Original Article

Patient determinants as independent risk factors for postoperative complications of breast reconstruction

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Background: Breast reconstruction is an essential component in the treatment of breast cancer. Postoperative complications after breast reconstruction are common and affect patient satisfaction. Determining independent risk factors using patient characteristics could be advantageous for patient assessment and counseling.

Methods: We retrospectively enrolled 623 consecutive patients who underwent reconstruction with a deep inferior epigastric perforator flap (DIEP), latissimus dorsi flap (LD), lateral thoracodorsal flap (LTDF), or tissue expander with a secondary implant (EXP) in this study. Information on demographic and perioperative factors was collected, as well as information on all postoperative complications. Logistic regression was used to analyze associations between possible patient-related risk factors and postoperative complications.

Results: Smoking was associated with the highest number of early overall complications [odds ratio (OR) 2.05, 95% confidence interval (CI) 1.25–3.37, P=0.0005], followed by body mass index (BMI) (OR 1.07, 95% CI 1.01–1.13, P=0.017). High BMI was associated with the highest number of late overall postoperative complications (OR 1.06, 95% CI 1.00–1.11, P=0.042), followed by history of radiotherapy (OR 1.66, 95% CI 1.01–2.74, P=0.046). When the risk factors were combined, the risk for postoperative complications rose exponentially.

Conclusions: Our results provide evidence that patients should cease smoking and overweight patients should lose weight before undergoing breast reconstruction. Additionally, if the patient has received radiotherapy, the reconstruction method should be carefully chosen. High BMI, history of radiotherapy, and smoking are independent risk factors for many types of both early and late postoperative complications in breast reconstructive surgery. Combining these risk factors multiplies the risk of postoperative complications.

Keywords: Breast cancer; breast reconstruction; deep inferior epigastric perforator (DIEP) flap; implant reconstructions; latissimus dorsi (LD) flap; postoperative complications

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Introduction

There is lack of large cohort analyses using patient determinants as risk factors for postoperative outcomes after breast reconstruction. Complications after breast reconstructive surgery are common (1-6), and it has been shown that complications affect patient emotional well-being, health-related quality of life and satisfaction (5,7-10). Patients' satisfaction and health-related quality of life are frequently used as parameters for outcome measurement in plastic surgery.

Identifying independent risk factors for complications could have multiple advantages, such as making the treatment of patients with breast cancer requesting reconstruction more effective and aiding in selection of the best reconstruction method for each patient.

The effect of radiotherapy on breast reconstruction

Many studies on radiotherapy and complications after breast reconstruction have been performed. In the majority of studies, radiotherapy is shown to adversely affect outcome after implant-based breast reconstructions, with increased late failure rates (5,11,12), poor aesthetic results, loss of symmetry (13-15), capsular contracture, and infection, even when using the latest generation of implants (5,11,12,14,16-24).

Results from studies on radiotherapy and autologous reconstructions are more conflicting. Radiotherapy after mastectomy but before reconstruction has not been shown to increase complications after autologous reconstruction (25); however, not all studies are in agreement (26,27). Certain studies show that postoperative radiotherapy to the breast reconstructed with a deep inferior epigastric perforator flap (DIEP) or transverse rectus abdominis myocutaneous (TRAM) flap has no effect on the reconstruction (28,29), while several others show a considerable negative effect on the final results of autologous reconstruction (24,26,30-34).

The effect of chemotherapy and hormone therapy on breast reconstruction

Studies on the effect of adjuvant chemotherapy on postoperative complications are also not conclusive. Chemotherapy has been reported to be associated with a high rate of complications and reconstruction failure (18), but several other studies show no association between adjuvant chemotherapy and adverse events after breast reconstruction (12,35).

In the case of adjuvant hormone therapy, there is no agreement regarding its effect on complications. Some studies show an association with overall complications (36) and, especially, capsular contraction (16,37), while other studies have shown no such association (18,38-41).

The effect of patient characteristics on breast reconstruction

Several studies have examined the relationship between several patient characteristics (other than adjuvant therapy) and complications (2,6,42-45), but there was variation in the factors studied, and inconclusive results.

