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ORIGINAL PAPER

Early postoperative complications of breast reconstruction by history of radiotherapy and reconstruction approach

Pavla Ticha[1,2] · Ondrej Mestak[3] · Meagan Wu[2] · Andrej Sukop[1]

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Abstract

Background For patients undergoing postmastectomy breast reconstruction, early postoperative complications may represent remarkable physical and emotional burden. Preoperative risk assessment is essential to minimizing such complications. The aim was to compare postoperative inpatient stay and early postoperative complications by radiotherapy status and different types of breast reconstruction.

Methods A total of 95 patients who had undergone postmastectomy primary breast reconstruction in a delayed manner in our institution were reviewed. A retrospective analysis was performed on the clinical data of patients with or without history of radiation therapy who had undergone implant, autologous, or combined reconstruction. The Kruskal–Wallis test, chi-square test of independence, and one-way ANOVA were used for data analysis.

Results Patients with a history of radiotherapy as well as patients who had undergone autologous reconstruction had the longest operative times ($p=0.020$; $p<0.001$), length of stay in the ICU ($p=0.010$; $p<0.001$), and overall length of postoperative inpatient stay ($p=0.049$; $p<0.001$). The rate of postoperative complications was 40% with previous radiotherapy compared to 12.3% without previous radiotherapy ($p=0.002$), and 42.1% with autologous reconstruction compared to 8.3% with implant reconstruction and 6.1% with combined reconstruction ($p<0.001$).

Conclusions History of radiotherapy and autologous reconstruction were associated with significantly longer operative times, inpatient stays, and a higher risk of early postoperative complications. Despite use of the patient's own tissue in combined reconstruction, there were no significant differences between the implant and combined reconstruction methods.
Level of evidence: Level III, risk/prognostic study.

Keywords Breast reconstruction · Combined reconstruction · Radiation therapy · Inpatient stay · Early postoperative complications

Introduction

Postmastectomy breast reconstruction has become the standard of care for breast cancer survivors, and the number of reconstructions has been increasing in recent years. However, there remain concerns regarding early postoperative complications. Adverse effects of breast reconstruction surgery are influenced by various factors, such as the patient's body habitus and BMI, comorbidities, smoking status, and/or type and extent of oncological treatment (e.g., the state of local tissues following mastectomy).

Radiation therapy in particular has a detrimental effect on breast reconstruction outcomes [1]. Therefore, our first aim was to analyze breast reconstruction outcomes by radiotherapy status. Whereas patient risk factors cannot be changed by the plastic surgeon, risk-informed planning of the surgical

Comparison of Early Postoperative Complication Rates Among Common Techniques for Postmastectomy Breast Reconstruction

✉ Andrej Sukop
andrej@sukop.cz

[1] Department of Plastic Surgery, 3rd Faculty of Medicine and University Hospital Kralovske Vinohrady, Charles University in Prague, Srobarova 50, 10034 Praha 10, Czech Republic

[2] Division of Plastic and Reconstructive Surgery, Department of Surgery, Stanford University School of Medicine, 1651 Page Mill Road, Palo Alto, CA 94304, USA

[3] Department of Plastic Surgery, Bulovka Hospital, 1st Medical Faculty of Charles University in Prague, Budinova 2, 18081 Praha 8, Czech Republic

procedure beforehand can positively impact surgical outcome. Our second aim was thus to analyze the outcomes by different types of breast reconstruction. Moreover, although many studies have examined the long-term outcomes and complications of breast reconstruction, short-term postoperative data are inconsistent. This prompted us to focus our comparisons on inpatient stay characteristics and early postoperative complications.

A postoperative complication was defined by Sokol et al. (2008) as "…any undesirable, unintended, and direct result of an operation affecting the patient, which would not have occurred had the operation gone as well as could reasonably be hoped" [2]. Importantly, Wilkins et al. (2018) clarified a complication as "…adverse postoperative, surgery-related event requiring additional treatment" [3]. There exist studies focusing on the negative aesthetic outcomes of breast reconstruction (e.g., breast asymmetry [4, 5]) in which additional treatment is *optional* or *favorable* but not *required*). However, data on postoperative complications that *require* additional treatment, which is an important consideration during the preoperative decision-making process, are inconsistent and thus the focus of this study.

