The significance of timing in breast reconstruction after mastectomy: An ACS-NSQIP analysis

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Background

Globally, more than 2 million patients are diagnosed with breast cancer each year.[1] Breast cancer often necessitates mastectomy, with breast reconstruction (BR) significantly improving the quality of life of patients. Different techniques (implants versus autologous tissue) and time points (immediately or at a delayed time after mastectomy) are available.[2] Patient eligibility for alloplastic and autologous BR should be critically evaluated on a case-by-case basis, accounting for patient preferences and procedure-specific advantages. Although the implant-based option is generally associated with lower invasiveness and shorter operative and downtime, autologous tissue is characterized by superior tolerance to radiation, triggers no immune/encapsulation reactions, and offers a (more) natural appearance and feel.[3-6]

During the last decade, the number of immediate BRs has been on the rise, with more than three out of four BR cases now performed at the same time as mastectomy surgery.[7] This popularity of immediate BR is likely due to the reported lower costs, superior esthetic outcome, and increased levels of psychosocial well-being compared to delayed BR.[8] Yet, the delayed approach may also have its benefits, for example, in cases involving planned post-mastectomy radiation therapy or when the patient is incapable of making well-considered decisions due to the emotional and psychological burden of cancer.[9]

For surgical decision-making, the outcomes after each procedure play a key role. Previous studies investigating the incidence of complications after immediate versus delayed and implant-based versus autologous BR report conflicting results.[8,10-18] Such discordance may be due to three reasons: (i) non-distinction between autologous and alloplastic BR, (ii) inconsistent capturing and reporting of complications, and (iii) single-center or single-surgeon experience with small sample size. As a result, transferability and comparability remain limited, with scarce evidence on accurate differences in perioperative success. Analyses of a multicenter database would help overcome these limitations and address this knowledge gap by pooling standardized patient data with geographic, racial, and institutional variations.

The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) collects data from more than 700 hospitals. In the field of breast surgery, available literature includes numerous studies evaluating the ACS-NSQIP.[19-25] However, the ACS-NSQIP database has not yet been analyzed to compare the perioperative outcomes following implant-based and autologous BR in the immediate or delayed setting. Of note, in the ACS-NSQIP, postoperative follow-up is limited to 30 days. Yet, short-term outcomes and complication occurrence in the early postoperative period have been shown to significantly affect patient satisfaction in the long term.[26,27] Ultimately, the herein-presented insights can guide both patients and physicians in informed decision-making regarding the optimal timing for BR.

Methods

Data source

Data were acquired from the ACS-NSQIP database over a 14-year period (2008–2021). At the time of analysis, more recent data were unavailable. Available to participating institutions, the ACS-NSQIP is a risk-adjusted, case-mix-adjusted, and outcomes-based data registry of surgical patients and their procedures. It collects information from more than 700 hospitals in 11 different countries on more than 150 preoperative, perioperative, and postoperative data points of surgical patients. The quality and validity of the patient/procedural metrics are guaranteed by spot audits and peer reviews. The analyzed data contain de-identified information. Ethical approval to perform this study was obtained from REDACTED our institution (Brigham and Women's Hospital, Boston, MA, USA; protocol number: 2013P001244).

Patient selection

The ACS-NSQIP captures surgical cases of patients aged ≥18 years. We excluded all male and non-binary patients. In the first step, the datasets were filtered for the codes ICD-9-CM 174 ("Malignant neoplasm of the female breast"), 233.0 ("Carcinoma in situ of the breast"), and V10.3 ("Personal history of malignant neoplasm of the breast") as well as ICD-10-CM C50 ("Malignant neoplasm of the breast"), D05 ("Carcinoma in situ of the breast"), and Z85.3 ("Personal history of malignant neoplasm of the breast"). Cases with other and/or more extensive diagnoses were not eligible. We then searched this pre-filtered cohort for all patients who underwent implant-based or autologous BR using Current Procedural Terminology (CPT) codes (Supplementary Table 1). All cases with immediate-delayed BR (i.e., CPT code 19357 ["Tissue expander placement in breast reconstruction"]) were excluded, as the removal of the expander and insertion of a breast implant at a later time point cannot be adequately tracked in the database. Accordingly, in this manuscript, the term "implant-based" always refers to the insertion of breast prostheses without interim tissue expansion. We excluded all patients who underwent invasive (concurrent) surgery other than BR. Cases with physiologically impossible body mass index (BMI) values (< 7 kg/m^2 or > 250 kg/m^2) and vague coding (e.g., missing CPT numbers or procedural descriptions) were also excluded. The final cohort was manually checked by two investigators (S.K. and L.K.), with a third investigator (A.C.P.) resolving controversies. Finally, we compiled a cohort of adult female patients who had been diagnosed with breast cancer and underwent implant-based or autologous BR, either immediately or at a delayed stage. Figure 1 illustrates the screening process.

