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Breast

Opioid-sparing Strategies in Alloplastic Breast Reconstruction: A Systematic Review

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Introduction: Pain and discomfort are frequently experienced following mastectomy with concomitant breast implant- or tissue expander-based alloplastic breast reconstruction (AlBR). Unfortunately, postoperative opioids have decreased efficacy in AlBR, short-term complication profiles, and are fraught by long-term dependence. This systematic review aims to identify opioid-sparing pain management strategies in AlBR.

Methods: A systematic literature search of MEDLINE, Embase, Web of Science, and Cochrane Central Register was performed in September 2018. PRISMA guidelines were followed, and the review was prospectively registered in PROSPERO (CRD42018107911). The search identified 1184 articles. Inclusion criteria were defined as patients 18 years or older undergoing AlBR.

Results: Fourteen articles were identified assessing opioid-sparing strategies in AlBR. This literature included articles evaluating enhanced recovery protocols (two), intercostal blocks (two), paravertebral blocks (four), liposomal bupivacaine (three), diclofenac (one), and local anesthesia infusion pumps (two). The literature included five randomized trials and nine cohort studies. Study characteristics, bias (low to high risk), and reporting outcomes were extensively heterogeneous between articles. Qualitative analysis suggests reduced opioid utilization in enhanced recovery after surgery (ERAS) pathways, paravertebral blocks, and use of liposomal bupivacaine.

Conclusions: A variety of opioid-sparing strategies are described for pain management in AlBR. Multimodal analgesia should be provided via ERAS pathways as they appear to reduce pain and spare opioid use. Targeted paravertebral blocks and liposomal bupivacaine field blocks appear to be beneficial in sparing opioids and should be considered as essential components of ERAS protocols. Additional prospective, randomized trials are necessary to delineate the efficacy of other studied modalities. *(Plast Reconstr Surg Glob Open 2021;9:e3932; doi: 10.1097/GOX.0000000000003932; Published online 16 November 2021.)*

INTRODUCTION

Breast cancer is estimated to affect over 260,000 individuals in the United States annually, making it the most common carcinoma in women.[1] Therapeutic strategies rely on ablative surgery, chemoradiation, and subsequent reconstruction. Restoring form, function, and quality of life,[2–4] postmastectomy implant- or tissue expander (TE)-based breast reconstruction (collectively, "alloplastic") remains the most commonly performed reconstructive modality.[5]

Patients who undergo immediate alloplastic breast reconstruction (AlBR) tend to experience more postoperative pain than those undergoing mastectomy without reconstruction.[6] This occurs despite high opioid use, suggesting poor opioid efficacy in this patient population.[6] Significant postoperative pain impairs recovery, contributes to poor patient satisfaction, and is correlated to increased rates of chronic postmastectomy pain.[7–11] There is a subsequent need to definitively and effectively treat postmastectomy pain through multimodal approaches which involve the overall reduction or minimization of opioid narcotics.

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Excessive postoperative opioid use is not without morbidity, and its use has effects of associated nausea, vomiting, altered mentation, and respiratory depression.[12–14] More troubling, opioid overprescription, as is observed in a number of plastic surgery procedures, can lead to opioid dependence.[15–21] Subsequent opioid use, misuse, and overdose seen in the current nationwide epidemic has contributed to a decline in the US life expectancy for two consecutive years.[22]

These conclusions necessitate judicious prescribing practices and promote implementation of alternatives to opioid-based pain management. Subsequent evaluation of opioid use in plastic surgery highlights a new era of patient safety and practice progression. To derive the methodological clarity and efficacy of various pain protocols, we aim to systematically review the literature and identify opioid-sparing pain management strategies in AlBR.

Takeaways

Question: What approaches or medical means can surgeons utilize to reduce the number of opioid narcotics that patients require for pain following breast reconstruction?

Findings: Multimodal analgesia should be provided via ERAS pathways including targeted paravertebral blocks and liposomal bupivacaine field blocks, as these techniques appear to treat pain effectively and reduce postoperative opioid consumption.