Although assessments of implant and abdominal-based autologous reconstruction outcomes are relatively abundant in the literature [6–8], data on combined reconstruction are limited. Some authors even state that patients have three main options following mastectomy: no reconstruction, reconstruction with implant, or reconstruction using the patient's own tissue [9]. To address this knowledge gap, we included patients who had undergone combined reconstruction with implant and autologous tissue in this study and compared their outcomes to those of patients with implant or abdominal-based autologous reconstruction.

Although breast reconstructions are predominantly performed immediately following mastectomy in the USA [10], the majority of postmastectomy breast reconstructions are delayed in many European countries, such as France, Germany, the UK, Sweden, or the Czech Republic [11–15]. Given the differences between European and American approaches to postmastectomy breast reconstruction, we focused on outcomes for patients undergoing delayed breast reconstruction to provide data relevant to European clinicians and patients.

In sum, the results of this study would contribute to informed planning of such reconstruction procedures.

Materials and methods

Sample

Data from patients who had undergone delayed breast reconstruction between 2009 and 2014 at facilities of the Department of Plastic Surgery, University Hospital Kralovske Vinohrady, Charles University in Prague, Czech Republic, were collected. Data were obtained from the medical records from the clinic's patient records system. A retrospective study was conducted. The inclusion criteria were women ≥ 18 years of age who had undergone mastectomy for a primary breast cancer diagnosis followed by primary reconstruction with an implant (Fig. 1a–d), abdominal-based autologous reconstruction with free transverse rectus abdominis myocutaneous flap or free deep inferior epigastric artery flap (Fig. 2a–d), or a combination of an implant and a latissimus dorsi flap or thoracodorsal artery perforator flap. Reconstruction must have been performed in a delayed manner and in a single procedure. The exclusion criteria were as follows: patients who had undergone mastectomy for breast cancer prophylaxis or for benign neoplasm treatment. The study was approved by the Ethics Commission of the Third Faculty of Medicine, Charles University in Prague, and the manuscript was prepared in accordance with STROBE guidelines.

Procedure

The primary independent variables were history of radiotherapy and reconstruction procedure type. Data that were analyzed included the following characteristics of the inpatient stay: operative time, length of overall inpatient stay and stay at the intensive care unit (ICU), therapeutic intervention scoring system (TISS) records, postoperative pain scale score, requirement of transfusions, catecholamine support, therapy with vasodilation infusions, intravenous therapy with antibiotics, consumption of intravenous opioid/non-opioid analgesics and antipyretics, and consumption of anxiolytics, hypnotics, antidepressants, antitussives, expectorants, antiemetics, and prokinetics. Furthermore, we analyzed postoperative complications that occurred during the inpatient stay (early postoperative complications), including perfusion disorders, bleeding, necrosis/dehiscence, swelling, seroma, and infection.

Statistical analysis

The collected data were recorded in Excel (Microsoft Corporation, Redmond, WA). Mean values and standard deviations (SDs) were calculated. The Kruskal–Wallis test was employed to compare > 2 groups, the chi-square test of independence was used for contingency tables, and one-way ANOVA was employed to compare 2 groups. The level of statistical significance was set at $p < 0.05$.