Variable extraction

Preoperative data: we evaluated patient demographics (sex, age, race, and BMI), comorbidities (diabetes, history of chronic obstructive pulmonary disease [COPD], congestive heart failure [CHF], sepsis, dialysis, renal insufficiency, medically treated hypertension, ascites, dyspnea, nicotine use in the past year, corticosteroid use, weight loss more than 10% of body weight in the 30 days before surgery, disseminated cancer, bleeding disorders, preoperative transfusion of ≥1 unit of whole/packed red blood cells 72 h prior to surgery, wound infection, and functional health status), preoperative scores (American Society of Anesthesiology [ASA]) physical status classification [score 1-4], and wound classification [score 1-4].

Perioperative variables: surgical setting (inpatient or outpatient), type of anesthesia (general and other/unknown), specialty (plastic surgery, general surgery, and other/unknown), and year of surgery. Cases were manually reviewed and classified based on technique (implant-based versus autologous) and timing (immediate versus delayed), according to the reported CPT codes. We sub-specified the types of autologous surgery (latissimus dorsi flap, free flap, transverse rectus abdominis myocutaneous [TRAM; single-pedicled versus single-pedicled and supercharged versus bi-pedicled], and other/unknown) and lymph node surgery (sentinel lymph node biopsy [SLNB] or axillary lymph node dissection [ALND]).

Thirty-day outcomes: operative time, length of hospital stay (LOS), discharge destination (home, non-home, and other/unknown), and complication occurrence. Any complication was defined as the occurrence of mortality and/or reoperation and/or readmission and/or unplanned readmission and/or any surgical, and/or any medical complication. General complications included mortality and/or reoperation and/or readmission, and/or unplanned readmission. All surgical complications recorded in the ACS-NSQIP database were evaluated (namely, superficial and deep incision site infections, organ space infections, dehiscence, and bleeding/transfusion). We considered all medical complications captured by the ACS-NSQIP (i.e., pneumonia, reintubation, pulmonary embolism, ventilator dependence > 48 h, renal insufficiency, renal failure, urinary tract infection, cerebral vascular accident/stroke, cardiac arrest, myocardial infarction, deep vein thrombosis/thrombophlebitis, sepsis, and septic shock).

Statistical analysis

The raw data were converted to Microsoft Excel files (V.16, Microsoft Corporation, Redmond, WA, USA) via SPSS for Windows (V.29, IBM Corporation, Armonk, NY, USA). The data were stored in an electronic laboratory notebook (LabArchives, LLC, San Marcos, CA, USA) and analyzed using the R statistical software (V. 4.1.2). Categorical data are presented as absolute numbers (n) and percentages (%), and continuous variables as mean ± standard deviation. Risk factors for any, surgical and medical complications were evaluated exploratory using t-tests for continuous variables and chi-square tests for categorical variables. To compare differences in outcomes after immediate versus delayed implant-based BR, we used a propensity score weighting (PSW) approach with overlap weights.[31] The propensity scores were estimated by logistic regression and adjusted for possible confounders – all preoperative and perioperative variables as stated above – using package PSweight with the option weight = "overlap." The causal odds ratios (ORs) for the outcomes of interest were compared in the overlap population, i.e., for patients being eligible for both immediate and delayed implant-based BR. As a sensitivity analysis, we compared the causal ORs to the results of univariable and multivariable logistic regression, adjusting for the aforementioned confounding factors. Adjusted ORs for the other risk factors were obtained from the same analyses. Statistical significance was set at $p < 0.05$.

Results

Preoperative patient demographics and health characteristics

A total of 21,560 female breast cancer patients were included, with 10,323 (47.9%) receiving autologous and 11,237 (52.1%) undergoing implant-based BR (Table 1). In the autologous cohort, 8378 (81.2%) women underwent immediate surgery, while 1945 (18.8%) had delayed procedures. Among implant-based BR, the majority (n = 9791; 87.1%) were