Meaning: Postoperative opioid usage can be reduced by employing specific forms of multimodal pain control. This will likely translate into better patient satisfaction and reduce overall opioid consumption.

METHODS

Study Design

This study protocol was prospectively registered with PROSPERO, an international register of systematic reviews (Study ID: CRD42018107911).[23] The systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement guidelines.[24,25]

Study Criteria

Inclusion criteria were defined as patients 18 years or older undergoing breast reconstruction. Only cases of AlBR (TE or implants) were included. Patients undergoing nonreconstructive breast surgery (ie, mastectomy alone, oncoplastic reduction, and augmentation) were excluded. Interventions assessed included opioid-sparing pain management techniques. The primary outcome was defined as mean morphine equivalent units utilized. Secondary outcomes included time to ambulation, hospital length of stay (HLOS), hospital expenditures/costs, patient reported pain-scales, opioid-related adverse events, postoperative complications, and postoperative opioid use.

No time limit was placed on published articles. Only English-language literature was included. Randomized or nonrandomized controlled trials and cohort studies were included. Studies with less than 10 patients were excluded. Animal studies were excluded. “Gray literature” was assessed and included if methodology was accessible and scientifically sound.

Search Strategy

The search was conducted on September 17, 2018, by an experienced research librarian at the Countway Medical Library at the Harvard Medical School. The following four databases were searched: MEDLINE (Pubmed/Ovid), Embase (Elsevier), Web of Science (Clarivate Analytics), and Cochrane Central Register of Controlled Trials (Wiley). Our full-text search strategy is accessible at PROSPERO.[23]

Data Extraction, Bias Assessment, and Statistical Analysis

Extracted articles were imported into Covidence. Duplicate references were removed (n = 412). Titles and abstracts were screened by two authors (D.T.C. and L.L.B.). Split decisions were made by an independent reviewer (N.G.C.). Final article selection and full-text analysis was performed by two reviewers (D.T.C. and A.M.S.I.). Study-level bias was assessed utilizing the risk of bias in nonrandomized studies of interventions (ROBINS-I) tool.[26] Assessments of study bias were dependent on confounding, bias in intervention classification, bias from intervention deviations, bias in missing data and selective result reporting, and bias in outcome measurements. Missing data are highlighted in the discussion as appropriate. Due to the heterogenous nature of study and outcome measures, meta-analysis and sensitivity-analyses were not performed. Mean outcome values were compared based on article test statistics.

RESULTS

Articles Identified

A branching-logic diagram of search results and article processing is depicted in Figure 1. Fourteen articles meeting defined criteria were included in this review (Table 1).

“Enhanced Recovery after Surgery” Protocols

Chiu et al describe implementation of an enhanced recovery after surgery (ERAS) protocol (Table 2) for mastectomy with submuscular AlBR in a proposed 23-hour hospitalization. Their intention-to-treat analysis included 276 pre-ERAS (traditional management) and 96 ERAS patients. ERAS implementation increased preoperative acetaminophen, gabapentin, scopolamine, and regional anesthesia utilization. The total mean morphine equivalent units utilized were statistically reduced in the ERAS cohort, (111.4 ERAS versus 168.3 pre-ERAS) with statistically significant reductions in morphine equivalents used throughout other hospital settings [intraoperative, postanesthesia care unit (PACU), and on the wards]. On average, ERAS patients had lower maximal pain scores. Multivariate regression demonstrated decreased opioid

