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Enhanced Recovery Pathway in Microvascular Autologous Tissue-Based Breast Reconstruction: Should it Become the Standard of Care?

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Abstract

Background—Enhanced Recovery Pathway (ERP) programs have demonstrated improved perioperative care and shorter length of hospital stay (LOS) in several surgical disciplines. The purpose of this study was to compare outcomes of patients undergoing autologous tissue-based breast reconstruction (ABR) before and after the implementation of an ERP program.

Methods—We retrospectively reviewed consecutive patients who underwent ABR by two surgeons before and after the implementation of the ERP at a university center over a three-year period. Patient demographics, perioperative data, and 45-day postoperative outcomes were compared between the traditional standard of care (pre-ERP) and ERP patients. Multivariate logistic regression was performed to identify risk factors for LOS. Cost analysis was performed.

Results—Between April 2014 and January 2017, 100 consecutive women were identified; 50 in each group. Both groups had similar demographics, co-morbidities, and reconstruction types. Postoperatively, the ERP cohort used significantly less opiate and more acetaminophen when compared to the pre-ERP cohort. Median LOS was shorter with the ERP cohort, which resulted in an extrapolated $279,258 savings from freeing up inpatient beds and increase in overall contribution margins of $189,342. Participation in an ERP program and lower total morphine equivalent use were independent predictors for decreased LOS. Overall 45-day major complication

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rates, partial flap loss rates, emergency room visits, hospital readmissions, and unplanned reoperations were similar between the groups.

Conclusions—ERP program implementation should be considered as the standard approach for perioperative care in ABR since it does not affect morbidity and is associated with accelerated recovery with reduced postoperative opiate use and decreased LOS leading to downstream healthcare cost savings.

Keywords

Enhanced recovery pathway; Enhanced recovery after surgery; Enhanced recovery after surgery in microvascular breast reconstruction; Autologous breast reconstruction

INTRODUCTION

There has been a steady growth in breast reconstructive procedures, with a 39% increase in procedural volume since 2000.[1] Although microvascular autologous breast reconstruction accounts for a small overall portion of these procedures, it has remained steady over the years which implies that the actual number of procedures contunues to increase. Excellent perioperative care for this patient population is essential to expedite recovery and optimize resource utilization. Implementation of enhanced recovery pathways (ERPs) have been proposed as one way to accomplish these goals, however, this has not been universally adopted.[2,3,4,5]

ERPs are collective standardized evidence-based preoperative, intraoperative, and postoperative multidisciplinary protocols involving collaboration of several specialties including surgeons, anesthesiologists, nurses, dieticians, pharmacists, and home care specialists.[6] These programs challenge and reevaluate traditional practices to improve quality of care. Their success is attributed to the attenuation of the neurohormonal stress response to surgery, thereby limiting physiologic stress, and consequently diminishing complications and organ dysfunction.[6] The benefits of ERP programs have been well established in several surgical disciplines including general, colorectal, bariatric, neurologic, orthopedic, and gynecologic surgery.[6,7,8,9,10,11,12,13,14,15,16] Although these programs have not yet been widely implemented in plastic surgery, emphasis on cost-effective quality initiatives has driven several institutions around the country to consider this quality measure. However, current literature on ERP for microvascular breast reconstruction is scarce. Some of the limitations of previous studies include small number of subjects, inequalities between the study groups, and use of expensive medications, such as liposomal bupivacaine, as part of the multimodal analgesic regimens.[2,3,4,5] Continued critical evaluation of ERP programs in plastic surgery is necessary, not only to demonstrate that the previously observed positive impact on LOS and other patient outcomes is replicable, but also to further optimize existing ERP protocols.

This study compared perioperative outcomes of patients who underwent microvascular breast reconstruction before and after the implementation of our institution’s ERP, examined risk factors for LOS and performed a cost analysis.

METHODS

Study design and data collection

This is a single-center retrospective cohort study comparing perioperative outcomes following microvascular breast reconstruction, immediate or delayed, among consecutive patients who were managed with the traditional standard of care (pre-ERP) and post implementation of an ERP program. The ERP for women undergoing microvascular breast reconstruction was designed through collaboration of healthcare professionals from Plastic Surgery, Anesthesia, Nursing and Pharmacy at our institution (Table 1). Following implementation in August 2015, all patients undergoing microvascular breast reconstruction by two surgeons participating in the study were subjected to the ERP. Exclusion criteria included allergies or adverse reactions to any of the medications used, pregnancy, prisoners, and age<18. The study was approved by the Institutional Review Board (Study number: 160806).

Patient demographics and clinical characteristics, intraoperative data, postoperative outcomes and complications were recorded. Data was gathered by two un-blinded investigators and entered into a Microsoft™ Excel spreadsheet using prepared de-identified codes. Unresolved data points or entry errors were reviewed and clarified by the principal investigators.

