

Forskningsrapport



Huvudsökande:

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Frågeställning:

Hur stor är risken för cancerrecidiv vid bröstrekonstruktion med egen vävnad?

Tre frågor till Maria:

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

Någonstans mellan 20 och 30 procent av alla kvinnor som får bröstcancer genomgår en mastektomi, där man tar bort hela bröstet/brösten. Många av dessa kvinnor önskar rekonstruktion vilket kan göras med olika metoder; antingen med hjälp av implantat eller med hjälp av egen vävnad. Olika metoder har sina för- och nackdelar. Frågetecknen har funnits, huruvida rekonstruktioner med egen vävnad skulle öka risken för återfall i bröstcancer.

Den studie som gjordes på Akademiska sjukhuset i Uppsala, jämförde 225 kvinnor som genomgick rekonstruktion med egen vävnad från buken med 450 kvinnor som fick rekonstruktion med implantat alternativt ingen rekonstruktion. I denna studie kunde man inte påvisa någon skillnad mellan de två jämförda grupperna, vad gäller återfall i bröstcancer. Det här resultatet hjälper oss som vårdgivare att på ett säkert sätt kunna erbjuda kvinnor olika typer av bröstrekonstruktion utifrån de önskemål och fysiska förutsättningar varje individ har.

Hur viktigt har stödet från Bröstcancerförbundet varit för er forskning?

Stödet från Bröstcancerförbundet har möjliggjort denna studie som är en del i avhandlingen för en av klinikens doktorander.

Vad vill du hälsa alla Bröstcancerförbundets givare?

Genom att ge ett bidrag till Bröstcancerförbundet hjälper du till att säkerställa att vi kan fortsätta forskningen, inte bara kring bröstcancer i sig, utan det omhändertagande och den vård vi vill ge kvinnor efter att deras cancer färdigbehandlad.

Marias populärvetenskapliga rapport finns att läsa på efterföljande sidor.

Risk för cancerrecidiv vid bröstrekonstruktion med egenvävnad från buken

Populärvetenskaplig sammanfattning

Bakgrund

Någonstans mellan 20 och 30 procent av alla kvinnor som får bröstcancer genomgår en mastektomi, där man tar bort hela bröstet/brösten. Flera av dessa kvinnor önskar rekonstruktion vilket kan göras med olika metoder; antingen med hjälp av implantat eller med hjälp av egen vävnad. Olika metoder har sina för- och nackdelar. Frågetecken har funnits, huruvida rekonstruktioner med egen vävnad skulle öka risken för återfall i bröstcancer. Det har funnits teorier om att större kirurgi såsom bröstrekonstruktioner med egenvävnad kan aktivera mikrometastaser och orsaka recidiv eller spridning av cancer. Målet med den här studien var att utvärdera om en bröstrekonstruktion med vävnad från buken, ökar risken för återfall i bröstcancer, eller påverkar dödligheten för kvinnor som tidigare behandlats för bröstcancer.

Metod

Den studie som gjordes på Akademiska sjukhuset i Uppsala, jämförde 225 kvinnor som genomgått bröstrekonstruktion med egen vävnad från buken med 450 kvinnor som genomgått rekonstruktion med implantat alternativt inte genomgått bröstrekonstruktion.

Grupperna liknande varand (var matchade) avseende år för diagnos (+/- 3 år), ålder vid diagnos (+/- 5 år), typ av cancer och hemregion. Man tittade på lokala återfall eller spridning av cancer, samt den totala överlevnaden. Den totala risken för sjukdomsåterfall och dödlighet analyserades och man gjorde uppskattningar av relativa risker. Kvinnorna följdes upp över en median tid på 125 månader.

Resultat

Vi såg ingen ökad risk för återfall i bröstcancer vid bröstrekonstruktion med egenvävnad från buken och inte heller någon ökad dödlighet i denna grupp. Man kan med andra ord utifrån den utförda studien erbjuda olika former av bröstrekonstruktion utan att det ökar risker för återfall.