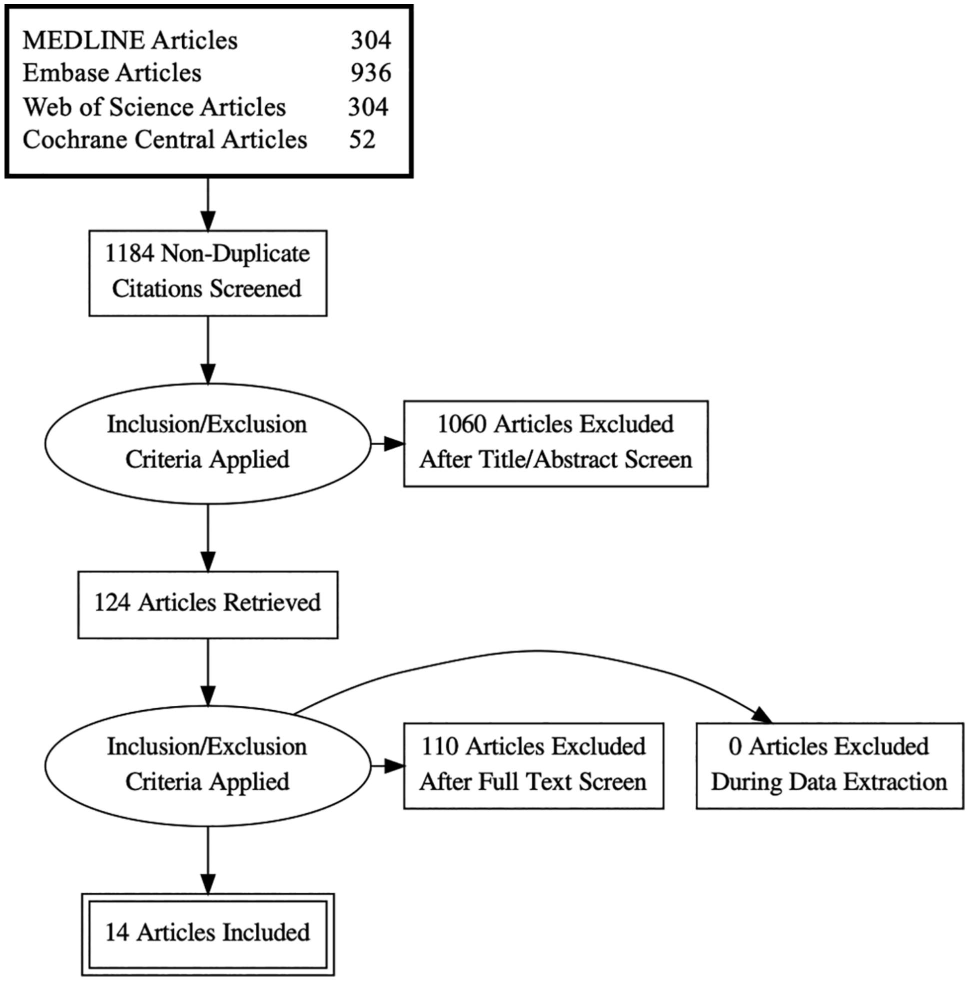

Fig. 1. PRISMA flow diagram of article exclusion and inclusion.

use in the ERAS cohort. ERAS patients demonstrated significant reductions in lorazepam use (−10%) and postoperative nausea/vomiting (−23%). No statistical change in HLOS was observed in the setting of 23-hour admission.

Dumestre et al[28] evaluated 29 patients in an outpatient model ERAS pathway undergoing immediate, subpectoral AlBR. ERAS patients were compared to 29 controls and 11 patients operated on during a "transition" period before full ERAS implementation. HLOS was reduced among ERAS patients: 1.6 nights among controls compared to less than 24 hours for ERAS patients. Compared to the transition cohort, the ERAS cohort described statistically significant improvements in "severe pain," "nausea," and "sleep" defined by a recovery questionnaire. There were no cohort differences in reported postoperative complications. Follow-up communication with ERAS patients were "overall positive" without comparison to other cohorts.

Paravertebral Blocks

A nonblinded, randomized control trial by Wolf et al described patients undergoing AlBR randomized to ropivacaine paravertebral blocks (PVBs, n = 35) or no PVB (n = 39) with standardized nausea prophylaxis, opioids, and pain assessments. A statistical reduction in opioid consumption was observed in the PVB cohort (108 versus 246 fentanyl equivalents). Those receiving PVB had significantly less pain at 0–1 and 3–6 hours, in addition to reduced 24-hour "worst" pain ratings (1.50 ± 3.22 PVB versus 2.39 ± 3.49 control). PVB patients consumed statistically fewer antiemetics tablets (0.71 versus 2.1) despite nonstatistically different rates of nausea. Patients in the PVB cohort received promethazine, dexamethasone, and ondansetron postoperatively for nausea prophylaxis, but dosages and frequency of administration were not noted.