It is well established that high body mass index (BMI) increases the risk for surgical complications and overall morbidity in all types of breast reconstructions, both implant-based and autologous (46-54). It is also well established that smoking has a negative influence on free flap breast reconstruction (6,45,55-59), although some studies have failed to establish this relationship (4,60-62). The same seems to be true for implant-based reconstructions (16,35,44,63-65), but not all studies can confirm these findings (52). Many studies show no relationship between age and risk for complications (45,57,60-62,66-71), while other studies show that elderly patients have more risk (44,53,63). Diabetes has been associated with postoperative complications after autologous reconstruction, but the results after implant-based breast reconstruction are more conflicting (52,72-75). Patients with renal disease seem to be more prone to complications (75,76). Very little has been published on the history of DVT and postoperative complications, but one study showed an increased risk for thrombosis in free flap surgery in hypercoagulative patients and a very low salvage rate of the affected flaps (77). No reports seem to exist on the effect of concurrent rheumatic or neurologic disease and outcome after breast reconstruction.

The aim of the present study was to investigate the effect of numerous patient-related determinants (adjuvant therapy and concurrent diseases) on postoperative complication frequency among four different methods of breast reconstruction by systematically evaluating the outcome with identical criteria on a consecutive series of breast reconstruction cases.

Methods

The present study is a retrospective analysis of 623 consecutive patients who underwent surgery between 2003 and 2009 with one of four delayed breast reconstruction methods at the Department of Plastic Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden.

The patients were enrolled from the operation database of the clinic (Operätt, C&S Healthcare Software AB, Mölndal, Sweden). The inclusion criteria were as follows: first time delayed reconstruction with (I) DIEP (78); (II) latissimus dorsi flap with silicone implant (LD) (79); (III) lateral thoracodorsal flap (LTDF) with silicone implant (80);

or (IV) tissue expander with a secondary silicone implant (EXP) (81). The primary (expander) and secondary (implant) procedures were registered separately, as well as compiled, in the EXP group.

Existing data on at least 30 days of follow-up was required for inclusion; patients lost to follow-up were not included. Data were collected from the chart filing systems (Melior, Siemens Health Care, Upplands Väsby, Sweden, and Operätt) from the patients' first referral to the last follow-up visit.

Demographic data

Demographic parameters registered were age, BMI, smoking status, previous radio- or chemotherapy, medications (hormone therapy, acetylsalicylic acid, corticosteroids, thyroid supplements, and anticoagulants), concurrent morbidity (diabetes, hypothyroidism, cardiovascular disease, history of thromboembolism, coagulopathy, and rheumatic, neurological, kidney, liver, or lung disease) as well as follow-up-time. Patient demography, perioperative parameters, and frequency of postoperative complications with respect to the different reconstructive methods for this group has previously been published (82).

Registered postoperative complications

Follow-up parameters and complications encountered were divided into early (≤30 days after surgery) and late (>30 days after surgery). The registered complications can be seen in *Table 1*. Detailed definitions of the registered complications have been previously published (82). The data was processed in a secure FileMaker database (Filemaker Inc., Santa Clara, CA, USA).

Statistics

Univariate and multivariate logistic regression was used to analyze the association between the independent (possible risk factors) and the dependent outcome parameters (postoperative complications). As the reconstruction methods varied significantly regarding the duration of surgery, blood loss during surgery, and the incidence of postoperative complications, all models were adjusted to the reconstructive method. Therefore, the reconstructive method itself was not a factor biasing the results of the statistical analysis. To analyze whether patient-related factors had an independent effect on the outcome variables, a multivariate logistic regression with adjustment for patient demographic parameters acting as confounding factors was performed. Thus, all demographic factors that acted as confounding factors were statistically adjusted for and did not bias the results of the statistical analysis. Relationships between independent (possible risk factors) and dependent (outcome) variables are presented with odds ratio (OR), 95% confidence interval (CI), and P value (P). All significance tests were two-sided and conducted at the 5% significance level. P values below 0.05 were considered statistically significant. Statistical analysis was performed with SPSS 23 (IBM Corp., Armonk, NY, USA). The study was approved by the Gothenburg Ethical Committee (No. 043-08).