Survival and risk of breast cancer recurrence after breast reconstruction with deep inferior epigastric perforator flap

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Background: Women who undergo autologous breast reconstruction have been reported to have an increased risk of breast cancer recurrence compared with those who have mastectomy alone. It has been suggested that more extensive surgery possibly activates dormant micrometastases. The aim of this study was to evaluate whether delayed unilateral deep inferior epigastric perforator (DIEP) flap reconstruction after mastectomy increases the risk of breast cancer recurrence or affects mortality among women previously treated for breast cancer.

Methods: This was a matched retrospective cohort study including women with a previous unilateral invasive breast cancer who received a delayed DIEP flap breast reconstruction and a control cohort of individually matched women with unilateral breast cancer who underwent mastectomy but no autologous breast reconstruction. Matching criteria comprised: year of diagnosis (± 3 years), age at diagnosis (± 5 years), type of cancer and demographic region. The primary endpoints were local recurrence or distant metastasis, and overall mortality was a secondary endpoint. Absolute risk of recurrent disease and mortality was analysed, and relative risks were estimated using Cox proportional hazards analysis.

Results: There were 225 women in the DIEP cohort and 450 in the no-DIEP cohort. The median follow-up time was 125 months. There was no difference in absolute risk of recurrence between the cohorts. The hazard ratio for breast cancer recurrence in DIEP *versus* no-DIEP cohorts was 0.76 (95 per cent c.i. 0.47 to 1.21).

Conclusion: There is no increased risk in breast cancer recurrence after delayed DIEP flap reconstruction compared with mastectomy alone.

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Introduction

Breast cancer is the most common cancer affecting women worldwide, representing approximately 25 per cent of all cancers in women¹. The incidence of breast cancer is increasing and women with a history of breast cancer now constitute the largest group of cancer survivors². Breast-conserving surgery (BCS) is becoming increasingly common, but mastectomy is still performed in around 23–33 per cent of patients^{3,4}.

Many women who undergo mastectomy are interested in having a breast reconstruction, either directly or at a later stage⁵. Breast reconstruction can be performed using autologous tissue, implants or a combination of these. Previous studies^{6,7} have demonstrated that implant-based breast reconstruction does not increase the risk of breast cancer recurrence, nor does it have a negative effect on adjuvant oncological treatments. Isern and colleagues⁸ reported an increased risk of recurrence among women

who underwent delayed large-flap breast reconstructions with autologous tissue compared with women who underwent mastectomy without reconstruction. This potential association has, however, not yet been replicated⁹. Reconstruction may delay or hide recurrence; in addition, extensive reconstructive surgery has been suggested to possibly activate dormant micrometastases, resulting in early local recurrence or distant metastatic disease^{10–13}.

As autologous reconstructions are becoming increasingly popular, it is pertinent to clarify any potential associations between autologous breast reconstruction and cancer recurrence. The aim of the present study was to assess whether there is an increase in breast cancer recurrence and decrease in survival after delayed breast reconstruction with deep inferior epigastric perforator (DIEP) flap surgery. The DIEP cohort was compared with an individually matched cohort of patients who did not receive an autologous reconstruction after mastectomy.

Methods

The study was approved by the Regional Ethics Committee in Uppsala (2014/354).

All consecutive women who had a delayed unilateral DIEP flap reconstruction after mastectomy for breast cancer between January 2000 and December 2009 were identified from the local operation registry at Uppsala University Hospital (UU). This hospital is a tertiary referral centre, and is the only centre providing microsurgical breast reconstructions for a region of approximately two million people. DIEP flap reconstruction was defined as delayed when there was an interval of more than 6 months between mastectomy and reconstruction. Patients who had a bilateral DIEP flap reconstruction were excluded as they have significantly longer operating times and this group also includes prophylactic procedures. To be eligible for inclusion in the study, the primary breast cancer surgery had to be performed after 1992, when the Regional Breast Cancer Registry (RBCR) was created, to allow for the matching of control (no DIEP) patients. Patients in whom BCS had initially been attempted were eligible for inclusion if mastectomy was performed within 3 months after BCS. In these situations, residual tumour tissue after BCS was the reason for this mastectomy; it was considered as a part of the primary surgery. All patients who underwent reconstruction at UU were included, even if the mastectomy had been performed at another hospital, given that the other hospital was within the geographical region covered by UU.