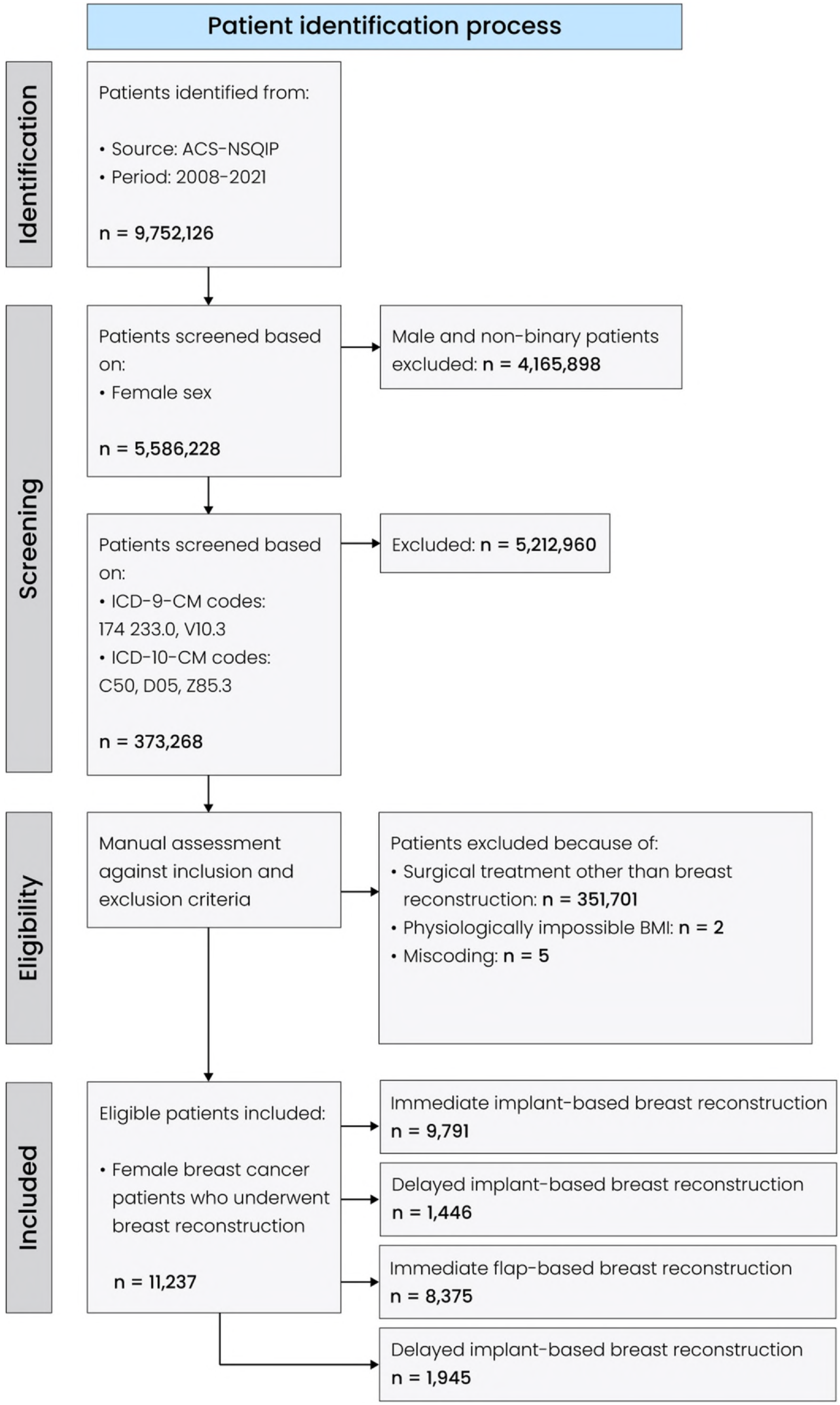

Figure 1 Flow chart of the screening and selection process.

Table 1 Demographics and preoperative health characteristics of all patients undergoing alloplastic and autologous BR at immediate or delayed time points. Reported as n (%), unless otherwise stated.