Table 1 Complications registered early (≤30 days after surgery) and late (>30 days after surgery)

Complications registered early and late
Overall complications
Signs of infection
Administration of antibiotics
Overall local complications
Skin necrosis
Fat necrosis
Hematoma
Seroma
Wound rupture
Early resurgery for complications
Scars in need of treatment (late only)
Late resurgery/cosmetic corrections

Results

The median of follow-up time was 26.1 (Q_1–Q_3 15.1–41.8) months.

Early complications

Table 2 displays the associations between the patient-related factors and early complications. In the multivariate model, the patient factor related to the highest number of the early complications subgroups was smoking, and was associated with early overall complications, early administration of

Table 2 Statistically significant results of both univariate and multivariate logistic regression models between patient related factors and early postoperative complications

Complications	Univariate model		Multivariate model	
	OR (95% CI)	P	OR (95% CI)	P
Early overall complications				
BMI	1.08 (1.03–1.14)	0.002	1.07 (1.01–1.13)	0.017
Smoking	1.65 (1.07–2.54)	0.023	2.05 (1.25–3.37)	0.005
Radiotherapy	1.87 (1.32–2.65)	<0.001	NS	NS
Early signs of infection				
BMI	1.08 (1.01–1.16)	0.018	NS	NS
Early administration of antibiotics				
BMI	1.13 (1.06–1.20)	<0.001	1.10 (1.04–1.18)	0.002
Smoking	1.84 (1.11–3.03)	0.017	2.10 (1.19–3.71)	0.010
Hormone therapy	1.56 (1.01–2.43)	0.046	NS	NS
Radiotherapy	1.77 (1.15–2.73)	0.009	2.03 (1.24–3.30)	0.005
Early overall local complications				
Smoking	2.28 (1.40–3.72)	0.001	2.77 (1.61–4.75)	<0.001
Radiotherapy	3.20 (2.04–5.01)	<0.001	2.03 (1.09–3.75)	0.025
Early skin necrosis				
Smoking	2.70 (1.36–5.33)	0.004	3.64 (1.67–7.93)	0.001
Radiotherapy	3.13 (1.55–6.30)	0.001	NS	NS
Early fat necrosis				
BMI	1.22 (1.10–1.36)	<0.001	NS	NS
Smoking	3.00 (1.29–6.95)	0.010	NS	NS
Radiotherapy	7.29 (2.47–21.51)	<0.001	NS	NS
Early hematoma				
Smoking	3.52 (1.48–8.36)	0.004	NS	NS
Early seroma				
Age	0.96 (0.93–1.00)	0.030	0.95 (0.92–0.99)	0.016
Radiotherapy	2.18 (1.12–4.24)	0.022	NS	NS
Early resurgery				
BMI	1.11 (1.04–1.19)	0.003	1.09 (1.01–1.17)	0.029
Radiotherapy	1.73 (1.05–2.83)	0.031	NS	NS

BMI, body mass index (kg/m^2); NS, not significant.

antibiotics, early overall local complications, and early skin necrosis. Increased BMI was ranked second, and was associated with early overall complications, early administration of antibiotics, and early resurgery. History of radiotherapy ranked third, and was associated with early administration of antibiotics, and early overall local complications. Age seemed to be a protective factor regarding development of early seroma.

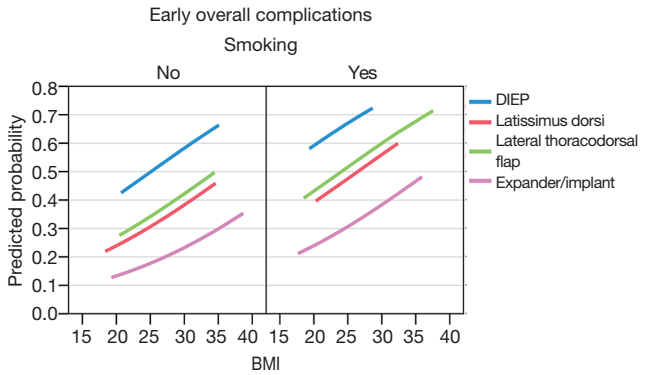

Figure 1 The diagram illustrates the relationship between the independent risk factors of smoking and BMI, and their probability for early overall complications. The combination resulted in a considerably increased risk compared to the presence of only one risk factor. DIEP, deep inferior epigastric perforator; BMI, body mass index.