The following exclusion criteria were applied to both cohorts: other cancer diagnoses within 5 years before primary breast cancer surgery, which could influence survival and represent a selection bias for not receiving a DIEP flap; reconstruction for breast cancer recurrence that needed a DIEP flap for chest wound coverage (not breast reconstruction); any preoperative chemotherapy; distant metastasis other than regional lymph node metastasis at the time of breast cancer diagnosis or before DIEP flap reconstruction; immediate DIEP flap reconstruction; and less than 6 months between mastectomy and DIEP reconstruction (*Fig. 1*). Flap loss was also an exclusion criterion because all such patients underwent a rescue breast reconstruction with a latissimus dorsi flap within days of flap loss. Of eight excluded women who lost a DIEP flap, four were also excluded for one or more of the following reasons: primary surgery outside the region; BCS; breast cancer diagnosis before 1992; no invasive breast cancer; distant disease at the time of breast cancer diagnosis; early reconstructions; bilateral reconstruction; and neoadjuvant therapy. They were not eligible for the study but, in addition, they lost the DIEP flap. This left a total of four women with flap loss for a sensitivity analysis.

Matching of cohorts

For each patient who underwent DIEP flap reconstruction, six patients without an autologous reconstruction were selected randomly from the RBCR, with the intention of having at least two matched patients for each patient in the DIEP group, after applying the exclusion criteria. The RBCR has been linked to the national Swedish Breast Cancer Registry since 2008 and covers 97 per cent of patients with breast cancer¹⁴.

The no-DIEP cohort comprised women who had undergone mastectomy, matched for year of cancer diagnosis (\pm 3 years), age at cancer diagnosis (\pm 5 years), type of cancer (invasive cancer *versus* ductal carcinoma *in situ*) and demographic region. The medical records were checked to verify that the patients had invasive cancer and not carcinoma *in situ*.

After applying the exclusion criteria, there were two valid matched patients without an autologous reconstruction for each patient in the DIEP group, of whom at least one had no reconstruction at all. To avoid biased results with a large number of women with early recurrence in the no-DIEP cohort, a reference date was created. The reference date for the DIEP group was the date of breast reconstruction. All patients in the no-DIEP cohort had to be free from recurrence for at least the interval between mastectomy and reconstruction of the matched patient in the DIEP group.