Characteristic	Immediate implant-based BR (n = 9791)	Delayed implant-based BR (n = 1446)	*P* value	Immediate flap BR (n = 8378)	Delayed flap BR (n = 1945)	*P* value
Demographics						
Age, mean ± SD	51 ± 11	52 ± 11	0.39	53 ± 9.7	52 ± 9.9	**0.0003**
BMI, mean ± SD	27 ± 6.1	27 ± 6.4	**< 0.0001**	29 ± 5.9	29 ± 5.7	0.17
Race						
American Indian or Alaskan Native	18 (0.2)	1 (0.1)	**0.02**	14 (0.2)	4 (0.2)	**0.0008**
Asian	442 (4.5)	72 (5.0)		491 (5.9)	67 (3.4)	
Native Hawaiian or Pacific Islander	18 (0.2)	9 (0.6)		18 (0.2)	6 (0.3)	
Black or African American	624 (6.4)	123 (8.5)		1217 (15)	302 (16)	
White	6640 (68)	1122 (78)		5326 (64)	1208 (62)	
Other/Unknown	2049 (21)	119 (8.2)		20 (0.2)	1 (0.1)	
Preoperative health and comorbidities						
Diabetes	479 (4.9)	81 (5.6)	0.27	576 (6.9)	138 (7.1)	0.12
Insulin-treated diabetes	117 (1.2)	21 (1.5)	0.11	108 (1.3)	37 (1.9)	
COPD	59 (0.6)	14 (1.0)	0.15	53 (0.6)	11 (0.6)	0.77
Obesity	2375 (24)	406 (28)	**0.0006**	3348 (40)	795 (41)	0.42
CHF	8 (0.1)	1 (0.1)	> 0.99	13 (0.2)	4 (0.2)	0.85
Dialysis	9 (0.1)	0 (0.0)	0.51	2 (0.0)	3 (0.2)	0.07
Renal insufficiency	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Hypertension	2121 (22)	379 (26)	**0.0001**	2289 (27)	521 (27)	0.65
Ascites	0 (0.0)	0 (0.0)		1 (0.0)	0 (0.0)	> 0.99
Dyspnea	170 (1.7)	35 (2.4)	0.10	141 (1.7)	36 (1.9)	0.67
Current smoker	836 (8.5)	113 (7.8)	0.38	651 (7.8)	144 (7.4)	0.62
Corticosteroid use	195 (2.0)	23 (1.6)	0.35	154 (1.8)	35 (1.8)	0.98
Weight loss > 10%	25 (0.3)	3 (0.2)	0.93	27 (0.3)	5 (0.3)	0.81
Disseminated cancer	221 (22)	25 (1.7)	0.24	163 (1.9)	37 (1.9)	0.97
Bleeding disorders	85 (0.8)	12 (0.9)	> 0.99	40 (0.5)	10 (0.5)	0.98
Preoperative transfusions	2 (0.0)	2 (0.1)	0.14	16 (0.2)	2 (0.1)	0.59
Wound infection	10 (0.1)	3 (0.2)	0.51	61 (0.7)	33 (1.7)	**< 0.0001**
History of sepsis	16 (0.2)	3 (0.2)	0.97	36 (0.4)	3 (0.2)	0.11
Tumor characteristics/type			**< 0.0001**			**< 0.0001**
In situ	2193 (22)	59 (4.1)		1900 (23)	52 (2.7)	
Invasive	7428 (76)	834 (58)		6258 (75)	1352 (70)	
Other/unknown	170 (1.7)	553 (38)		220 (2.6)	541 (28)	
ASA class			**< 0.0001**			**< 0.0001**
1 - No disturbance	682 (7.0)	56 (3.9)		341 (4.1)	48 (2.5)	
2 - Mild disturbance	6879 (70)	981 (68)		5453 (65)	1119 (58)	
3 - Severe disturbance	2178 (22)	405 (28)		2544 (30)	767 (39)	
4 - Life-threatening	39 (0.4)	2 (0.1)		36 (0.4)	10 (0.5)	
5 - Other/unknown	13 (0.1)	2 (0.1)		4 (0.0)	1 (0.1)	
Wound class			0.15			**0.003**
1 - Clean	8714 (89)	1297 (90)		7284 (87)	1664 (86)	
2 - Clean/Contaminated	98 (1.0)	23 (1.6)		115 (1.4)	42 (2.2)	
3 - Contaminated	14 (0.1)	5 (0.3)		23 (0.3)	13 (0.7)	
4 - Dirty/Infected	5 (0.1)	1 (0.1)		22 (0.3)	5 (0.3)	
5 - Other/unknown	960 (9.8)	121 (8.4)		934 (11)	221 (11)	
Functional status						0.51
Independent	9772 (100)	1443 (100)	> 0.99	8313 (99)	1934 (99)	
Partially or totally dependent	19 (0.2)	3 (0.2)		48 (0.6)	8 (0.4)	

ASA, American Society of Anesthesiology; BMI, body mass index; BR, breast reconstruction; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; SD, standard deviation.
Significant findings are highlighted in bold.

immediate procedures, with 1446 (12.9%) patients receiving implants at a later time point. Mean age (51 ± 11 years) and BMI (27 ± 6.1 kg/m^2) were lowest in the immediate implant-based cohort, whereas women with immediate autologous BR were on average older (53 ± 9.7 years) and had higher BMI values (29 ± 5.9 kg/m^2). In all four 4 groups, obesity and hypertension were the most common comorbidities.

Surgical characteristics

Among patients with immediate and delayed autologous BR, free flap reconstruction was the most common procedure (n = 5875, 70% and n = 1311, 67%, respectively). Latissimus dorsi flaps were more frequently performed as a delayed procedure (n = 340; 17% versus Immediate: n = 801; 10%), a higher percentage of immediate autologous BR patients received a TRAM flap (n = 1702; 20% versus n = 294; 15%). More than one in two (n = 5094; 52%) patients with immediate implant-based BR underwent SLNB. In the same cohort, 1714 (18%) patients received ALND. Similar patterns were noted among patients having immediate autologous BR, with 3960 (47%) recorded SLNB cases and 1323 (16%) ALND cases. By contrast, in patients undergoing delayed autologous BR, SLNB, and ALND were rarely performed. Among women with immediate implant-based BR, an even distribution between inpatient (n = 4844; 49%) and outpatient (n = 4947; 51%) care was recorded, whereas the vast majority (n = 1357; 94%) sought delayed implant-based BR in the ambulatory setting (Table 2). Both immediate (n = 7959; 95%) and delayed (n = 1771; 91%) autologous BRs were most commonly managed as inpatient procedures.

