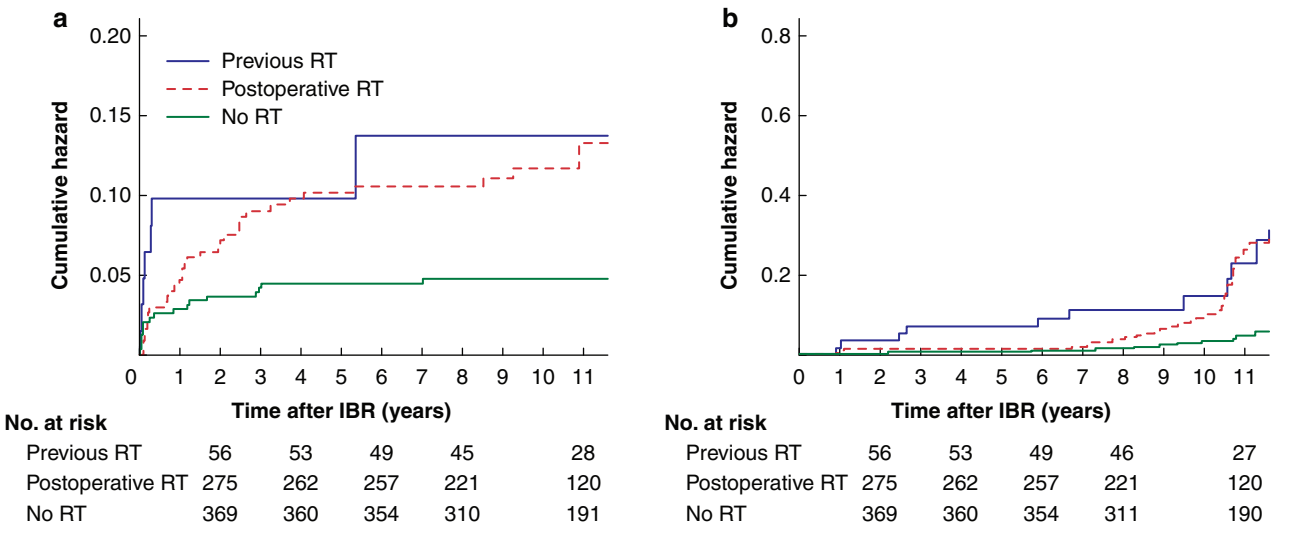

Fig. 1 Cumulative hazard curves showing the likelihood of implant removal owing to **a** surgical complications and **b** patient preference. RT, radiotherapy. **a** $P = 0.002$, **b** $P < 0.001$ (log rank test)

over time, underlining the importance of evaluating long-term implant removal rates, conversion to autologous reconstruction, as well as longitudinal PROs[41]. The present study included a relatively small number of women with previous RT, which was associated with the highest implant removal rate. This is in line with previously published results, suggesting that history of RT is an independent risk factor for IBR failure regardless of surgical technique[42–45]. In accordance with earlier conclusions, autologous alternatives for immediate or delayed breast reconstruction should be strongly considered in this setting[25].

Some authors have suggested that delayed autologous reconstruction is the most sensible approach in the setting of PMRT[46]. Other studies have shown that implant-based IBR can be performed successfully after PMRT, whereas others have advised a delayed-immediate reconstructive strategy[40,47–49]. Clinical guidelines are still lacking and many centres rely on a varying concoction of expert opinion, local tradition and resources, surgeon preferences or patient choice, resulting in a discrepancy in reconstructive strategies and outcome.

Table 3 Mean BREAST-Q scores on each subscale in 2020, and comparison between radiotherapy groups by linear regression

BREAST-Q subscale	No. of responses	Crude analysis		Adjusted analysis†	
		Mean score*	P	Mean score	P
Satisfaction with breasts					
No RT	225	54.63 (52.35, 56.48)	Reference	51.70	Reference
Previous RT	21	43.95 (35.53, 52.24)	0.001	41.06	0.001
Postoperative RT	144	52.73 (47.43, 57.95)	0.218	49.20	0.219
Satisfaction with overall outcome					
No RT	225	66.36 (63.70, 68.81)	Reference	70.02	Reference
Previous RT	21	53.16 (42.71, 63.35)	0.001	57.81	0.001
Postoperative RT	144	66.20 (59.77, 64.84)	0.995	69.64	0.995
Psychosocial well-being					
No RT	224	71.32 (68.14, 74.06)	Reference	62.45	Reference
Previous RT	21	65.83 (53.62, 77.51)	0.222	55.94	0.157
Postoperative RT	142	70.07 (62.53, 77.24)	0.503	61.42	0.662
Sexual well-being					
No RT	212	53.13 (49.56, 56.56)	Reference	49.13	Reference
Previous RT	21	39.03 (25.10, 52.97)	0.009	35.38	0.012
Postoperative RT	138	48.95 (40.07, 57.84)	0.135	44.80	0.129
Physical well-being					
No RT	225	81.03 (79.16, 83.10)	Reference	72.57	Reference
Previous RT	21	74.86 (67.0, 82.74)	0.038	65.05	0.014
Postoperative RT	144	76.14 (71.09, 81.19)	0.001	68.13	0.005

Values in parentheses are 95 per cent confidence intervals. *Mean score on scale ranging from 0 to 100. †Adjusted for age (categorical) and year of immediate breast reconstruction. RT, radiotherapy.