Breast reconstruction with deep inferior epigastric perforator flap

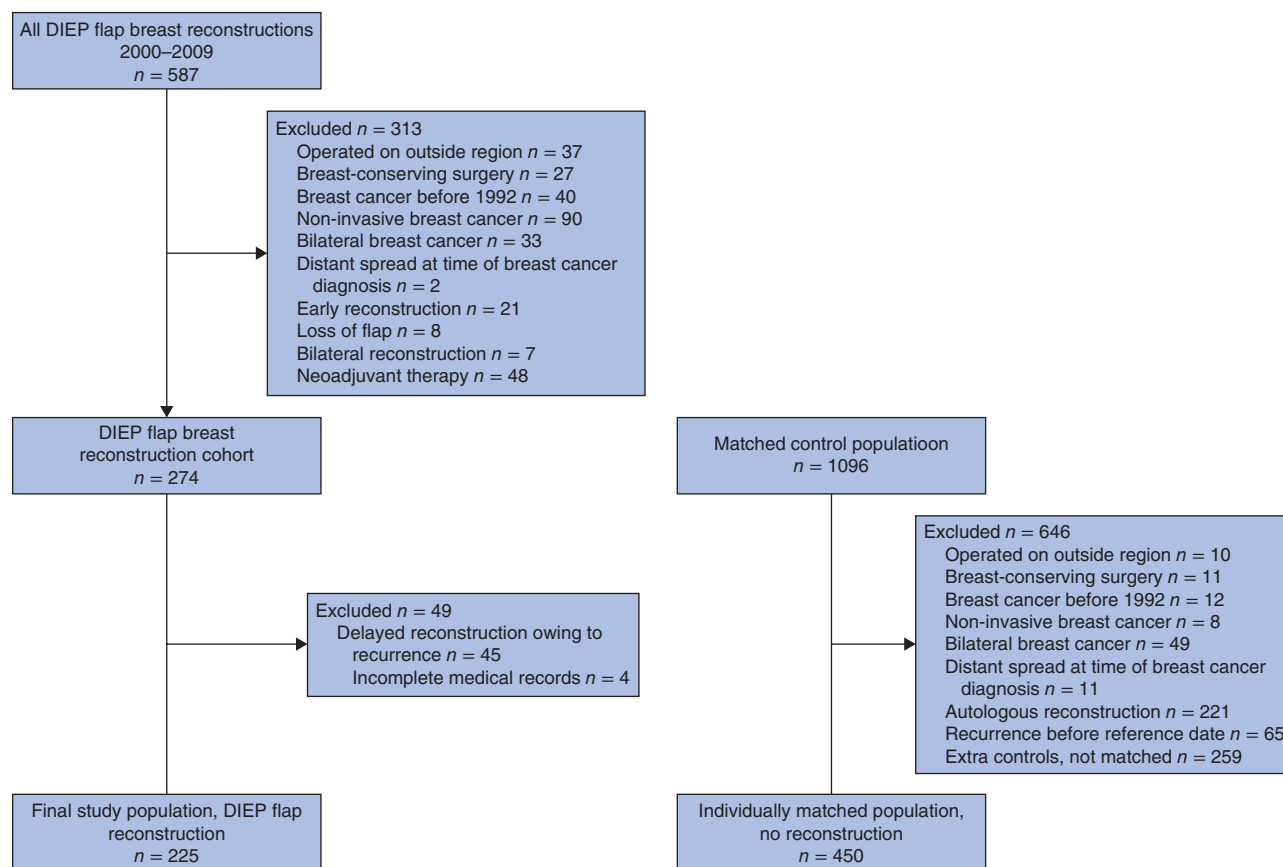


Fig. 1 Inclusion and exclusion criteria to achieve matched populations for the study. DIEP, deep inferior epigastric perforator

Any woman in either cohort who developed recurrence before the reference date was excluded.

Data retrieval

The following data were retrieved from patients' medical records and not from the RBCR: tumour size, tumour type, oestrogen receptor status, progesterone receptor status, human epidermal growth factor receptor 2 (HER2) status (available from 2003 onwards), lymph node status, adjuvant treatment, type of breast cancer recurrences, and time elapsed between reconstructive surgery and recurrence.

Endpoint retrieval

All patients' medical records were searched during December 2016 at the treating hospital to ascertain the last date of clinical follow-up and cause of death. For most patients, an electronic journal was searched, but medical charts were also reviewed if data were missing. The last note in

the patient's medical record was set as the last follow-up date. Primary endpoints were local recurrence or distant metastasis. Contralateral breast cancer was not defined as recurrence. The secondary endpoint in this study was overall mortality.

Follow-up time for all analyses was the interval between the reference date and recurrence, death or end of follow-up (31 December 2016). Cause of death was one of the primary or secondary outcomes and was thus not ascertained.