Microvascular autologous tissue-based breast reconstruction standard of care pathway (pre-ERP)

In this pathway, patients were kept nil by mouth for six hours prior to surgery and continued until the morning of postoperative day 1. The patients' diet was then slowly advanced as tolerated over the following 24 hours. Maintenance intravenous fluids were used until the patient tolerated an unrestricted diet. Analgesic regimens, intraoperative management, and postoperative nausea and vomiting prophylaxis were not standardized, but at the discretion of the attending anesthesiologists. No regional nerve blocks, such as transverse abdominis plane (TAP) blocks, were performed. Prophylactic Enoxaparin was started the evening of surgery, and 81mg daily aspirin was started the following morning for 30 days. Antibiotic prophylaxis was similar to ERP. Postoperatively, patient's hospital admission and flap monitoring were similar to ERP. Pain management was not standardized and included intravenous opiate analgesics or patient-controlled analgesia (PCA) pump until at least postoperative day 1 when the patient's diet was advanced. Once the patient was tolerating a diet, acetaminophen and oral narcotics were used on as needed basis, with intravenous narcotics for breakthrough pain. Perioperative nausea and vomiting prophylaxis was used for symptomatic relief. Early ambulation was encouraged but not expected. Foley catheters were removed on postoperative day 1 or 2 depending on the progress of the patient. Discharge home was at the discretion of the surgeon.

Microvascular autologous tissue-based breast reconstruction ERP

The ERP protocol was developed through a literature review followed by a multidisciplinary consensus (Table 1). Pre-admission education and counseling was provided to all patients elected to proceed with microvascular autologous reconstruction and met the study inclusion

criteria. Unlike the pre-ERP cohort, bilateral TAP blocks (containing bupivacaine 0.25%, dexamethasone 4 mg, possible clonidine to extend block duration) were performed by the Anesthesia team, either in the preoperative holding area or in the operating room immediately after induction of anesthesia, as part of the multimodal analgesic regimen. Postoperatively, pain control was managed by the Anesthesia Perioperative Consult Service. Patients were encouraged to be up and walking the evening of surgery. Foley catheters were removed at 6AM on the first postoperative day. Discharge planning was begun the day after surgery, along with education on drain management at home. Discharge criteria included sufficient oral intake without nausea and vomiting, adequate ambulation, good urine output, and satisfactory pain control with an oral analgesic regimen.

Surgical technique

All operations were performed by two participating attending microvascular surgeons. The surgical technique was similar for all the flaps without a learning curve for this procedure in either cohort. Standard flap harvest techniques were used. The internal mammary vessels were used as recipient vessels in all flaps.

Outcomes

The primary outcome was LOS, which was defined as the number of nights the patient spent in the hospital from admission until discharge. Postoperative day 0 was defined as day of surgery.

Secondary endpoints included postoperative inpatient analgesic and anti-emetic requirements, as well as minor and major complications within 45 days from the index operation. Analgesic requirements were divided into acetaminophen and opiate use. Opiate use was calculated by converting all forms of opioid intake, parenteral and oral, into oral morphine equivalents.[17] The need for a PCA pump and duration of use was also recorded. Major complications were defined as complications that were directly related to the index admission and required hospital readmission or reoperation within 45 days from the index operation. Partial or complete flap loss was also included in the major complications. Partial flap loss was defined as <40% of the total flap volume secondary to vascular compromise of an area of the flap. Complete flap loss was defined as irreversible vascular compromise of the flap due to microvascular arterial or venous thrombosis requiring explantation. All other complications were considered as minor.

Our institution utilizes a cost accounting system that allows assignment of fixed and variable expenses at the charge level for both Professional and Technical Services. For example, the system can assign nursing salary to inpatient room and board charges, actual medical supply costs to the individual charge items, and on the professional side the actual physician salary to Current Procedural Terminology codes and services. This allows for an accurate assessment of the cost of specific services for the organization. In order to understand the impact of the ERP on autologous breast reconstruction we examined all financial information (e.g., charges, payments, fixed and variable costs) associated with each study patient before and after the implementation of the program.

Statistical analysis

Patient characteristics, operative details, and postoperative outcomes were compared between pre-ERP and ERP groups. Descriptive statistics were reported as mean ± standard deviation or median with range, or as the number of patients or flaps with percentages. Categorical variables were compared using Pearson chi-square and Fisher exact tests. Continuous variables were compared with two-tailed Student's t-test. All group comparisons were unpaired and p-values two-tailed with statistical significance set at $p<0.05$. IBM SPSS Statistics Software version 23.0 (IBM Corporation, Armonk, New York, USA) was used for univariate analyses.