Additional articles analyzing PVBs in AlBR were retrospective in design.[31–33] Table 3 illustrates principal findings. Fahy et al[31] described outcomes of mastectomy with bupivacaine PVBs in 232 patients (55% with AlBR), compared to 294 patients without PVB (51% with AlBR). Although HLOS, opioid use, and antiemetic use were statistically reduced in the total cohort, subgroup analysis demonstrated that opioid reductions were only significant in cases of bilateral reconstruction (48.8 ± 14.4 mg PVB versus 63.1 ± 20.2 mg non-PVB). Reductions in antiemetic use were not observed for bilateral reconstruction, and neither opioid nor antiemetic use were reduced in unilateral reconstructions. Coopey et al[32] reported a faster transition to oral opioid agents in 190 PVB patients

Table 1. Characteristics of Studies Meeting Inclusion Criteria

	Study Characteristics			
Study	**Study Type (LOE)**	**Intervention**	**Primary Outcome(s)**	**Bias**
Chiu et al[27]	Retrospective (2)	ERAS protocol	Total perioperative opioid consumption (oral morphine equivalents)	Low-to-moderate Risk
Dumestre et al[28]	Prospective cohort with retrospective arm (2)	ERAS protocol	Length of stay and proof of concept safety	High-to-severe risk
Shah et al[12]	Retrospective (2)	Thoracic intercoastal blocks	Postoperative pain, antiemetic use, and HLOS	Moderate risk
Lanier et al[29]	Randomized controlled trial (1)	Intercostal and pectoral nerve blocks vs placebo saline injection	Global 40-item Quality of Recovery Questionnaire, pain scores, opioid consumption	Low risk
Wolf et al[30]	Randomized controlled trial (1)	PVB vs no PVB	Postoperative pain and opioid consumption	Low risk
Fahy et al[31]	Retrospective (2)	PVB	Hospital discharge <36 hrs, PACU LOS, opioid consumption, and antiemetic use	High risk
Coopey et al[32]	Retrospective (2)	PVB	HLOS	Moderate risk
Aufforth et al[33]	Retrospective (2)	PVB	Opioid consumption	Moderate risk
Abdelsattar et al[34]	Retrospective (2)	LB compared PVB	Oral morphine equivalents consumed, pain scores, HLOS, time to first opioid	Moderate-to-high risk
Motakef et al[35]	Randomized controlled trial (1)	LB vs bupivacaine blocks	Opioid and benzodiazepine consumption, and HLOS	Low-to-moderate risk
Butz et al[36]	Retrospective (2)	LB	Mean morphine equivalents, and HLOS	High-to-severe risk
Legeby et al[37]	Randomized controlled trial (1)	Diclofenac suppository vs placebo suppository	Postoperative pain (rest and dynamic) and opioid consumption	Low-to-moderate risk
Lu and Fine[38]	Prospective cohort with retrospective arm (2)	Bupivacaine IP	Postoperative PACU pain; opioid consumption	Moderate risk
Strazisar et al[39]	Randomized (1)	Levobupivacaine pump compared to piritramide infusion	Opioid consumption, antiemetic requirements, and sedation	High risk

LOE, level of evidence; LOS, length of stay.

undergoing mastectomy with AlBR compared to 154 controls (Table 3). Comparatively, Aufforth et al[33] evaluated 59 patients undergoing mastectomy and AlBR, 45 received bupivacaine PVBs and 14 were controls. They found significant reductions in morphine equivalent use on the subgroup analysis of reconstruction (25.3mg PVB versus 42.8mg non-PVB), but this did not persist among the total cohort's (317 patients) opioid use. No cases of pneumothorax, epidural spread, or PVB site complications were noted in the manuscripts.