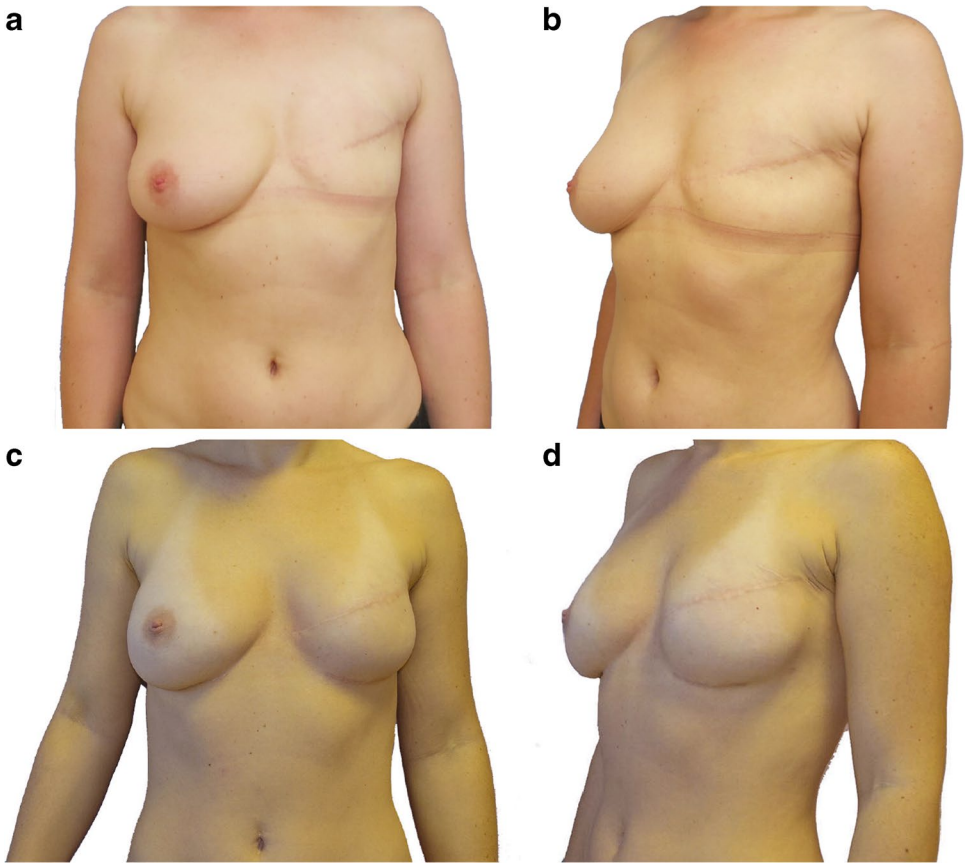

Fig. 1 **a**–**d** Reconstruction with an implant

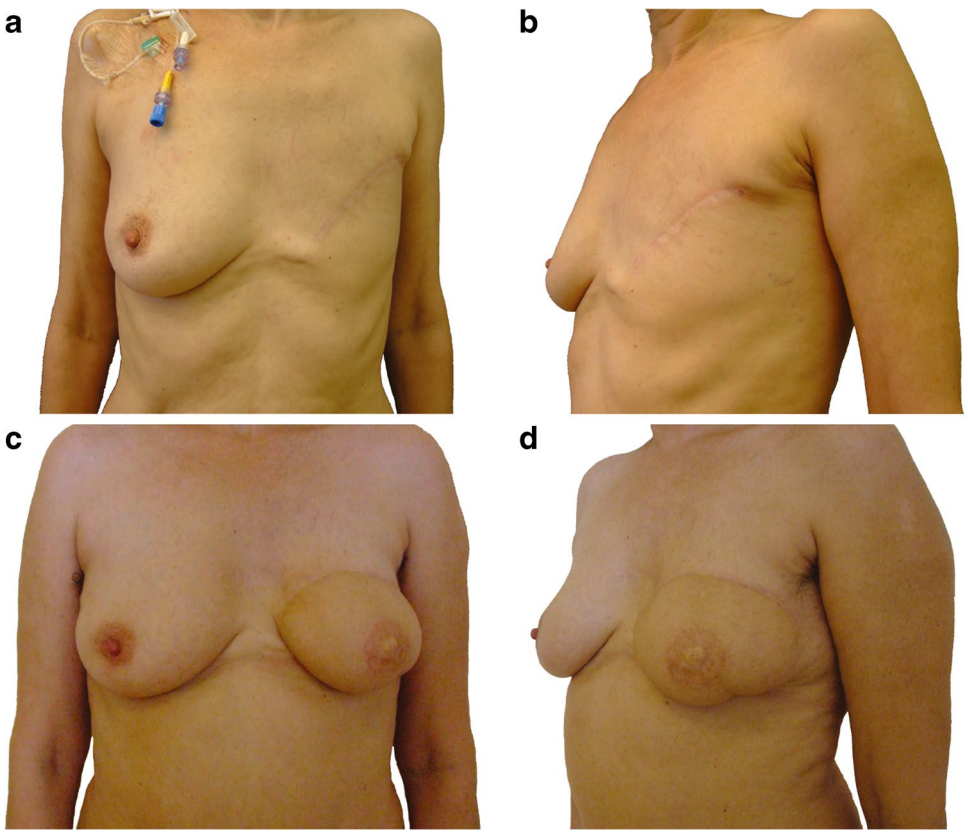

Fig. 2 **a**–**d** Abdominal-based autologous reconstruction

Results

The medical records of a total of 95 patients were analyzed. The average age and BMI of the patients were 48.8 years and 23.8 kg/m^2, respectively. Thirty-seven patients had cardiovascular comorbidities, 20 patients had endocrine (including diabetes) comorbidities, and 35 patients had orthopedic comorbidities (e.g., vertebrogenic algic syndrome). Seventeen patients were smokers. The mean delay between the last oncologic surgery and breast reconstruction was 35.3 months.

Thirty patients had radiation therapy prior to reconstruction, and 65 patients had no irradiation at all. Twenty-four of the patients underwent implant reconstruction, 38 underwent abdominal-based autologous reconstruction, and 33 underwent combined reconstruction with implant and autologous tissue performed in a single reconstruction procedure. Distribution of reconstruction types among the patients with previous radiotherapy versus patients with no radiotherapy is listed in Table 1. Within the radiotherapy group, the largest proportion of patients (63.3%) had undergone autologous reconstruction, followed by combined reconstruction (23.3%), and implant reconstruction (13.3%). Within the no radiotherapy group, 40.0% of patients had undergone combined reconstruction, 30.8% had undergone implant reconstruction, and 29.2% had undergone autologous reconstruction.

Table 1 Distribution of reconstruction approaches among patients with and without history of radiotherapy