Statistical analysis

Absolute risks were assessed by estimating cumulative incidence, using the Kaplan–Meier method. Log rank tests were used to test the hypothesis that incidence curves were not significantly different. In multivariable models, missing data were replaced by means of multiple imputation by chained equations, as described by van Buuren¹⁵, using ten imputation data sets. Relative risks were estimated by pooling Cox regression models across all ten imputation data

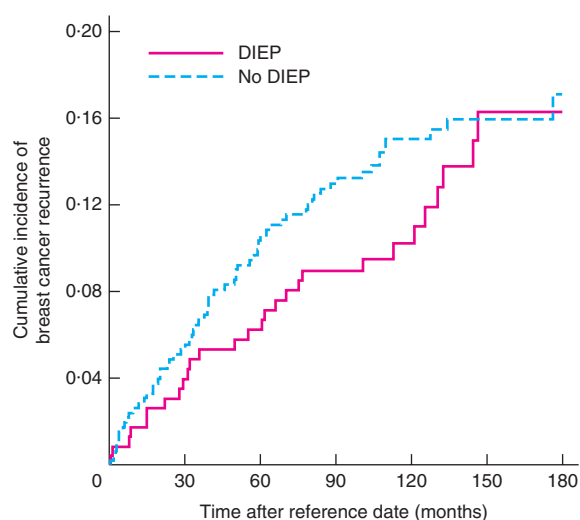
Table 1 Clinical, histopathological and biological characteristics, and adjuvant treatment in women who did and those who did not undergo deep inferior epigastric perforator flap reconstruction

	DIEP (n = 225)	No DIEP (n = 450)	P**
Age at reference date (years)*	52 (46–57)	53 (47–58)	0.203††
Reference year			0.186
1999–2004	62 (27.6)	148 (32.9)	
2005–2009	163 (72.4)	302 (67.1)	
Primary operation at university hospital			<0.001
Yes	69 (30.7)	42 (9.3)	
No	156 (69.3)	408 (90.7)	
Histological type (WHO classification)			<0.001
Ductal/tubular	143 (63.6)	345 (76.7)	
Lobular	49 (21.8)	71 (15.8)	
Other	15 (6.7)	34 (7.6)	
Missing	18 (8.0)	0 (0)	
Elston–Ellis grade			0.052
1	21 (9.3)	46 (10.2)	
2	104 (46.2)	219 (48.7)	
3	59 (26.2)	137 (30.4)	
Missing	41 (18.2)	48 (10.7)	
Tumour size (mm)*	20 (14–30)	21 (15–30)	0.386
0–20	101 (44.9)	220 (48.9)	
21–50	87 (38.7)	196 (43.6)	
> 50	7 (3.1)	28 (6.2)	
Missing	30 (13.3)	6 (1.3)	
No. of positive lymph nodes			0.022
0	98 (43.6)	205 (45.6)	
1–3	78 (34.7)	156 (34.7)	
> 3	36 (16.0)	82 (18.2)	
Missing	13 (5.8)	7 (1.6)	
ER status			0.011
Positive†	162 (72.0)	326 (72.4)	
Negative	42 (18.7)	106 (23.6)	
Missing	21 (9.3)	18 (4.0)	
PR status			0.001
Positive†	141 (62.7)	283 (62.9)	
Negative	59 (26.2)	148 (32.9)	
Missing	25 (11.1)	19 (4.2)	
HER2 status			0.256
Positive‡	20 (8.9)	55 (12.2)	
Negative	160 (71.1)	322 (71.6)	
Missing	45 (20)	73 (16.2)	
Chemotherapy§			<0.001
Yes	161 (71.6)	243 (54.0)	
No	52 (23.1)	140 (31.1)	
Missing	12 (5.3)	67 (14.9)	
Radiotherapy¶			<0.001
Yes	166 (73.8)	270 (60.0)	
No	54 (24.0)	116 (25.8)	
Missing	5 (2.2)	64 (14.2)	

Table 1 continued

	DIEP (n = 225)	No DIEP (n = 450)	P**
Endocrine therapy#			<0.001
Yes	167 (74.2)	242 (53.8)	
No	43 (19.1)	130 (28.9)	
Missing	15 (6.7)	78 (17.3)	

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). The reference date is the date of deep inferior epigastric perforator (DIEP) flap reconstruction for women with a DIEP flap and a date matched by time since mastectomy for women without a DIEP flap. †At least 10 per cent positive cells. ‡Score 3+ on immunohistochemistry or amplified by fluorescence *in situ* hybridization; analysed routinely after 2003. §Any chemotherapy; usually six rounds. ¶Locoregional. #Usually antioestrogen. ER, oestrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2. ** χ^2 test, except ††Mann–Whitney *U* test.