Intercostal Blocks

In their randomized controlled trial, Lanier et al[29] describe intercostal and pectoral blocks on patients undergoing immediate AlBR randomized to bupivacaine and dexamethasone injections (n = 23) or placebo saline injections (n = 22). Pain regimens were standardized patient-controlled anesthesia (PCA) transitioning to per os (PO) agents. There was a nonsignificant decrease in morphine equivalent use among nerve block patients (92 units treatment versus 114 units control, $P = 0.31$). Despite nerve block patients trending toward reduced PACU pain scores, there were no statistical pain score differences between cohorts. Discharge quality of recovery questionnaires did not differ.

Shah et al[12] described retrospective results of bupivacaine thoracic intercostal blocks (ICBs) in 89 immediate AlBR patients compared to 43 patients undergoing AlBR without ICB. Morphine requirements were reduced in patients who received ICBs for bilateral (5.15mg ICB versus 12.68mg non-ICB) and unilateral (2.80mg ICB versus 8.17mg non-ICB) reconstructions. ICB patients trended ($P > 0.05$) toward less oral oxycodone consumption. In bilateral reconstructions, statistically decreased HLOS (1.87 ICB versus 2.32 days non-ICB) and diazepam consumption (22.24mg ICB versus 31.13mg non-ICB) were noted in ICB patients. No difference in antiemetics use was observed. A pneumothorax occurred in one ICB patient.

Liposomal Bupivacaine

Motakef et al[35] presented randomized trial data for liposomal bupivacaine (LB) among 24 patients undergoing TE or direct-to-implant AlBR. Twelve patients received LB, whereas 12 received bupivacaine field blocks. Cohorts were well matched and excluded chronic pain patients. Postoperatively, patients received standing diazepam and as needed opioids and ondansetron. Motakef et al[35] found significant reductions in benzodiazepine use and morphine equivalents utilized among LB patients (0.76 versus 1.43 morphine equivalent dosing/hr). The LB cohort required significantly shorter HLOS (29.8 versus 46.7 hours) and reduced hospital expenditures ($10,828 versus $18,632). Hospital expenditures were largely based on HLOS. Average pain scores were similar with no significant adverse events.

Abdelsattar et al[34] retrospectively reviewed patients who underwent unilateral or bilateral mastectomy with TE AlBR. Fifty-three patients received a preoperative ultrasound-guided PVB compared to 44 who received local, intraoperative LB. Patients were discharged once ambulating on PO analgesics. On multivariable analysis, opioid use in the recovery room was significantly lower in the LB group compared to the PVB group (mean ± SD; 9.4 ± 16.4 LB versus 24.8 ± 23.9 PVB morphine equivalents; P: 0.03), as were day of surgery pain scores via a numeric rating scale (3.2 LB versus 4.2 PVB; score range 0–10, P: 0.05). However, HLOS, antiemetic consumption, and total opioid consumption were not different.

Table 2. Summary of ERAS Protocol Interventions

	Intervention Time		
Intervention	**Preoperative**	**Intraoperative**	**Postoperative**
Oral acetaminophen	Dumestre et al[28] and Chiu et al[27]: 1000 mg		
Oral NSAIDS	Dumestre et al[28]: Celecoxib 400 mg		Chiu et al[27]: Ibuprofen PRN for mild pain Dumestre et al[28]: Celecoxib 200 mg q12hr for 2 doses Dumestre et al[28]: Ibuprofen 200–400 mg q6-8hr PRN after celecoxib administered
Oral gabapentin	Chiu et al[27]: 600 mg Dumestre et al[28]: 300 mg		Dumestre et al[28]: 200 mg q8hr for 2 doses total
Oral aprepitant	Dumestre et al[28]: 80 mg		
Oral oxycodone	Dumestre et al[28]: 10 mg		
Acetaminophen with hydro/oxycodone			Chiu et al[27]: For moderate pain
IV hydromorphone			Chiu et al[27]: For severe pain unrelieved by oral agents,
Lorazepam			Chiu et al[27]: For muscle spasm
Scopolamine patch	Chiu et al[27]: 1.5 mg*		
Ondansetron		Chiu et al[27]: 4 mg, IV	
Dexamethasone		Chiu et al[27]: 8 mg, IV	
Opioids		Chiu et al[27]: "Minimal"†	
Regional blocks		Chiu et al[27]: Ropivacaine or bupivacaine type 1 or 2 pectoralis blocks, or ropivacaine paravertebral blocks at T4, at provider discretion Dumestre et al[28]: Subcutaneous breast blocks with bupivacaine:epinephrine	
Anesthesia notes		Chiu et al[27]: TIVA (Propofol) with limited fentanyl/hydromorphone† and avoidance of volatile anesthetics Dumestre et al[28]: Intraoperative medications at anesthesia's discretion	
Avoidance of prolonged fasting	Chiu et al[27]: CLD 2 hrs before surgery Dumestre et al[28]: CLD 3 hrs before surgery		
Other	Dumestre et al[28]: 125 cc/hr Ringers lactate 1 hr before procedure	Chiu et al[27]: Euvolemia (<2 L crystalloids) and normothermia,	Chiu et al[27]: Early mobilization and oral intake