Table 2 Surgical characteristics. Reported as n (%).

Characteristic	Immediate implant-based BR (n = 9791)	Delayed implant-based BR (n = 1446)	*P* value	Immediate flap BR (n = 8378)	Delayed flap BR (n = 1945)	*P* value
Type of surgery						**< 0.0001**
Free flap				5875 (70)	1311 (67)	
Latissimus dorsi flap				801 (10)	340 (17)	
TRAM flap				1702 (20)	294 (15)	
Single-pedicled				1245 (15)	212 (11)	
Single-pedicled and supercharged				261 (3.1)	56 (2.9)	
Bi-pedicled				196 (2.3)	26 (1.3)	
Lymph node surgery			**< 0.0001**			**< 0.0001**
SLNB	5094 (52)	3 (0.2)		3960 (47)	29 (1.5)	
ALND	1714 (18)	0 (0.0)		1323 (16)	10 (0.5)	
Surgical specialty			**< 0.0001**			**< 0.0001**
General surgery	6849 (70)	50 (3.5)		4182 (50)	134 (6.9)	
Plastic surgery	2932 (30)	1396 (97)		4181 (50)	1808 (93)	
Other/Unknown	10 (0.1)	0 (0.0)		15 (0.2)	3 (0.2)	
Type of anesthesia			**0.003**			> 0.99
General	9761 (100)	1434 (99)		8354 (100)	1940 (100)	
Other/unknown	30 (0.3)	12 (0.8)		23 (0.3)	5 (0.3)	
Setting			**< 0.0001**			**< 0.0001**
Inpatient	4844 (49)	89 (6.2)		7959 (95)	1771 (91)	
Outpatient	4947 (51)	1357 (94)		419 (5.0)	174 (8.9)	
Year of surgery			**< 0.0001**			**< 0.0001**
2008	306 (3.1)	37 (2.6)		335 (4.0)	63 (3.2)	
2009	375 (3.8)	54 (3.7)		377 (4.5)	88 (4.5)	
2010	290 (3.0)	31 (2.1)		402 (4.8)	47 (2.4)	
2011	108 (1.1)	59 (4.1)		208 (2.5)	32 (1.6)	
2012	583 (6.0)	89 (6.2)		567 (6.8)	114 (5.9)	
2013	736 (7.5)	90 (6.2)		662 (7.9)	98 (5.0)	
2014	609 (6.2)	102 (7.1)		616 (7.4)	105 (5.4)	
2015	683 (7.0)	116 (8.0)		697 (8.3)	127 (6.5)	
2016	749 (7.6)	70 (4.8)		637 (7.6)	111 (5.7)	
2017	915 (9.3)	139 (9.6)		757 (9.0)	230 (12)	
2018	1139 (12)	169 (12)		728 (8.7)	271 (14)	
2019	1299 (13)	220 (15)		815 (9.7)	249 (13)	
2020	1039 (11)	149 (10)		643 (7.7)	189 (9.7)	
2021	960 (10)	121(8.4)		934 (11)	221 (11)	

ALND, axillary lymph node dissection; BR, breast reconstruction; SLNB, sentinel lymph node biopsy; TRAM, transverse rectus abdominis myocutaneous.
Significant findings are highlighted in bold.

Table 3 Operative and postoperative outcomes following implant-based BR. Reported as n (%), unless otherwise stated.