Multivariate analysis was performed to further analyze factors contributing to LOS using statistical software R version 3.3.0. LOS was described as a median with interquartile ranges and compared between pre-ERP and ERP groups using the Wilcoxon rank sum test. Since the distribution of LOS was highly skewed, a multivariable ordinal logistic regression was used to evaluate the difference between the two groups with adjustment for age, body mass index (BMI), bilateral reconstruction, operative time, total intraoperative fluid amount, total oral morphine equivalent use, and total acetaminophen use. Variables were examined for their distribution and transformations were made when needed. Results were presented as interquartile-range odds ratios (OR) for continuous predictors and simple OR for categorical predictors.

RESULTS

Between April 2014 and January 2017, a cohort of 100 consecutive women, who underwent a total of 145 microsurgical autologous breast reconstructions (45 bilateral procedures), were identified; 50 women were managed with the pre-ERP and 50 with the ERP. Baseline patient demographics and clinical characteristics were not significantly different between the two groups (Table 2). There were no significant differences between the two groups in the surgical timing (immediate *vs* delayed), laterality, or type of reconstruction (Table 3).

Data related to the intraoperative course is shown in Table 4. Overall operative times were found to be higher in the pre-ERP cohort. Unilateral reconstructions had a significantly longer operative time in the pre-ERP cohort, but no difference was noted between the two groups for patients undergoing bilateral reconstructions. There were no differences between the two groups in terms of intraoperative transfusions, intraoperative vasopressor use, and the use of mesh for abdominal wall reinforcement. Reduction in intraoperative fluid administration was seen in the ERP group.

A comparison of postoperative outcomes between the two groups is presented in Table 5. The ERP cohort had a significantly shorter median LOS, and less total oral morphine equivalents. The use of PCA pump was significantly less common for the ERP group, however when used, there was no difference in duration of use between groups. The ERP group had significantly higher use of acetaminophen in the first 48 hours, equal to pre-ERP group on postoperative day 3, and less on subsequent days. Additionally, the ERP cohort used significantly less ondansetron during the overall hospitalization, as well as specifically on postoperative days 0, 1, and 5. Table 6 compares the two groups with regards to 45-day

postoperative complications. There was no difference in frequency of minor or major complications, emergency room visits, hospital readmissions, or unplanned reoperations. However, there was a significant difference between the two groups in donor site wound healing, with higher rates of delayed wound healing in the ERP cohort. Of note, the majority of these cases were managed non-operatively with local wound care in the outpatient setting with complete resolution. Only 3 cases, 2 in the pre-ERP and 1 in the ERP cohort, required operative intervention.

Multivariate logistic regression analysis of risk factors for LOS is shown in Table 7. Participation in an ERP program and lower total morphine equivalent use were independent predictors for decreased LOS.

Implementation of the ERP decreased mean LOS by 1.7 days, resulting in a decrease of 108 inpatient days. This translated to a saving of $4,400 per patient. Contribution Margin is equivalent to the cost savings on a per patient basis and driven by payer mix and the corresponding payer mix. For our study, we identified an extrapolated $279,258 savings from freeing up inpatient beds and increase in overall contribution margins of $189,342.

DISCUSSION

The ERP program utilized at our institution encompasses core features from ERP literature including preoperative patient education, avoidance of prolonged preoperative fasting, goal-directed fluid management, standardized multimodal analgesic and anesthetic regimens, prevention of postoperative nausea and vomiting, venous thromboembolism prophylaxis, antibiotic prophylaxis, early ambulation and early resumption of diet postoperatively.[18,19] To the best of our knowledge, currently only four other studies have proposed a standardized care pathway in microvascular breast reconstruction and evaluated its efficacy by comparing outcomes after its implementation. Batdorf et al. examined the role of ERP in 100 consecutive patients (pre-ERP 51, ERP 49) undergoing microvascular breast reconstruction by two surgeons.[2] Afonso et al. retrospectively reviewed 91 patients (pre-ERP 49, ERP 42) undergoing deep inferior epigastric artery perforator (DIEP) or muscle-sparing transverse rectus abdominis myocutaneous (TRAM) flaps for breast reconstruction by multiple surgeons.[3] Bonde et al. presented their results before and after the establishment of a fast-track surgery protocol for unilateral microsurgical breast reconstruction (pre-ERP 292, ERP 177), and later revised their protocol and re-examined their outcomes on 16 consecutive patients.[4,5] Although all studies highlighted the conceivable success of ERP program in microvascular breast reconstruction, a few limitations were noted. The initial protocol of fast-track surgery that Bonde et al. used was not comprehensive since it did not include some key components of the current ERPs. When that protocol was revised, only the results of 16 patients were reported. The study by Batdorf et al. had patients with a significantly lower BMI and less chronic pain diagnosis in the ERP cohort. The ERP cohort also had a higher number of patients who underwent DIEP flaps (compared to muscle-sparing TRAM flaps), as well as less number of abdominal wall reconstructions with mesh compared to the non-ERP group. These differences might have confounded their outcomes. Afonso et al. attempted to account for these differences and included multiple surgeons with different practice patterns for better generalizability of their results. However, intraoperative and