Reconstruction approach	Radiotherapy ($n=30$) % (n)	No radiotherapy ($n=65$) % (n)
Implant ($n=24$)	13.3 (4)	30.8 (20)
Autologous ($n=38$)	63.3 (19)	29.2 (19)
Combined ($n=33$)	23.3 (7)	40.0 (26)

Postoperative characteristics by radiotherapy status are listed in Table 2. The mean operative time was 195.2 min in the radiotherapy group compared to 137.7 min in the no radiotherapy group ($p=0.020$). The mean overall length of inpatient stay was 12.3 days in the radiotherapy group and 10.6 days in the no radiotherapy group ($p=0.049$), of which the mean length of stay in the ICU was 5.2 days in the radiotherapy group and 3.2 days in the no radiotherapy group ($p=0.010$). The mean TISS 15–19 was recorded at an average of 1.5 days in the ICU in the radiotherapy group and 0.7 days in the no radiotherapy group ($p=0.004$). The mean TISS 9–14 was recorded at an average of 3.0 days in the ICU in the radiotherapy group and 1.9 days in the no radiotherapy group ($p=0.024$). Pain scores, on a scale of 1–10, were recorded on each day during the inpatient stay. The average pain score was 5.9 in the radiotherapy group and 5.1 in the no radiotherapy group ($p=0.036$). The mean number of transfusion products administered per patient was 0.3 in the radiotherapy group and 0.1 in the no radiotherapy group ($p=0.035$). Catecholamine support was required for an average of 0.5 days in the radiotherapy group and 0.2 days in the no radiotherapy group ($p=0.058$). Postoperative

Table 2 Comparison of inpatient stay characteristics in patients with and without history of radiotherapy