Characteristic	Immediate implant-based BR (n = 9791)	Delayed implant-based BR (n = 1446)	*P* value	Immediate flap BR (n = 8378)	Delayed flap BR (n = 1945)	*P* value
LOS, Mean days ± SD	1.4 ± 2.3	0.3 ± 2.5	**< 0.0001**	3.9 ± 2.8	3.8 ± 2.9	**0.01**
LOS ≥1 day	3082 (31)	50 (3.5)	**< 0.0001**	7980 (95)	1749 (90)	**< 0.0001**
Operative time, Mean minutes ± SD	202 ± 92	99 ± 55	**< 0.0001**	444 ± 185	418 ± 186	**< 0.0001**
Any complication	1112 (11)	64 (4.4)	**< 0.0001**	2073 (25)	417 (21)	**< 0.0001**
General complication	889 (9.1)	50 (3.5)	**< 0.0001**	1245 (15)	240 (12)	**0.005**
Mortality within 30 days	2 (0.0)	1 (0.1)	0.84	5 (0.1)	2 (0.1)	0.86
Reoperation	718 (7.3)	29 (2.0)	**< 0.0001**	985 (12)	191 (9.8)	**0.02**
Readmission	423 (4.3)	31 (2.1)	**< 0.0001**	467 (5.6)	103 (5.3)	0.46
Unplanned readmission	395 (4.0)	30 (2.1)	**0.0003**	419 (5.0)	93 (4.8)	0.52
Surgical complication	555 (5.7)	30 (2.1)	**< 0.0001**	1310 (16)	283 (15)	0.25
Superficial incisional infection	211 (2.2)	15 (1.0)	**0.006**	356 (4.2)	90 (4.6)	0.50
Deep incisional infection	74 (0.8)	3 (0.2)	**0.03**	101 (1.2)	40 (2.1)	**0.005**
Organ space infection	146 (1.5)	7 (0.5)	**0.003**	58 (0.7)	17 (0.9)	0.48
Dehiscence	91 (0.9)	7 (0.5)	0.12	129 (1.5)	33 (1.7)	0.69
Bleeding	64 (0.7)	1 (0.1)	**0.01**	777 (9.3)	133 (6.8)	**0.0008**
Medical complication	86 (0.9)	7 (0.5)	0.15	255 (3.0)	58 (3.0)	0.97
Pneumonia	7 (0.1)	1 (0.1)	> 0.99	28 (0.3)	6 (0.3)	> 0.99
Reintubation	2 (0.0)	0 (0.0)	> 0.99	14 (0.2)	8 (0.4)	0.07
Pulmonary embolism	16 (0.2)	0 (0.0)	0.24	53 (0.6)	7 (0.3)	0.21
Ventilator dependence > 48 h	3 (0.0)	0 (0.0)	> 0.99	8 (0.1)	6 (0.3)	0.05
Renal Insufficiency	1 (0.0)	0 (0.0)	> 0.99	5 (0.1)	3 (0.2)	0.37
Urinary tract infection	26 (0.3)	1 (0.1)	0.26	51 (0.6)	10 (0.5)	0.74
Cerebral vascular accident/stroke	1 (0.0)	0 (0.0)	> 0.99	3 (0.0)	1 (0.1)	> 0.99
Myocardial infarction	2 (0.0)	0 (0.0)	> 0.99	8 (0.1)	4 (0.2)	0.36
Deep vein thrombosis/Thrombophlebitis	9 (0.1)	2 (0.2)	0.94	69 (0.8)	12 (0.6)	0.43
Sepsis	30 (0.3)	3 (0.2)	0.70	60 (0.7)	14 (0.7)	> 0.99
Septic shock	3 (0.0)	0 (0.0)	> 0.99	9 (0.1)	1 (0.1)	0.76
Discharge destination			0.39			0.35
Home/Permanent residence	8782 (90)	1318 (91)		7192 (86)	1735 (89)	
Non-home	32 (0.3)	2 (0.2)		65 (0.8)	11 (0.6)	
Other/unknown	977 (10)	126 (8.7)		1121 (13)	199 (10)	

BR, breast reconstruction; LOS, length of hospital stay; SD, standard deviation.
Significant findings are highlighted in bold.

Perioperative and postoperative outcomes

Patients undergoing immediate implant-based BR (202 ± 92 minutes) had significantly longer ($p < 0.0001$) operating times than those with delayed implant-based BR (99 ± 55 minutes; Table 3). Concurrent mastectomy significantly ($p < 0.0001$) prolonged the operation time in autologous BR. In the implant-based cohort, 8782 (90%) patients with immediate and 1318 (91%) patients with delayed surgery could return home after a LOS of 1.4 ± 2.3 days and 0.3 ± 2.5 days, respectively. Among patients with autologous BR, immediate surgery had significantly ($p = 0.01$) longer LOS (3.9 ± 2.8 days) with lower rates of home discharge (n = 7192; 86%) compared to delayed surgery (3.8 ± 2.9 days and n = 1735; 89%, respectively).

More than one in ten patients (n = 1112; 11%) with immediate implant-based BR experienced a complication, most of which were reoperations (n = 718; 7.3%) and surgical complications (n = 555; 5.7%). The respective risk was significantly (all $p < 0.0001$) lower in delayed implant-based BR, with 64 (4.4%) cases of any complication recorded, 29 (2.0%) patients returning to the operating room, and 30 (2.1%) experiencing complications. In the implant-based cohort, medical complications were rare, with 86 (0.9%) events occurring in the immediate cohort and 7 (0.5%) in the delayed cohort.

Table 4 Comparative overview of the PSW-based causal ORs for the occurrence of any, general, surgical, and medical complications across different groups. Statistically significant values are highlighted in bold.