No. at risk	0	30	60	90	120	150	180
DIEP	225	214	207	198	114	63	17
No DIEP	450	418	388	348	227	135	68

Fig. 2 Risk of breast cancer recurrence among women with and without breast reconstruction with a deep inferior epigastric perforator (DIEP) flap. The reference date is the date of DIEP flap reconstruction for women with a DIEP flap and a date matched by time since mastectomy for women without a DIEP flap. $P = 0.433$ (log rank test)

sets. Time to death or recurrence was the outcome of interest and stratification was employed to handle the matched study design. Selection of co-variables included in models was based on clinical reasoning; for example, oestrogen receptor status was included but not HER2 status, because the latter was not assessed in a majority of patients undergoing primary mastectomy before 2003. The proportional

Table 2 Pooled Cox regression models predicting breast cancer recurrence after reference date across ten multiple imputation data sets, stratified by matching variable

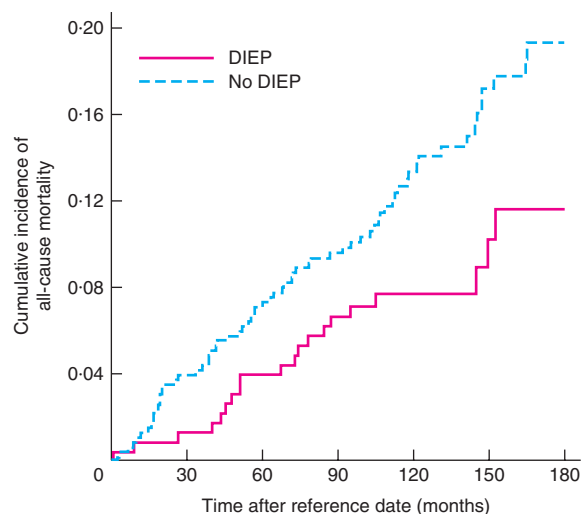
	n*	Hazard ratio†	
		Univariable	Multivariable
DIEP flap			
No	450 (66.7)	1.00 (reference)	1.00 (reference)
Yes	225 (33.3)	0.77 (0.49, 1.21)	0.76 (0.47, 1.21)
Missing	0 (0)		
Elston–Ellis grade			
1–2	390 (57.8)	1.00 (reference)	1.00 (reference)
3	196 (29.0)	1.35 (0.79, 2.32)	1.26 (0.69, 2.32)
Missing	89 (13.2)		
Tumour size (mm)			
≤ 20	321 (47.6)	1.00 (reference)	1.00 (reference)
> 20	318 (47.1)	1.75 (1.04, 2.95)	1.68 (0.99, 2.87)
Missing	36 (5.3)		
No. of positive lymph nodes			
0	303 (44.9)	1.00 (reference)	1.00 (reference)
≥ 1	352 (52.1)	1.12 (0.68, 1.84)	1.06 (0.63, 1.78)
Missing	20 (3.0)		
ER status			
Negative	148 (21.9)	1.00 (reference)	1.00 (reference)
Positive	488 (72.3)	0.89 (0.47, 1.67)	1.12 (0.55, 2.27)
Missing	39 (5.8)		

Values in parentheses are *percentages and †95 per cent confidence intervals. The distribution of patients with missing data for any co-variable in the models was 48 (21.3 per cent) in the deep inferior epigastric perforator (DIEP) cohort and 58 (12.9 per cent) in the no-DIEP cohort. ER, oestrogen receptor.

hazards assumption was investigated by studying incidence curves and Schoenfeld residuals¹⁶. Sensitivity analyses were undertaken to evaluate model assumptions, but also inclusion and exclusion criteria. One sensitivity analysis excluded all matched women who later underwent a reconstruction. Another analysis included women who received a DIEP flap and subsequently had it removed, along with their matched women. Complete-case analyses were carried out to compare with imputation results. All tests were two-sided and $P < 0.050$ was considered statistically significant. Data management was performed using SAS[®] version 9.4 (SAS Institute, Cary, North Carolina, USA) and R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria) for all analyses.