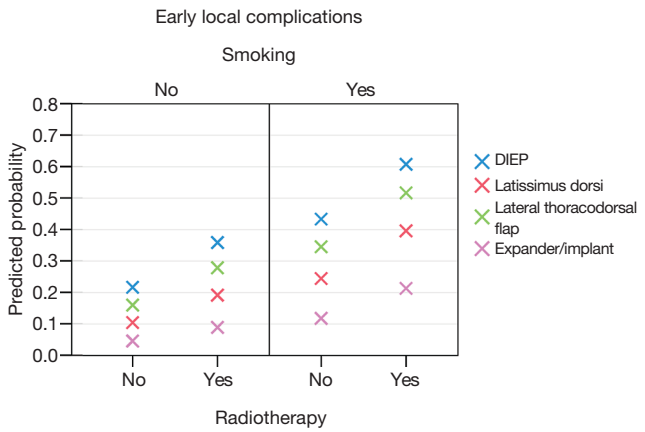

Figure 2 The diagram illustrates the relationship between the independent risk factors of smoking and history of radiotherapy and their probability for early local complications. The combination resulted in a considerably increased risk compared to the presence of only one risk factor. DIEP, deep inferior epigastric perforator.

Independent risk factors combined

The patient-related factors of BMI and smoking were independent risk factors for overall early complications: BMI (OR 1.07, 95% CI 1.01–1.13, P=0.017) and smoking (OR 2.05, 95% CI 1.25–3.37, P=0.005). Thus, the risk for encountering overall early complications rose by 7% for each unit of BMI increase, and the risk increased over 200% if the patient was a smoker. When both risk factors were combined, the mean predicted probability was 230% higher for smokers with a BMI of 30 compared to non-smokers

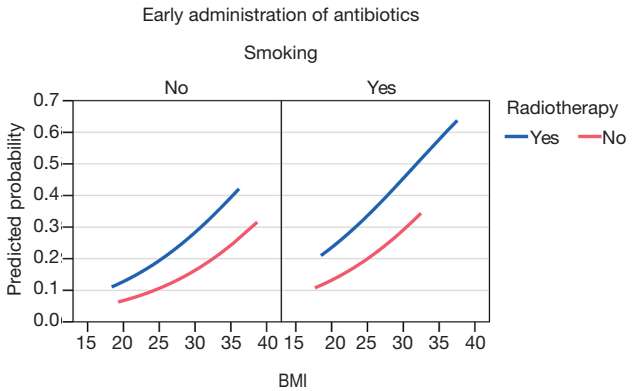

Figure 3 The diagram illustrates the relationship between the independent risk factors of increased BMI, smoking, and radiotherapy, and their risk for early administration of antibiotics when they are combined. All curves, irrespective of method, show a positive association between increased risk factor and risk for complication. As BMI increases, and is combined with smoking and history of radiotherapy, the risk curves are shifted upwards. The combination resulted in a considerably increased risk compared to the presence of only one risk factor. BMI, body mass index.

with a BMI of 20. The patients in the expander group had the greatest increase at 3.8-fold for the combination of high BMI and being a smoker (*Figure 1*).

The patient related factors of smoking (OR 2.77, 95% CI 1.61–4.75, P<0.0001) and radiotherapy (OR 2.03, 95% CI 1.09–3.75, P=0.025) were independent risk factors for early local complications. Therefore, the risk for encountering early local complications rose by 277% if the patient was a smoker, and the risk increased over 200% if the patient was irradiated. The predicted probability for all methods increased a mean 3.6-fold for smokers who had undergone radiotherapy compared to patients who were neither smokers and had not undergone radiotherapy. The patients in the expander group had the greatest increase of 4.6-fold for the combination of smoking and radiotherapy (*Figure 2*).