Comparison	Any complication		General complication		Surgical complication		Medical complication	
	OR (95% CI)	*P* value	OR	95% CI	OR	95% CI	OR	95% CI
Immediate implant-based versus delayed implant-based BR	2.41 (1.69, 3.44)	**< 0.0001**	2.48 (1.68, 3.68)	**< 0.0001**	3.66 (2.11, 6.36)	**< 0.0001**	1.26 (0.39, 4.01)	0.70
Immediate flap versus delayed flap BR	1.28 (1.09, 1.50)	**0.003**	1.37 (1.12, 1.67)	**0.002**	1.13 (0.93, 1.36)	0.21	1.15 (0.77, 1.71)	0.49
Immediate versus delayed BR	1.33 (1.16, 1.52)	**< 0.0001**	1.52 (1.28, 1.80)	**< 0.0001**	1.19 (1.01, 1.41)	**0.04**	1.05 (0.72, 1.51)	0.82

BR, breast reconstruction; CI, confidence interval; OR, odds ratio; PSW, propensity score weighting.

The autologous cohort had a similar pattern: the complication rate was significantly ($p < 0.0001$) higher in patients in the immediate cohort (n = 2073; 25%) compared to the delayed cohort (n = 417; 21%). A total of 985 (12%) patients with immediate autologous BR required reoperation, whereas less than 1 in 10 patients (n = 191; 9.8%) with delayed surgery returned to the operating room. The rates of surgical and medical complications were comparable between immediate (n = 1310; 16% and n = 255; 3.0%, respectively) and delayed (n = 283; 15% and n = 58; 3.0%, respectively) autologous BR.

Propensity score weighting

When comparing immediate versus delayed implant-based BR, a causal OR of 2.41 (95% confidence interval [CI]: 1.69, 3.44; $p < 0.0001$) and 3.66 (95% CI: 2.11, 6.36; $p < 0.0001$) for the occurrence of any and surgical complications, respectively, was noted (Table 4). We found a 1.28-fold (causal OR: 1.28; 95% CI: 1.09, 1.50; $p = 0.0003$) and 1.37-fold (causal OR: 1.37; 95% CI: 1.12, 1.67; $p = 0.002$) increased odds for the occurrence of any and general complications among patients seeking immediate autologous BR compared to the delayed alternative.

Univariable and multivariable analyses

Univariable and multivariable analyses confirmed the ORs obtained via PSW. A detailed overview of the ORs can be found in Supplementary Tables 2 and 3.

Discussion

Arnold et al. predicted that the worldwide breast cancer incidence will continue to increase, exceeding 3 million new cases per year by 2040.[28] In the USA alone, there are more than 4 million breast cancer survivors, of whom patients with flat closure after mastectomy may be potential candidates for delayed BR.[29,30] According to research, less than 50% of women undergoing mastectomy are offered BR surgery, with 20% opting for immediate BR.[31] Even more, three out of four women do not understand the spectrum of BR options available.[31] Thorough and early-stage patient education with comparative presentation of the clinically available options is, therefore, imperative. In this study, we queried the multi-institutional ACS-NSQIP database to compare early postoperative outcomes of immediate and delayed BR, in both the implant-based and autologous options.

We found a higher percentage of invasive tumors in the immediate reconstruction cohort for both implant-based and flap-based BRs. This finding seems intuitively contradictory as delayed BR is often recommended for high -invasive cancers.[32] However, the ACS-NSQIP does not include data on the specific cancer entity and the degree of invasiveness, which may complicate the interpretation of this finding. While further studies are warranted to elucidate the exact rationale, we hypothesize that immediate flap-based BR provides a robust therapeutic base and wound bed for adjuvant treatments including radiotherapy. The radiation tolerance of reconstructive flaps is well documented.[33] For instance, Wang et al. reviewed 14 pre-flap radiations and 74 post-flap radiations and found that both success and healing rates were lower in the pre-flap radiation group (86% versus 99% for success, 64% versus 95% for healing).[34]

For both implant-based and flap BR, the literature regarding optimal timing is inconsistent and yields conflicting results. In fact, although a series of studies point to immediate flap BR as the safer option, a robust body of evidence finds immediate flap BR to be associated with an increased risk of postoperative complications.[10] Such contradictions can also be seen in the field of alloplastic BR: Sanati-Mehrizy et al. reported that immediate BR with implants/tissue expanders was associated with a significantly decreased risk of medical and surgical complications, whereas Saheb-Al-Zamani et al. noted slightly increased and statistically significant higher risks for minor and major complications, respectively, among patients with implant-based immediate BR.[21,35]