Characteristic	Radiotherapy ($n=30$) mean (SD)	No radiotherapy ($n=65$) mean (SD)	p-value
Operative time (minutes)	195.2 (116.9)	137.7 (99.0)	0.020
Overall inpatient stay (days)	12.3 (4.7)	10.6 (3.5)	0.049
Intensive care unit stay (days)	5.2 (3.9)	3.2 (3.3)	0.010
TISS 9–14 (days)	3.0 (2.5)	1.9 (2.1)	0.02
TISS 15–19 (days)	1.5 (1.5)	0.7 (1.2)	0.004
Pain scale (1–10)	5.9 (1.2)	5.1 (1.5)	0.036
Transfusions (total)	0.3 (0.8)	0.1 (0.3)	0.035
Administration of catecholamines (days)	0.5 (0.8)	0.2 (0.6)	0.058
Vasodilation therapy (days)	4.3 (3.8)	2.0 (3.2)	0.003
Antibiotics IV therapy (days)	5.3 (3.7)	3.4 (2.9)	0.011
Opioids, non-opioid analgesics, and antipyretics IV therapy (days)	2.8 (2.5)	1.9 (1.8)	0.047
Use of anxiolytics (days)	5.5 (5.3)	2.6 (3.6)	0.003
Use of hypnotics (days)	3.0 (4.8)	2.1 (3.2)	0.289
Use of antidepressants (days)	1.7 (4.0)	1.2 (3.6)	0.574
Use of antitussives and expectorants (days)	0.8 (2.0)	0.4 (1.6)	0.228
Use of antiemetics and prokinetics (days)	0.3 (1.3)	0.4 (1.9)	0.748

TISS therapeutic intervention scoring system, *IV* intravenous

vasodilation therapy was administered for an average of 4.3 days in the radiotherapy group compared to 2.0 days in the no radiotherapy group ($p = 0.003$). Patients in the radiotherapy group received intravenous antibiotics for an average of 5.3 days during their inpatient stay compared to 3.4 days in patients with no radiotherapy ($p = 0.011$). The mean duration of intravenous administration of opioids, non-opioid analgesics, and antipyretics was 2.8 days in the radiotherapy group compared to 1.9 days in the no radiotherapy group ($p = 0.047$). The mean duration of anxiolytic consumption was 5.5 days in the radiotherapy group and 2.6 days in the no radiotherapy group ($p = 0.003$). There were no significant differences in the consumption of hypnotics, antidepressants, antitussives and expectorants, and antiemetics and prokinetics between the radiotherapy group and the no radiotherapy group.

Postoperative clinical characteristics by breast reconstruction type are listed in Table 3. The mean operative time in the autologous group was 263.1 min compared to 81.7 min in the combination group and 74.1 min in the implant group ($p < 0.001$). The mean overall length of inpatient stay was 13.6 days in the autologous group, 10.7 days in the combination group, and 7.7 days in the implant group ($p < 0.001$), of which the mean length of stay in the ICU was 7.7 days in the autologous group, 1.5 days in the combination group, and 0.8 days in the implant group ($p < 0.001$). The mean TISS 15–19 was an average of 2.4 days in the autologous group; in the implant and combination groups, the averages were close to 0 days ($p < 0.001$). The mean TISS 9–14 was an average of 4.5 days in the autologous group, 0.8 days in the combination group, and 0.6 days in the implant group. The average pain score was highest in the autologous group (5.7), followed by the combination group (5.5) and then the implant group (4.6) ($p = 0.005$). In the autologous group, the mean number of transfusion products administered was 0.4 per patient, whereas no transfusions were administered in the implant and combination groups. Patients in the autologous group required postoperative catecholamine support for an average of 0.8 days, whereas patients in the implant and combination groups did not receive any postoperative catecholamine support ($p < 0.001$). Postoperative vasodilation therapy was administered on average for 6.7 days in the autologous group; no vasodilation therapy was required for patients in the other two groups, except for one patient in the combination group ($p < 0.001$). Patients in the autologous group received intravenous antibiotics for an average of 7.6 days compared to 1.7 days in the implant group and 1.6 days in the combination group ($p < 0.001$). The mean duration of intravenous analgesia was 4 days in the autologous group compared to 1 day in both the implant and combination groups ($p < 0.001$). The mean duration of anxiolytic consumption was also highest in the autologous group at 6.7 days compared to 1.9 days in the implant group and 1.0 days in the combination group ($p < 0.001$). Patients with autologous reconstruction received hypnotics for an average duration of 4.3 days, antidepressants for 2 days, antitussives and expectorants for 1.3 days, and antiemetics and prokinetics for 0.9 days; in the implant and combination groups, there was almost no administration of these medications. Given the high proportion of patients with previous