Results

During the study interval, a total of 587 DIEP flap reconstructions were performed, of which 225 met the



No. at risk							
DIEP	225	222	216	208	120	68	18
No DIEP	450	432	415	377	248	148	75

Fig. 3 All-cause mortality among women with and without breast reconstruction with a deep inferior epigastric perforator (DIEP) flap. The reference date is the date of DIEP flap reconstruction for women with a DIEP flap and a date matched by time since mastectomy for women without a DIEP flap. $P = 0.037$ (log rank test)

inclusion criteria (Fig. 1). Among 450 patients in the control no-DIEP cohort, 49 underwent reconstruction with an implant (all without the use of acellular dermal matrices). The median follow-up time was 125 (i.q.r. 103–158) months. In terms of baseline characteristics, a higher proportion of patients in the DIEP cohort received adjuvant treatment than in the no-DIEP cohort (94.6 versus 80.0 per cent; $P < 0.001$). There was no difference in tumour characteristics between the DIEP and no-DIEP cohorts (Table 1).

Recurrence was observed in 97 women (14.4 per cent), 68 (15.1 per cent) in the no-DIEP cohort and 29 (12.9 per cent) in the DIEP cohort. Sixty-five (67 per cent) of the women who developed recurrence experienced only distant metastasis, 17 (18 per cent) had only a locoregional recurrence, and 15 (15 per cent) had a locoregional recurrence followed by distant metastases. The patients who developed a recurrence were more likely not to have received chemotherapy or radiation.

There was no statistically significant difference in absolute risk of breast cancer recurrence between the groups (Fig. 2). Time-to-event analyses including potential confounders did not reveal any differences between the DIEP and no-DIEP groups (Table 2). Larger tumour

Table 3 Pooled Cox regression models predicting all-cause mortality after the reference date across ten multiple imputation data sets, stratified by matching variable

	n*	Hazard ratio†	
		Univariable	Multivariable
DIEP flap			
No	450 (66.7)	1.00 (reference)	1.00 (reference)
Yes	225 (33.3)	0.57 (0.34, 0.94)	0.64 (0.38, 1.08)
Missing	0 (0)		
Elston–Ellis grade			
1–2	390 (57.8)	1.00 (reference)	1.00 (reference)
3	196 (29.0)	1.55 (0.87, 2.78)	1.07 (0.53, 2.16)
Missing	89 (13.2)		
Tumour size (mm)			
≤ 20	321 (47.6)	1.00 (reference)	1.00 (reference)
> 20	318 (47.1)	1.71 (1.02, 2.87)	1.57 (0.88, 2.79)
Missing	36 (5.3)		
No. of positive lymph nodes			
0	303 (44.9)	1.00 (reference)	1.00 (reference)
≥ 1	352 (52.1)	1.63 (0.96, 2.77)	1.31 (0.74, 2.33)
Missing	20 (3.0)		
ER status			
Negative	148 (21.9)	1.00 (reference)	1.00 (reference)
Positive	488 (72.3)	0.50 (0.26, 0.98)	0.58 (0.27, 1.25)
Missing	39 (5.8)		

Values in parentheses are *percentages and †95 per cent confidence intervals. The distribution of patients with missing data for any co-variable in the models was 48 (21.3 per cent) in the deep inferior epigastric perforator (DIEP) cohort and 58 (12.9 per cent) in the no-DIEP cohort. ER, oestrogen receptor.

size was associated with a higher risk of breast cancer recurrence in the unadjusted analysis (Table 2) and a higher risk of distant metastasis in the adjusted analysis (Table S1, supporting information). The no-DIEP cohort had a higher overall mortality rate than the DIEP cohort (Fig. 3), with a hazard ratio of 0.57 (95 per cent c.i. 0.34 to 0.94), in the univariable Cox regression model, although this association disappeared after multivariable adjustments (Table 3). These findings were compared with those of complete-case models, and models with imputations with and without adjustment for adjuvant therapy. None of these altered the findings in a significant way.