In our study, the delayed option was associated with a significantly lower risk of postoperative complications in both alloplastic and autologous BR. Specifically, we found that one in four patients undergoing flap BR in the immediate setting experienced any postoperative complication compared with one in five patients who received delayed flap BR (Table 3). The PSW and multivariable analyses revealed that patients with immediate flap BR had a 28% of any and 37% higher risk of general complications (Table 4 and Supplementary Table 3). In implant-based BR, the differences between immediate and delayed time points were even more significant: we calculated a more than twofold and nearly fourfold increased risk of any (OR: 2.41) and surgical (OR: 3.66) complication occurrence, respectively, in patients seeking immediate implant-based BR in comparison to the delayed alternative (Table 4). In the immediate patient cohort, the OR for medical adverse events was also markedly higher (OR: 1.26). However, in a broader context, clinicians and BR providers should critically weigh slightly differing complication rates of immediate versus delayed implant-based BR (e.g., wound dehiscence in 0.9% of immediate versus 0.5% of delayed BR) against the financial and esthetic challenges of delayed BRs.[36] Further, the difference in complication rates after immediate (25%) versus delayed (21%) autologous BR may be considered minor and should be interpreted in light of the limited postoperative follow-up period, thereby calling for prospective long-term studies.

Therefore, through a clinician's lens focused exclusively on postoperative morbidity, reconstruction of the breast on a separate day from mastectomy may be recommended. The process of surgical decision-making, however, should not be limited to such a mono-perspective approach. Instead, both patients and surgeons ought to take into account potential downsides of delayed BR: living without breasts can heavily affect the patient's body image and self-esteem, translating to higher rates of anxiety and depression.[37,38] In addition, patients must be informed about the necessity of a second surgical intervention, which can be technically challenging (due to intermediate skin contracture and scarring), and potentially less optimal cosmesis.[39] In contrast, after immediate BR, patients wake up with a breast mound without requiring additional surgery, thereby dampening the psycho-emotional burden of mastectomy.[40]

Despite our findings, although there appears to be an equal distribution of implant-based and autologous procedures, the majority of procedures in both these groups were performed immediately after mastectomy, with less than 20% of patients undergoing delayed reconstruction. This phenomenon may represent patients' wishes, for example, due to the awareness of the aforementioned downsides of BR, particularly the effect on body image and self-esteem. It should be mentioned, however, that a large multicenter US study found that women undergoing delayed reconstruction experience significantly worse quality of life before BR than women who underwent immediate BR, but this effect was no longer present in the 2-year post-reconstruction follow-up.[8]

Limitations

This study is the first to compare perioperative outcomes between immediate and delayed implant-based and autologous BR – based on multi-institutional data collected over 14 years. It is important to consider the limitations of this study when interpreting the results. The retrospective nature of the ACS-NSQIP database is associated with inherent biases.[41,42] The accuracy of the data varies depending on the expertise/experience of the data collectors, both within and between participating hospitals. Yet, Shiloach et al. report low variance in the database's heterogeneity.[43] While standardized data acquisition maximizes comparability, it can also result in the omission of potentially relevant and procedure-specific determinants, for example, information on the laterality of reconstruction as well as exact mastectomy technique/approach were unavailable. The NSQIP data on (neo)adjuvant chemotherapeutic regimens or radiotherapy were only recorded up to 2012/2013 and could, therefore, not be included in our analyses. We were, therefore, unable to determine how many complications ultimately led to reconstruction failure and how radiotherapy influenced the complication rates in our patient cohort.

While future research is needed to elucidate the reason(s) for the lower complication rates in delayed versus immediate autologous BRs, we speculate that such differences are due to clinical variables not captured in the ACS-NSQIP database (e.g., cancer progression, closer postoperative monitoring, and specialized care in BR center). In this context, it is important to note that delayed autologous BR does not automatically imply that patients underwent radiotherapy and/or chemotherapy, but only refers to the staged approach of mastectomy and BR. The ACS-NSQIP database lacks data on certain short-term complications (<30 days), such as hematoma or seroma, and any long-term outcomes (>30 days), including capsular contracture, esthetic appearance, or sensation. It is also noteworthy that delayed BRs are nowadays less frequently performed due to the financial burden and aesthetic drawbacks (e.g., disruption of key anatomic borders such the inframammary fold).[36] We excluded nonbinary patients as the ACS-NSQIP does not include data on hormone replacement therapy in such individuals. Hormone therapies, especially testosterone, however, have been shown to impact surgical outcomes and complication rates to a variable extent.[44,45]

Conclusion

Our analysis highlights the significance of timing in oncologic BR. We find that in both autologous and implant-based BR, patients with immediate surgery experienced significantly more short-term complications. Our insights can guide patients in making informed surgical decisions while surgeons ought to implement our findings in preoperative patient counseling and eligibility assessment. Ultimately, the choice of BR treatment remains a case-by-case evaluation, whereby patient preferences and evidence-based risk stratification should be critically considered.

Ethical approval

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Author contribution

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Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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None of the authors have a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.bjps.2023.11.049.

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