Table 3 Comparison of inpatient stay characteristics among different breast reconstruction approaches

Characteristic	Implant ($n = 24$) mean (SD)	Autologous ($n = 38$) mean (SD)	Combination ($n = 33$) mean (SD)	p-value
Operative time (minutes)	74.1 (36.9)	263.1 (80.7)	81.7 (25.3)	< 0.001
Overall inpatient stay (days)	7.7 (2.2)	13.6 (3.7)	10.7 (3.3)	< 0.001
Intensive care unit stay (days)	0.8 (1.2)	7.7 (2.3)	1.5 (1.0)	< 0.001
TISS 9–14 (days)	0.6 (0.8)	4.5 (2.0)	0.8 (0.7)	< 0.001
TISS 15–19 (days)	0.1 (0.3)	2.4 (1.0)	0.0 (0.2)	< 0.001
Pain scale (1–10)	4.6 (1.9)	5.7 (1.0)	5.5 (1.4)	0.005
Transfusions (total)	0.0 (0.2)	0.4 (0.8)	0.0 (0.0)	< 0.001
Administration of catecholamines (days)	0.0 (0.0)	0.8 (0.9)	0.0 (0.0)	< 0.001
Vasodilation therapy (days)	0.0 (0.0)	6.7 (1.9)	0.1 (0.4)	< 0.001
Antibiotics IV therapy (days)	1.7 (0.8)	7.6 (2.2)	1.6 (0.8)	< 0.001
Opioids, non-opioid analgesics, and antipyretics IV therapy (days)	1.0 (0.7)	4.0 (2.1)	1.0 (0.7)	< 0.001
Use of anxiolytics (days)	1.9 (2.1)	6.7 (5.3)	1.0 (0.8)	< 0.001
Use of hypnotics (days)	0.7 (1.2)	4.3 (4.8)	1.3 (2.4)	< 0.001
Use of antidepressants (days)	0.7 (1.9)	2.0 (4.7)	1.1 (3.5)	0.006
Use of antitussives and expectorants (days)	0.0	1.3 (2.6)	0.0 (0.0)	< 0.001
Use of antiemetics and prokinetics (days)	0.0	0.9 (2.7)	0.1 (0.3)	0.061

TISS therapeutic intervention scoring system, *IV* intravenous

radiotherapy in the autologous group, see Supplementary Table 1 for details on postoperative clinical characteristics by radiotherapy status within this group.

The frequencies of early postoperative complications by radiotherapy status are listed in Table 4. The occurrence of at least one early postoperative complication was significantly higher in the radiotherapy group (40.0%) than in the no radiotherapy group (12.3%) ($p=0.002$). In the radiotherapy group, 16.7% of patients had postoperative bleeding, 13.3% experienced necrosis or dehiscence, 6.7% had perfusion disorder(s), 6.7% suffered from postoperative swelling, 3.3% had seroma, and 3.3% experienced infection. In patients with no irradiation prior to reconstruction, 6% had bleeding, 3.1% experienced dehiscence or necrosis, 3.1% had perfusion disorder(s), and 3.1% had swelling complications. No patients without prior radiation therapy had seroma or infection.