postoperative ketorolac as an analgesic adjuvant was used inconsistently based on surgeon discretion, which might have introduced a selection bias. One significant difference between our multimodal analgesic regimen and that of the last two studies is the strict documented compliance with scheduled acetaminophen and the use of bupivacaine and dexamethasone for the TAP blocks, as opposed to liposomal bupivacaine. Our findings suggest that liposomal bupivacaine may not be necessary for TAP blocks given its higher cost and absence of strong evidence to suggest superiority to bupivacaine hydrochloride.[20,21] It is possible that plain bupivacaine when administered in combination with a medication that prolongs the duration of the nerve block, such as dexamethasone, may be equally beneficial.

Similar to prior studies, our primary endpoint was LOS. While a non-specific variable, it is readily available, and can be utilized as a proxy for the clinical recovery trajectory. Both Batdorf and Afonso's studies demonstrated a significant drop in LOS in the ERP group from from 5.5 to 3.9 days ($p<0.001$) and from 5 to 4 days ($p<0.0001$), respectively.[2,3] Bonde et al. demonstrated a decrease in mean LOS from 7.4 to 6.2 days with their initial fast-track protocol; however, after it was revised a dramatic reduction in mean LOS to 3.1 days was reported.[4,5] Our study showed a significant decrease in the median LOS for the ERP cohort from 4 to 3 days, without any increase in major complications, hospital readmissions or unplanned reoperations. A recently presented study of 3,666 patients examined the rates of free flap compromise requiring reoperation after autologous breast reconstruction, and identified a very low rate of reoperation after postoperative day 2.[22] The authors concluded that providers may consider discontinuing flap monitoring after the first 48 hours. In addition, it is possible that a procedure with shorter anticipated LOS is perceived as less invasive by patients, which when coupled with the high patient satisfaction rates observed in previous studies,[2] could make microvascular autologous breast reconstruction a more attractive option for appropriate candidates in the future. Our analysis went one step further to examine risk factors associated with LOS, and showed participation in an ERP program and lower total morphine equivalent use to be predictors of a decreased LOS. Based on these data, we do believe that improvement of the ERP programs has the potential to safely decrease the LOS further to 2 days, which could potentially generate tremendous savings for the health care system.

Consistent with Batdorf's findings, we demonstrated a significantly lower use of total and daily oral morphine equivalent in the ERP cohort.[2] Afonso and Batdorf's analyses showed no difference in anti-emetic use between groups, however, our study revealed a significantly lower total ondansetron use in the ERP cohort.[2,3] This may be related to the lower use of PCA in the ERP cohort; only 3 of 50 patients in the ERP group needed a PCA as opposed to all patients in the pre-ERP group. This may be related to the significantly higher intake of acetaminophen in the ERP cohort in the first 2 postoperative days seen in our study.

Intraoperative multidisciplinary optimization has been shown to be a critical component of surgical ERPs. In our study, goal-directed fluid management by the Anesthesia team for the ERP cohort resulted in administration of significantly lower volume of intravenous fluids. This might have improved our outcomes since previous authors have investigated the implications of perioperative intravenous fluid management on microsurgical breast reconstruction and concluded that excessive intravenous fluid administration significantly

predicted postoperative complications.[23,24] Furthermore, we observed a considerable decrease in the overall operative time for the ERP cohort, which was more noticeable in the unilateral cases. This could be indirectly related to the ERP program resulting in more standardized care that could increase the efficiency of the involved teams. It could have also contributed to some of the other positive outcomes noted in the ERP cohort, such as lower intraoperative fluid administration. This is especially meaningful as prior studies on breast reconstruction have demonstrated the risk of encountering any early postoperative complication increases by 5.2% for every 10 minutes additional duration of surgery.[25] Moreover, shorter duration of surgery has important implications in cost savings and resource utilization for the operating room, and as a result can make this operation a more viable option from a financial perspective for large institutions. The financial benefit of ERP implementation is further supported by our logistic regression analysis that demonstrated longer operative times to be a significant risk factor for increased LOS.