When BMI was added as a third risk factor, the association to early administration of antibiotics was multiplied. BMI (OR 1.10, 95% CI 1.04–1.18, P=0.002), smoking (OR 2.10, 95% CI 1.19–3.71, P=0.010) and radiotherapy (OR 2.03, 95% CI 1.24–3.30, P=0.005) were independent risk factors for early administration of antibiotics. A smoking, irradiated patient with a BMI of 30 had a 7.2-fold risk for early administration of antibiotics than a non-smoking, non-irradiated patient with a BMI of 20 (*Figure 3*).

Hypothyroidism, cardiovascular disease, coagulopathy,

liver disease, and lung disease had no statistically significant relationship to any of the complications registered.

Late complications

Table 3 displays the associations between the patient-related factors and late complications. In the multivariate model, the patient factors related to the highest number of the subgroups of late complications were high BMI (late overall complications, late signs of infection, late administration of antibiotics, and late fat necrosis), and history of radiotherapy (late overall complications, late administration of antibiotics, late overall local complications, and late fat necrosis). Smoking had a relationship with late resurgery only. Taking acetylsalicylic acid had a relationship with late administration of antibiotics.

Independent risk factors combined

The patient related factors of BMI and history of radiotherapy were independent risk factors for late overall complications; BMI (OR 1.06, 95% CI 1.00–1.11, P=0.042) and radiotherapy (OR 1.66, 95% CI 1.01–2.74, P=0.046). Thus, the risk of encountering overall late complications rose by 6% for each unit of BMI increased, and the risk rose by 66% if the patient was irradiated. When both risk factors were combined, an irradiated patient with a BMI of 30 had a 2.3-fold higher risk for late overall complications than a non-irradiated patient with a BMI of 20 (*Figure 4*).

The patient related factors of smoking and rheumatic disease were independent risk factors for late resurgery—smoking (OR 1.88, 95% CI 1.21–2.92, P=0.005) and rheumatic disease (OR 2.44, 95% CI 1.07–5.57, P=0.033). Thus, the risk for encountering late resurgery was 88% higher if the patient was a smoker, and 244% higher if the patient had rheumatic disease. A smoking patient with history of rheumatic disease had over 3-fold higher risk for late resurgery compared to that in a non-smoking patient without rheumatic disease (*Figure 5*).

The patient related factors of BMI and radiotherapy were independent risk factors for late fat necrosis: BMI (OR 1.18, 95% CI 1.05–1.33, P=0.005) and radiotherapy (OR 3.37, 95% CI 1.17–9.70, P=0.024). Therefore, the risk of encountering late fat necrosis rose by 18% for each unit of BMI increase, and the risk increased by 337% if the patient was irradiated. An irradiated patient with a BMI of 30 had a 16.4-fold higher risk for late fat necrosis than a non-irradiated patient with BMI of 20 (*Figure 6*).

Discussion

In the present study, we found that smoking, increased BMI, and history of radiotherapy were closely associated with several postoperative complications, both early and late, irrespective of reconstruction method. Interestingly, smoking was associated with several early complications (early overall complications, early administration of antibiotics, early overall local complications, and early skin necrosis), but only one late complication (late resurgery). Increased BMI affects both early complications (early overall complications, early administration of antibiotics, and early resurgery) and late complications (late overall complications, late signs of infection, late administration of antibiotics, and late fat necrosis). History of radiotherapy, on the other hand, generally affects late complications (late overall complications, late administration of antibiotics, late overall local complications, and late fat necrosis), but also has some effect on early complications (early administration of antibiotics and early overall local complications). Additionally, when the different independent risk factors are combined, the risks increased considerably.

Significant independent risk factors have been previously identified, both in plastic surgery and in other specialities (40,44,45,50,72,83-93). However, the advantage of the present study is the evaluation of four different reconstruction methods with the same criteria for complications. This is the first study on a large group of patients where the association between an extensive panorama of patient-related factors and meticulously registered postoperative complications was studied using the same stringent definition of complications applied to all reconstruction methods, and showing that the risk increases were independent of surgical method. The large number of patients also allows adjustment for all confounding factors, providing independent risk factors and the construction of risk models (*Figures 1-6*).