Table 4 Mean BREAST-Q scores by radiotherapy group for surveys in 2012 and 2020

BREAST-Q subscale	No. of patients in analysis	Mean score 2012	Mean score 2020	Change in mean	P*
Satisfaction with breasts					
No RT	217	59.30	55.30	−3.97	< 0.001
Previous RT	21	46.50	43.50	−3.00	0.279
Postoperative RT	144	52.04	52.64	0.60	0.615
Satisfaction with overall outcome					
No RT	216	71.36	67.68	−3.68	0.004
Previous RT	21	58.59	52.77	−5.82	0.242
Postoperative RT	144	65.79	66.66	0.87	0.554
Psychosocial well-being					
No RT	203	73.12	72.38	−0.75	0.590
Previous RT	21	61.41	62.41	1.00	0.752
Postoperative RT	144	65.70	69.81	4.11	0.011
Sexual well-being					
No RT	177	56.50	54.53	−1.97	0.189
Previous RT	21	42.57	35.48	−7.10	0.053
Postoperative RT	138	49.06	49.21	0.15	0.938
Physical well-being					
No RT	203	80.23	81.09	0.87	0.360
Previous RT	21	73.36	75.09	1.73	0.457
Postoperative RT	144	76.00	76.24	0.24	0.828

RT, radiotherapy. *Paired-samples *t* test.

Surgical complications were identified as an independent risk factor for IBR removal. The proportion of surgical complications did not differ between the cohorts, and the rate of postoperative infections is comparable to reported values after implant-based IBR[50,51]. Although a previous publication[25] on the same cohort reported higher postoperative infection rates in previously irradiated patients, the present long-term follow-up could not confirm these findings, possibly owing to late postoperative infections in the context of revisional surgery in the postoperative RT group. A meta-analysis by Fuertes and colleagues[52] showed a trend towards higher IBR failure rates after RT to temporary tissue expanders than to permanent implants, which was confirmed in the present analysis. The use of permanent implants could, however, be a surrogate marker for smaller breast volumes and, therefore, reconstructions at lower risk of complications. Unfortunately, information on breast volume or surgical specimen weight was not available for the present cohort. Patients with permanent implants or expanders underwent unplanned reoperations more often than those with a temporary expander, possibly because permanent expanders are commonly treated as temporary devices and used in a two-stage setting. One important factor to consider is that any reoperation entering the implant cavity poses a new risk of postoperative complications and IBR removal. Thus, an accumulation of IBR removals can be expected in patients who have undergone many reoperations.

Although the present study showed no significant changes over time in PROs in the irradiated groups, others[8,53–55] have reported that PROs improve over time when measured at two different time points. It must be considered that women suffering implant loss or choosing a new breast reconstruction using autologous tissue are likely to have experienced a decline in IBR-related PRO scores over time. It is a limitation of this study that patients could not report PROs after implant removal because the BREAST-Q module is impossible to complete for someone who has suffered implant loss or chosen an autologous reconstruction. It should also be noted that women receiving or having received RT are often those with more severe disease, and potentially more affected by their diagnosis and treatment. In agreement with this, Hamann and colleagues[56] reported that women with a history of RT, often suffering recurrent disease, have a significantly poorer quality of life than those who have received RT or have not had any RT.

The main strength of this study is its longitudinal design and long follow-up time with high response rates, allowing long-term evaluation of both IBR removal and PROs. An additional strength is the clinical data obtained from medical charts leading to minimal missing data on tumour characteristics, and detailed information on complications, reoperations, and IBR removal. Furthermore, all women included in this study had surgery in Stockholm, which reduces regional variations in treatment, selection criteria, or preoperative patient information regarding IBR.

The present results underline that previously irradiated patients should be evaluated primarily for autologous reconstructive alternatives. A negative impact of both previous and postoperative RT on IBR removal rates, unplanned reoperations, and PROs was confirmed. Long-term PROs in irradiated patients did not deteriorate, but remained stable over during follow-up.

Supplementary material

Supplementary material is available at *BJS* online.

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