In 2010, health-care expenditures in the United States neared $2.6 trillion, 10 times the amount spent in 1980.[26] It is thus not surprising that reduction in health-care expenditures and more effective utilization of resources has become an overriding health policy priority. While the cost savings resulting from ERPs have been documented across several surgical specialties, to the best of our knowledge, our study is the first in the plastic surgery literature to address this benefit.[27,28,29,30,31,32,33] There is a substantial effect of ERP implementation on healthcare expenditure with significant savings from freeing up inpatient beds and increased contribution margins, which warrants further evaluation.

This study has some limitations despite its overall contribution to the ERP literature. It is not a randomized-controlled trial and is therefore limited by the inherent drawbacks of a retrospective study design. Although we attempted to control for secular trends in our organization that may have occurred concurrently with our ERP implementation, it is possible that we did not capture confounding factors that might have affected our outcomes irrespective of the ERP. Also, our study is restricted by its single-center patient population and participation of only two surgeons, which may limit the generalizability of our results. We did not assess postoperative pain scores between the two groups, like prior studies, since opioid consumption is a more reliable and objective endpoint reflecting the patient’s need for analgesics. It has been previously shown that pain scores are fundamentally subjective and interpreted differently among individuals, making them less reliable measures of pain control.[34]

This study examined the effects of implementing a comprehensive ERP for microvascular autologous breast reconstruction at a large academic institution. Multiple benefits were observed including less postoperative narcotic and anti-emetic requirements, and decreased LOS without increasing patient morbidity. Of note, a higher rate of minor delayed wound healing problems that was managed with local wound care in the outpatient setting was observed in the ERP cohort, The etiology of this is unclear and has to be addressed with the patients in the preoperative setting. Equally important, in an era governed by policies to lower healthcare expenditures, our results suggest that implementation of such a program can assist in optimizing resource utilization with substantial cost savings. As advocates for our patients and our practices, we should start questioning whether such programs for breast

reconstruction should become standard of care and applied widely throughout the country. Even then, continued reassessment and research will be required to further refine and improve upon the components of the program for better outcomes.

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Table 1

Enhanced recovery pathway program.

Intervention Category	Intervention		
	Preop Holding Area	Intraoperative	Postoperative
Diet	Fasting: • Solid food: 6 hours before surgery • Clear liquids: 2 hours before surgery	Nil by mouth	Clear liquids immediately and unrestricted diet on POD1 7AM
Multimodal analgesia	1 hour before surgery: • Acetaminophen 1000 mg PO with sip of water ∫ • Gabapentin 600 mg PO with sip of water ∫∫ • Celecoxib 400 mg PO with sip of water ∫∫∫ Bilateral TAP blocks by Anesthesia team ¶	Lidocaine 1.5mg/kg bolus with induction, then 2 mg/min infusion until end of case $ Ketamine 0.5 mg/kg bolus with induction, then 5 mg/min infusion until completion of vessel anastomosis $$ IV Methadone 10–20 mg with induction $$$ Avoid opiate use Ketorolac 15–30mg IV at the end of the case	Continue lidocaine infusion for first 24 hours after termination of anesthesia † Acetaminophen 1000 mg PO q8h †† Gabapentin 300–900 mg PO q8h ††† Ketorolac 15–30 mg IV q6h – switch to Celecoxib 200 mg PO q12h when tolerating regular diet †††† Oxycodone 5–10 mg PO q3h as needed for pain score > 4/10 Hydromorphone 0.5 mg IV as needed for breakthrough pain *
Antiemetics	Scopolamine patch¶¶ if >2 risk factors for PONV	Prophylactic use of at least 2 agents from different classes or more if >2 risk factors: • Propofol drip or full TIVA for high risk PONV • Dexamethasone 8 mg IV ¥ • Ondansetron 4 mg IV • Scopolamine patch¶¶	Ondansetron 4 mg IV/PO q6h as needed Haloperidol 0.5–1 mg IV as needed Promethazine 6.25–12.5 mg IV/PO as needed Scopolamine patch up to 72 hours postoperatively
Fluid administration	None	Goal-directed to achieve euvolemia with zero balance and maintain urine output higher than 0.5 ml/kg/hr ^	Maintainance fluids until POD1 at 7AM
VTE prophylaxis	Sequential compression stockings	Sequential compression stockings Heparin 5000 IU S/C	Sequential compression stockings Prophylactic dose Enoxaparin to start at 10PM the night of surgery
Antibiotic prophylaxis	30–60 minutes before incision: Cefazolin 1–3 g IV or Clindamycin 600 mg IV if allergic to Cefazolin	Redose according to the specific antibiotic recommendations	Continue antibiotics for 24 hours

IV: Intravenous. PO: Per oral. POD: Postoperative day. PONV: Postoperative nausea and vomiting. TAP: Transverse abdominis plane. TIVA: Total intravenous anesthesia. VTE: Venous thromboembolism

∫ Reduce dose to 650 mg if weight is less than 70 kg or patient older than 65 years. Do not use if history of liver disease.