The frequencies of early postoperative complications by breast reconstruction type are listed in Table 5. While only 6.1% of patients in the combination group and 8.3% of patients in the implant group experienced early postoperative complication(s), 42.1% of patients with autologous reconstruction experienced complication(s) during their postoperative inpatient stay ($p<0.001$). In the autologous group, 18% of patients had postoperative bleeding, 15.8% suffered from necrosis or dehiscence, 7.9% experienced perfusion disorder(s), 7.9% had postoperative swelling, 1.2% had seroma, and 1.2% had infection. For details on the frequencies of early postoperative complications by radiotherapy status within the autologous group, see Supplementary Table 2. In the combination group, 3% of patients had perfusion disorder(s), and 3% of patients experienced postoperative bleeding complications. Combined reconstruction was not associated with any postoperative necrosis or dehiscence, swelling, seroma, or infection. In the implant group, 4.2% of patients experienced bleeding, and 4.2% of patients had swelling complications. No patients in the implant group had postoperative perfusion disorder(s), necrosis or dehiscence, seroma, or infection.

Table 4 Comparison of early postoperative complications in patients with and without history of radiotherapy

Characteristic	Radiotherapy ($n=30$) % (n)	No radiotherapy ($n=65$) % (n)	p-value
Total incidence of any early postoperative complication	40.0 (12)	12.3 (8)	0.002
Bleeding	16.7 (5)	6.2 (4)	0.106
Necrosis/dehiscence	13.3 (4)	3.1 (2)	0.057
Perfusion disorder(s)	6.7 (2)	3.1 (2)	0.423
Swelling	6.7 (2)	3.1 (2)	0.423
Seroma	3.3 (1)	0 (0)	0.142
Infection	3.3 (1)	0 (0)	0.142

Discussion

Given recent innovations in breast reconstructive surgery, patients and clinicians have more choices for surgical approaches than in the past [16]. The selection of reconstruction type should be discussed with all patients, taking into consideration their preference for the size and shape of the breast(s). However, clinicians should guide patients toward the appropriate option(s) with regard to the state of local tissues following mastectomy, body habitus and BMI, clinical risk factors (e.g., comorbidities or smoking status), and oncological diagnosis and treatment, particularly radiation therapy. Furthermore, patient understanding of the risks and benefits of different reconstruction types is essential to satisfaction with the postoperative course and reconstruction outcomes.

Postmastectomy radiation therapy improves oncological outcomes in patients with a high risk of local breast cancer recurrence [17]. However, despite its therapeutic advantages, radiation therapy increases the risk of breast reconstruction complications [18]. Radiation causes direct damage of tissues, leading to erythema, desquamation, and ulceration [19]. Late complications include radiation-induced fibrosis

Table 5 Comparison of early postoperative complications among different breast reconstruction approaches

Characteristic	Implant ($n=24$) % (n)	Autologous ($n=38$) % (n)	Combination ($n=33$) % (n)	p-value
Occurrence of any early postoperative complication	8.3 (2)	42.1(16)	6.1 (2)	<0.001
Bleeding	4.2 (1)	18.4 (7)	3.0 (1)	0.005
Necrosis/dehiscence	0.0 (0)	15.8 (6)	0.0 (0)	0.008
Perfusion disorder(s)	0.0 (0)	7.9 (3)	3.0 (1)	0.211
Swelling	4.2 (1)	7.9 (3)	0.0 (0)	<0.001
Seroma	0.0 (0)	2.6 (1)	0.0 (0)	<0.001
Infection	0.0 (0)	2.6 (1)	0.0 (0)	0.261

[19] and reduced healing capacity of irradiated tissues [20]. Some studies have suggested that breast cancer patients may need a lesser amount of radiation than they have been receiving [21, 22].

We demonstrated that a history of radiotherapy was associated with a significantly longer duration of reconstructive surgery and inpatient stay. As hypothesized, patients with a history of radiotherapy had a higher risk of early postoperative complications, particularly necrosis and dehiscence.

We then turned our analysis to a comparison of outcomes in patients who had undergone different types of breast reconstruction. Reconstruction with autologous tissue provides the most natural breast(s) in appearance and sensation [23]. Simultaneously, this type of reconstruction avoids common late postoperative complications associated with the use of foreign material, such as capsular contracture or implant rupture [24, 25]. Patients with abdominal-based autologous reconstruction also report higher health-related quality of life and satisfaction with reconstruction outcomes than patients with implant reconstruction [26]. However, the invasiveness of abdominal-based autologous reconstruction is notably higher than that of implant reconstruction; as our data show, abdominal-based autologous reconstruction was associated with a significantly longer inpatient stay and a notably higher risk of early postoperative complications (e.g., tissue necrosis). This should be taken into consideration, particularly with regard to preoperative planning in patients with serious clinical risk factors.