In this study, the negative findings are almost equally interesting. Hormone and chemotherapy did not appear to affect complication rates after breast reconstruction, which is in agreement with most other studies (1,12,35), but conflicts with one (18). Additionally, age does not appear to have an association with postoperative complications except for a protective effect on early seroma. History of chemotherapy, adjuvant hormone therapy, and concurrent morbidity (diabetes, hypothyroidism, cardiovascular disease, history of thromboembolism, coagulopathy, and rheumatic, neurological, kidney, liver, or lung disease) had

Table 3 Statistically significant results of both univariate and multivariate logistic regression models between patient related factors and late postoperative complications

Complications	Univariate model		Multivariate model	
	OR (95% CI)	P	OR (95% CI)	P
Late overall complications				
BMI	1.06 (1.01–1.12)	0.014	1.06 (1.00–1.11)	0.042
Rheumatic disease	2.27 (1.03–4.99)	0.041	NS	NS
Radiotherapy	1.79 (1.29–2.49)	<0.0001	1.66 (1.01–2.74)	0.046
Late signs of infection				
BMI	1.19 (1.10–1.28)	<0.0001	1.18 (1.09–1.28)	<0.0001
Late administration of antibiotics				
BMI	1.13 (1.05–1.21)	0.001	1.11 (1.03–1.20)	0.007
Acetylsalicylic acid	3.93 (1.65–9.33)	0.002	6.08 (2.29–16.11)	<0.0001
Radiotherapy	1.72 (1.01-2.93)	0.046	1.89 (1.04–3.42)	0.037
Late overall local complications				
Metabolic disease	2.47 (1.08–5.67)	0.033	NS	NS
Radiotherapy	3.31 (1.56–7.06)	0.002	3.79 (1.54–9.33)	0.004
Late skin necrosis				
Radiotherapy	9.27 (1.13–75.82)	0.038	NS	NS
Late fat necrosis				
BMI	1.20 (1.08–1.35)	0.001	1.18 (1.05–1.33)	0.005
Radiotherapy	3.48 (1.23–9.90)	0.019	3.37 (1.17–9.70)	0.024
Late hematoma				
Age (years)	1.21 (1.00–1.46)	0.046	NS	NS
Diabetes	33.5 (2.01–557.09)	0.014	NS	NS
Late seroma				
Metabolic disease	7.97 (1.11–57.50)	0.039	NS	NS
Late wound rupture				
Age	1.13 (1.026–1.21)	0.009	NS	NS
Radiotherapy	9.27 (1.13–75.82)	0.038	NS	NS
Late resurgery				
Smoking	1.92 (1.25–2.94)	0.003	1.88 (1.21–2.92)	0.005
Rheumatic disease	2.46 (1.15–5.29)	0.021	2.44 (1.07–5.57)	0.033
Radiotherapy	1.55 (1.12–2.14)	0.008	NS	NS

BMI, body mass index (kg/m^2); NS, not significant.

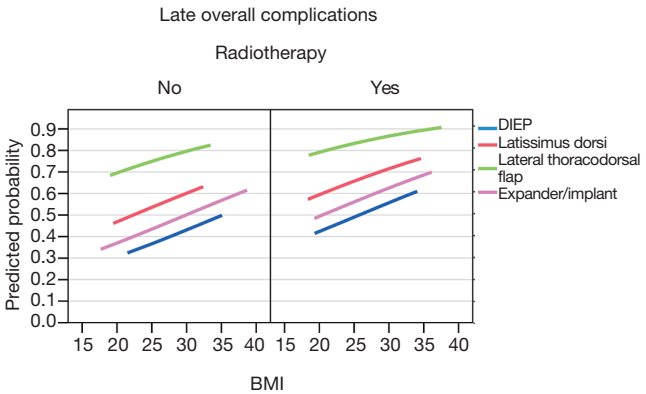

Figure 4 The diagram illustrates the relationship between the independent risk factor of increased BMI, combined with radiotherapy on the risk for late overall complications. The combination resulted in a considerably increased risk compared to the presence of only one risk factor. DIEP, deep inferior epigastric perforator; BMI, body mass index.