∫∫ Reduce dose to 300 mg in patients over the age of 65. Consider not giving or reducing to 100 mg in patients over the age of 75. Consider reducing the dose in patients with obstructive sleep apnea

∫∫∫ Reduce dose to 200 mg if moderate hepatic impairment. Do not use if severe hepatic or renal impairment, or history of gastrointestinal bleeding.

¶ Contains Bupivacaine 0.25% and dexamethasone 4 mg. Can also add clonidine to extend block duration. If unable to perform in preoperative holding area, can be completed in the operating room immediately after induction or postoperatively. If TAP blocks were not feasible, bilateral paravertebral blocks at T9–T10 level were considered.

¶¶ Do not use in patients over 65 years, and if there is concern for over-sedation or anti-cholinergic use.

^ Lactate ringers or plasmalyte were the preferred intravenous fluids administered. Normal saline was not used. Vasopressors were used only if the mean arterial pressure dropped 20% below the patient's baseline and it was not volume responsive. The preferred agents were ephedrine and dobutamine. Phenylephrine was avoided, if possible.

$ Contraindications: Unstable heart disease, recent myocardial infarction, heart block, heart failure, electrolyte disturbances, seizure disorder, current anti-arrhythmics such as amiodarone or sotalol

$$ Consider reducing dose to 0.25 mg/kg or not using bolus in patients over the age of 65

$$$ For patients with known preoperative chronic opiate use. May consider higher doses based on home opioid regimen. If opioids are required, consider methadone on emergence or in recovery room (5 mg IV boluses) every 5 to 10 minutes for a total of 20 mg prior to using other opioids.

¥ If not in TAP blocks.

† Dose is 1 mg/min IV if patient is < 70 kg, 1.5 mg/min IV if patient is 70–100 kg, and 2 mg/min IV if patient > 100 kg.

†† Decrease dose to 650 mg every 6 to 8 hours if patient is < 70 kg.

††† Use lower dose for patients older than 65 years or if patient is having significant sedation/dizziness.

†††† Use ketorolac 15–30 mg IV every 6 hours for 3 days if unable to take oral Celecoxib.

* Consider PCA if pain is refractory to all other pain medications. If pain continues to be uncontrolled, consider local anesthetic cream or postoperative local anesthesia.

Table 2

Demographic and clinical characteristics.

Characteristic	Patient group Pre-ERP N = 50	ERP N = 50	p-value
Age at surgery (years), mean ± SD	51.0 ± 10.0	51.9 ± 8.9	0.36
Body Mass Index (kg/m^2), mean ± SD	28.8 ± 4.0	29.7 ± 5.5	0.62
Smoking history, N (%)			0.51
Never	30 (60.0%)	34 (68.0%)	
Past user	19 (38.0%)	14 (28.0%)	
Current user	1 (2.0%)	2 (4.0%)	
Diabetes mellitus, N (%)	2 (4.0%)	6 (12.0%)	0.27
Hormonal therapy, N (%)			0.05
Never	21 (42.0%)	20 (40.0%)	
Prior use	1 (2.0 %)	8 (16.0%)	
Current use	28 (56.0%)	22 (44.0%)	
Oral contraceptive pill, N (%)	2 (4.0%)	0 (0 %)	0.50
Immunosuppressive medication, N (%)	1 (2.0%)	2 (4.0%)	1.00
Preoperative hypercoagulable state, N (%)	0	0	-
History of chest wall radiation, N (%)	23 (46.0%)	19 (38.0%)	0.42
History of systemic chemotherapy, N (%)	26 (52.0%)	29 (58.0%)	0.55
Chronic pain diagnosis, N (%)	3 (6.0%)	4 (8.0%)	1.00
Fibromyalgia, N (%)	3 (6.0%)	4 (8.0%)	1.00
Hypertension, N (%)	14 (28.0%)	18 (36.0%)	0.39
Chronic kidney disease, N (%)	0	0	-

(%): frequencies

ERP: enhanced recovery pathway. SD: standard deviation.

Table 3

Breast reconstruction data per patient.