Breast reconstruction using implants in combination with the patient's own tissue might have the benefits of both implant and autologous reconstruction methods. Implants in combination with autologous tissue provide a more natural appearance and sensation than implants only. Although late complications associated with the use of foreign material cannot be avoided, the use of autologous tissue at least facilitates wound healing and the process of tissue expansion, which might be particularly beneficial for patients who have undergone radiotherapy [27].

Given these long-term advantages of combined reconstruction, we were interested in whether the combination method is beneficial in the short-term and perioperative periods. The results of this study show that operative time and length of ICU stay were significantly shorter in patients who underwent combined and implant reconstruction procedures than in those who underwent abdominal-based autologous reconstruction. With regard to the length of overall postoperative inpatient stay in patients with combined reconstruction, the duration was significantly shorter than that in patients with abdominal-based autologous reconstruction but longer than that in patients with implant reconstruction. TISS values were significantly higher in patients with abdominal-based autologous reconstruction than in both patients with implant reconstruction and patients with combined reconstruction. The pain score on a scale of 1–10, recorded during the inpatient stay, was similar among patients with abdominal-based autologous and combined reconstruction and higher in these two groups than in patients with implant reconstruction. However, patients with combined reconstruction required intravenous analgesia for a significantly shorter period of time than patients with abdominal-based autologous reconstruction. Only patients with abdominal-based autologous reconstruction required postoperative transfusion(s) or catecholamine support. Abdominal-based autologous reconstruction was also associated with the longest duration of postoperative vasodilation therapy, antibiotic therapy, and consumption of anxiolytics, hypnotics, antidepressants, antitussives and expectorants, and antiemetics and prokinetics.

The frequencies of all types of examined early postoperative complications were highest in patients with abdominal-based autologous reconstruction. At least one postoperative adverse outcome was experienced by almost half of these patients. In contrast, there were almost no early postoperative complications in patients with implant and combined reconstruction procedures.

Although implant reconstruction is on the rise, reconstruction using autologous tissues yields better outcomes in patients with a history of radiation therapy [28]. Therefore, autologous reconstruction is typically preferred in such patients [29, 30]. This should be taken into consideration when evaluating postoperative outcomes of autologous reconstruction versus implant or combined reconstruction. Autologous reconstruction is a more complex surgical procedure compared to reconstruction using implant [31]; however, higher rate of irradiated patients might also contribute to longer inpatient stay and a higher rate of early postoperative complications after autologous reconstruction.

Conclusions

For patients who had undergone postmastectomy breast reconstruction, operative time and inpatient stay was longer if they had undergone radiation therapy prior to reconstruction, and if they had an abdominal-based autologous reconstruction versus an implant or combined reconstruction. Moreover, abdominal-based autologous reconstruction was associated with higher medicament consumption during inpatient stay. The risk of postoperative complications was also higher in irradiated patients compared to non-irradiated patients as well as in patients with abdominal-based autologous reconstruction compared to patients with implant or combined reconstruction.

Given no significant differences in outcomes between implant and combined reconstruction, combined reconstruction might be an interesting reconstruction option;

it provides a more natural appearance and sensation than implants only in addition to a lower risk of prolonged inpatient stay and early postoperative complications than abdominal-based autologous reconstruction.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00238-021-01918-x.

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Author contribution All authors contributed to the study conception and design. P.T., O.M., and A.S. performed material preparation. P.T. and A.S. performed data collection. P.T. and M.W. performed data analysis. The first draft of the manuscript was written by P.T., and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Code availability Not applicable.

Declarations

Ethics approval This retrospective study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Ethics Commission, Third Faculty of Medicine, Charles University in Prague approved this study.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest Pavla Ticha, Ondrej Mestak, Meagan Wu, and Andrej Sukop declare no competing interests.

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