Discussion

The present matched retrospective cohort study found no statistically significant difference in breast cancer recurrence rates between patients who had delayed breast reconstruction with a DIEP flap and those who underwent

mastectomy alone (with or without an implant-based reconstruction).

There is a theoretical risk that transposition of tissue on to the mastectomy site during the DIEP flap reconstruction procedure might hide or delay detection of local recurrence beneath the flap^{10–13}. An increased risk of breast cancer recurrence related to delayed autologous reconstructions was reported in a cohort study by Isern and colleagues⁸. The present results contradict these findings. A possible explanation for the results of Isern *et al.*⁸ is that only 33 DIEP flap reconstructions were included, which limits the statistical power of the analysis. In addition, transverse rectus abdominis myocutaneous and latissimus dorsi flaps were also included, which makes comparison difficult and may confound the outcomes. Furthermore, the reconstructed cohort had more lymph node metastases and more often had oestrogen receptor-positive tumours, but the findings remained significant after multivariable adjustment⁸. Fewer patients in the DIEP group had missing data at follow-up compared with the no-DIEP group, but the opposite was true regarding tumour data.

One strength of the present study is the homogeneity of the study population; only patients who had unilateral DIEP flap reconstructions following mastectomy for breast cancer were compared with women who had mastectomy alone with or without implant-based reconstruction without acellular dermal matrices. This study is, however, not generalized for all types of autologous breast reconstruction. A long follow-up of at least 7 years is advantageous. Normally breast cancer recurrence peaks during the first 2 years after cancer surgery¹⁷. Naturally, an even longer follow-up time would have been beneficial to capture any later peak.

The main limitations of the study relate to its retrospective design and the lack of randomization between the cohorts. To minimize selection bias, the groups were matched for year of cancer diagnosis (+/– 3 years), age at cancer diagnosis (+/– 5 years), type of cancer (invasive cancer *versus* ductal carcinoma *in situ*) and demographic region. To avoid overmatching, no further matching was performed and this also allowed measurement of the effect of different co-variables. Matching for more variables would have led to difficulties in obtaining suitable controls, and matching criteria would have had to be relaxed, leading to poor control for confounding. Another limitation of the study is that cause of death was not readily available, and so breast cancer-specific survival could not be included as an outcome.

A further limitation is the difference in baseline characteristics between the DIEP and no-DIEP cohorts, with a

higher proportion of patients in the DIEP cohort receiving adjuvant therapy. This may reflect a more aggressive initial cancer subtype, although this was not reflected in the tumour data registered. Another explanation for the tendency towards an increased survival rate in the DIEP cohort is selection bias, whereby these patients were healthier and fit enough to undergo free-flap breast reconstructions¹⁸. These women may represent a group with lower BMI, healthier lifestyles, better socioeconomic conditions and more motivation to travel for a DIEP flap reconstruction. It is also possible that socioeconomic factors could influence the type of adjuvant treatment the patient receives, and that the control group had less adjuvant treatment and therefore showed a trend towards higher overall mortality. It is also plausible that patients who had primary surgery at the tertiary unit received more information regarding DIEP flap reconstruction and had more support with decision-making than those in the no-DIEP group¹⁹. Breast reconstructions after breast cancer, both immediate and delayed, are financed completely by the national healthcare system in Sweden and carry no private expenses. Further research should include the impact of socioeconomic factors or medical co-morbidities on delayed breast reconstructions.

Even though the incidence is low, there is an association between implant-based reconstruction and breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), which is why a safe alternative to breast reconstruction without risk of BIA-ALCL is needed²⁰. In this context, delayed breast reconstruction with autologous flap surgery represents an important surgical option.

Acknowledgements

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.