Variable	Patient group		p-value
	Pre-ERP N = 50	ERP N = 50	
Reconstruction timing, N (%)			0.11
Immediate	6 (12.0%)	1 (2.0%)	
Delayed	44 (88.0%)	49 (98.0%)	
Reeonstruction laterality, N (%)			0.84
Unilateral	27 (54.0%)	28 (56.0%)	
Bilateral	23 (46.0%)	22 (44.0%)	
Type of reconstruction, N (%)			0.62
Unilateral DIEP flap	22 (44.0%)	25 (50.0%)	
Unilateral stacked DIEP flap	1 (2.0%)	2 (4.0%)	
Unilateral stacked DIEP flap with implant	0	1 (2.0%)	
Unilateral free MS TRAM flap	1 (2.0%)	0	
Unilateral SIEA flap	1 (2.0%)	0	
Unilateral PAP flap	1 (2.0%)	0	
Bilateral DIEP flap	19 (38.0.%)	17 (34.0%)	
Bilateral DIEP flap and free MS TRAM flap	3 (6.0%)	5 (10.0%)	
Bilateral DIEP flap and SIEA flap	1 (2.0%)	0	
Bilateral free MS TRAM flap	1 (2.0%)	0	

(%): frequencies

DIEP: deep inferior epigastric artery perforator. ERP: enhanced recovery pathway. MS: muscle-sparing. PAP: profunda artery perforator. TRAM: transverse rectus adbominis myocutaneous.

Table 4

Intra-operative data.

Variable	Patient group Pre-ERP N = 50	ERP N = 50	p-value
Operative time[†] (minutes), mean ± SD			
Total	464.1 ± 100.0	413.8 ± 107.1	0.02
Unilateral	418.0 ± 94.1	358.0 ± 89.8	0.02
Bilateral	518.2 ± 78.4	484.7 ± 83.4	0.17
Abdominal wall mesh use[‡]	3 (6.0%)	2 (4.0%)	1.00
Total intraoperative intravenous fluids (liters), mean ± SD	3.9 ± 1.2	3.2 ± 1.0	<0.01
Intraoperative transfusion, N (%)	3 (6.0%)	1 (2.0%)	0.62
Intraoperative vasopressor use, N (%)	16 (32.0%)	18 (36.0%)	0.67
Phenylephrine	16 (32.0%)	14 (28.0%)	0.66
Dobutamine	0 (0%)	4 (8.0%)	0.12

(%): frequencies

ERP: enhanced recovery pathway.

[†]Operative time is defined as skin incision to skin closure.

[‡]Mesh used was polypropylene.

Table 5

Postoperative outcomes.

Outcome	Patient group		p-value
	Pre-ERP N = 50	ERP N = 50	
Total length of hospital stay (days), mean ± SD	4.7 ± 2.3	3.0 ± 0.6	<0.01
Total length of hospital stay (days), median (range)	4.0 (3, 17)	3.0 (2, 5)	<0.01
Use of PCA, N (%)	50 (100%)	3 (6.0%)	<0.01
PCA duration (hours), mean ± SD	46.8 ± 16.0	40.8 ± 21.8	0.10
Oral morphine equivalent (mg), median (range)			
Total	276.3 (12.5, 1015.0)	67.5 (0, 432.5)	<0.01
POD 0	28.75 (0, 291.0)	7.50 (0, 88.0)	<0.01
POD 1	91.3 (5.0, 546.0)	26.3 (0, 100.0)	<0.01
POD 2	70.0 (0, 365.0)	22.5 (0, 90.0)	<0.01
POD 3	40.0 (0, 210.0)	7.5 (0, 145.0)	<0.01
POD 4	20.0 (0, 70.0)	0 (0, 97.5)	<0.01
POD 5	0 (0, 90.0)	0 (0, 60.0)	<0.01
Total acetaminophen use (mg), median (range)			
Total	5200.0 (0, 14000.0)	8000.0 (0, 16000.0)	<0.01
POD 0	325.0 (0, 3000.0)	1000.0 (0, 2000.0)	<0.01
POD 1	1000.0 (0, 3650,0)	3000.0 (0, 5000.0)	<0.01
POD 2	1300.0 (0, 3900.0)	3000.0 (1000.0, 5000.0)	<0.01
POD 3	1150.0 (0, 3000.0)	1000.0 (0, 4000.0)	0.25
POD 4	975.0 (0, 3000.0)	0 (0, 3000.0)	<0.01
POD 5	0 (0, 3000.0)	0 (0, 1000.0)	<0.01
Ondansetron (mg), mean ± SD			
Total	5.92 ± 7.01	2.56 ± 5.28	0.01
POD 0	1.92 ± 2.83	0.80 ± 1.81	0.02
POD 1	1.36 ± 2.63	0.32 ± 1.36	0.02
POD 2	1.12 ± 2.14	0.56 ± 1.81	0.16
POD 3	0.88 ± 2.72	0.72 ± 2.38	0.76
POD 4	0.40 ± 1.46	0.08 ± 0.57	0.15
POD 5	0.24 ± 1.26	0.08 ± 0.57	<0.01

(%): frequencies

ERP: enhanced recovery pathway. PCA: patient-controlled analgesia. POD: post-operative day. SD: standard deviation.