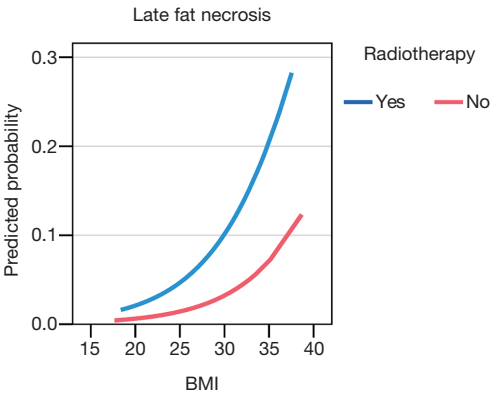

Figure 6 The diagram illustrates the relationship between the independent risk factor of increased BMI combined with history of radiotherapy on late fat necrosis. As BMI increases, the risk curves are shifted upwards. The combination results in a considerably risk compared to the presence of only one risk factor. BMI, body mass index.

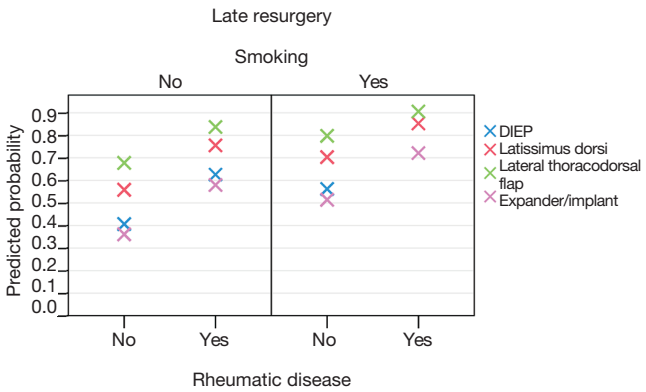

Figure 5 The diagram illustrates the relationship between the independent risk factor of smoking combined with rheumatic disease on the risk for late resurgery. The combination resulted in a considerably increased risk compared to the presence of only one risk factor. DIEP, deep inferior epigastric perforator.

no association with any of the registered complications.

The obviously increased risk associated with smoking and high BMI actualizes the question on whether healthcare providers should demand that patients cease smoking and reduce to normal BMI before surgery.

Radiotherapy is still one of the most beneficial treatments to increase survival in many types of breast cancer (94,95). Radiotherapy inevitably damages the tissue, and, as long as the modus of radiotherapy is unchanged, post-radiation breast reconstruction will be more challenging. Most studies find that radiotherapy in an implant-based reconstruction increases complications and late failure rates (5,11-23). The results of the present study are in line with those of other studies in this field (5,11-23,30,31,33).

Radiotherapy after mastectomy but before reconstruction has not been shown to increase complications of the flaps after autologous reconstruction (25), although not all studies agree on this (26,27). However, autologous breast reconstruction provides reduced morbidity than implant-based reconstruction in the setting of postoperative radiotherapy (2,26). In the present study, no patients received radiotherapy after the breast reconstruction, only before.

The association between radiotherapy and implant-based reconstruction has been addressed in many studies using various methodologies. However, in the present study, all complications were meticulously registered, and the same complication definitions were used for all four methods. The study group was large, which enabled the construction of a strong statistical model, allowing for adjustment for all factors acting as confounding factors. Consequently, the statistically significant associations are true associations, and unbiased by the surgical method or patient determinants acting as confounding factors in the model.

The aim for a successful breast reconstruction is to ensure the patient is satisfied with a breast that is almost never the same quality or has the same sensation compared to that before the mastectomy. One of the key elements to patient satisfaction is safety during the procedure. It is well established that postoperative complications influence

patient satisfaction (5,7,8). Therefore it is essential to minimize risks during the surgery. The present study contains an important piece of information to assist in optimal patient assessment before breast reconstruction and provides evidence for the goal of making an individual assessment of each patient to minimize the risks of the surgical procedure, and thereby maximal gain in health-related quality of life after breast reconstruction.

Conclusions

The present study firmly supports that, among a group of patients undergoing four different breast reconstruction methods, there is good evidence that patients should cease smoking and overweight patients should lose weight before surgery. Additionally, if the patient has had radiotherapy, the reconstruction method should be carefully chosen. This could reduce the likelihood of negative outcomes, reduce costs, and provide better cosmetic results and postoperative quality of life.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Gothenburg Ethical Committee (No. 043-08).

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