Table 6

Forty five-day postoperative complications *per patient*.

	Patient group		
Complication, N (%)	**Pre-ERP N = 50**	**ERP N = 50**	**p-value**
Number of complications			
None	23 (46.0%)	20 (40.0%)	0.55
One	17 (34.0%)	20 (40.0%)	0.53
Two	6 (12.0%)	8 (16.0%)	0.56
Three	3 (6.0%)	2 (4.0%)	1.00
Four	1 (2.0%)	0	1.00
Minor complications	24 (48.0%)	28 (56.0%)	0.42
Major complications	8 (16.0%)	3 (6.0%)	0.20
Emergency room visits	4 (8.0%)	5 (10.0%)	1.00
Hospital readmissions	4 (8.0%)	2 (4.0%)	0.68
Unplanned reoperations, Any	5 (10.0%)	2 (4.0%)	0.44
Breast recipient site complications, Any	32 (16.0%)	9 (18.0%)	0.11
Donor site complications, Any	18 (36.0%)	25 (51.0%)	0.13
Unplanned reoperations			
Deep SSI, recipient site	1 (2.0%)	0	1.00
Deep SSI, donor site	0	0	-
Delayed wound healing, recipient site	0	0	-
Delayed wound healing, donor site	2 (4.0%)	1 (2.0%)	1.00
Hematoma, recipient site	0	0	-
Hematoma, donor site	1 (2.0%)	0	1.00
Seroma, recipient site	0	0	-
Seroma, donor site	0	0	-
Flap vascular compromise	2 (4.0%)	1 (2.0%)	1.00
Breast recipient site complications			
Superficial SSI requiring oral antibiotics	1 (2.0%)	0	1.00
Superficial SSI requiring IV antibiotics	1 (2.0%)	1 (2.0%)	1.00
Deep SSI requiring oral antibiotics	0	0	-
Deep SSI requiring IV antibiotics	1 (2.0%)	1 (2.0%)	1.00
Wound dehiscence	0	0	-
Delayed wound healing	5 (10.0%)	0	0.06
Fat necrosis	0	4 (8.0%)	0.12
Hematoma managed non-operatively	1 (2.0%)	0	1.00
Hematoma requiring drainage in clinic	2 (4.0%)	0	0.50
Seroma managed non-operatively	0	0	-
Seroma requiring drainage in clinic	2 (4.0%)	0	0.50
Flap vascular compromise, non-operative	0	1 (2.0%)	1.00
Flap loss, partial	3 (6.0%)	0	0.24
Flap loss, total	0	0	-

	Patient group		
Complication, N (%)	**Pre-ERP N = 50**	**ERP N = 50**	**p-value**
Donor site complications			
Superficial SSI requiring oral antibiotics	2 (4.0%)	8 (16.0%)	0.09
Superficial SSI requiring IV antibiotics	1 (2.0%)	0	1.00
Deep SSI requiring oral antibiotics	1 (2.0%)	0	1.00
Deep SSI requiring IV antibiotics	1 (2.0%)	1 (2.0%)	1.00
Wound dehiscence	0	0	-
Delayed wound healing	8 (16.0%)	18 (36.0%)	0.02
Fat necrosis	4 (8.0%)	2 (4.0%)	0.68
Hematoma managed non-operatively	0	1 (2.0%)	1.00
Seroma managed non-operatively	0	0	-
Seroma requiring drainage in clinic	3 (6.0%)	0	0.24
Neoumbilicus necrosis	2 (4.0%)	1 (2.0%)	1.00
Deep vein thrombosis	0	0	-
Pulmonary embolism	0	0	-
Pneumonia	0	1 (2.0%)	1.00
Urinary tract infection	0	0	-
Cardiac complications	0	0	-
Gastrointestinal complications	0	0	-

(%): frequencies

ERP: enhanced recovery pathway. IV: intravenous. SSI: surgical site infection.

Table 7

Multivariable logistic regression analysis of risk factors for length of hospital stay.

Risk Factor	Odds Ratio	95% Confidence Interval	p-value *
Age	1.55	0.82 – 2.93	0.18
Body mass index	1.32	0.72 – 2.44	0.37
Bilateral breast reconstruction	0.81	0.28 – 2.34	0.70
Operative time	2.08	0.85 – 5.12	0.11
Intraoperative intravenous fluid amount	0.98	0.57 – 1.68	0.93
Total oral morphine equivalent use	6.56	2.64 – 16.30	< 0.01
Total acetaminophen use	1.51	0.92 – 2.46	0.10
Enhanced Recovery Pathway	0.07	0.02 – 0.28	< 0.01

* Significant p value < 0.05.