*If age <60 and a prior history of postoperative nausea/vomiting
†Anesthesia discretion.
CLD, clear liquid diet; IV, intravenous; TIVA, total intravenous anesthesia.

Butz et al[36] retrospectively evaluated 90 AIBR patients receiving either a bupivacaine pain pump (n = 30), LB field blocks (n = 30), or a control arm (n = 30) without regional anesthesia or a single intraoperative dose of bupivacaine or lidocaine. All patients received a PCA on postoperative day (POD) 0 and were transitioned to oral hydrocodone/acetaminophen by POD 1. There were no significant differences in antiemetic or opioid use (1137 ± 508 MME LB, 1275 ± 580 MME pain pump, 1205 ± 500 control; $P = 0.605$). The LB cohort had statistically lower subjective pain scores at 4-, 8-, 12-, 16-, and 24-hour time points. A significant association between LB and the same-day discharge was observed.

Diclofenac

Legeby et al[37] evaluated AIBR patients blinded and randomized to receive 50 mg diclofenac (n = 25) or placebo suppository (n = 23) every 8 hours. Perioperative medications were standardized per Table 4. The diclofenac cohort utilized significantly fewer opioids within the first 6 postoperative hours (16.9 versus 25.6 mg of opioids); however, no difference was observed during later time points (total use: 46.4 versus 53.3 mg of opioids, $P = 0.092$). In the first 20 postoperative hours, results controlling for axillary procedures and mastectomy laterality demonstrated reduced rest pain in the diclofenac cohort (analog scale 0–10, median: 2.1 diclofenac versus 3.0 placebo). No differences were observed in nausea and/or drowsiness. Diclofenac was a predictor of perioperative blood loss; however, no patients required reoperation for bleeding. One placebo patient required naloxone for opioid-induced hypoventilation.

Local Anesthetic IPs

Lu and Fine[38] described local anesthetic infusion pumps (IPs) in 35 patients receiving TE reconstruction with a catheter infusing 5.0–7.0 cc/hr of 0.25% bupivacaine compared to 39 controls. There was significantly less PACU hydromorphone consumption by IP patients (0.8 ± 0.8 and 1.4 ± 0.7 mg). Subgroup analysis of inpatients demonstrated a similar reduction in oral hydrocodone/acetaminophen consumption (2.1 ± 2.9 and 4.2 ± 3.2 tablets, $P = 0.02$). In the PACU, the authors noted statistically reduced pain scores in IP patients (2.0 ± 1.9 versus 4.1 ± 1.2). There were no significant differences in complications or HLOS.

Table 3. Summary of Retrospective Assessments of Paravertebral Blocks in Alloplastic Breast Reconstruction

		Study Outcomes				
Study	PVB Type	HLOS	Nausea/ Antiemetic Requirements	Opioid Requirements	Pain Scores	Multivariable Analysis
Aufforth et al[33]	0.25% bupivacaine injection at T1–T6	Significantly increased in PVB cohort (0.83 vs 0.58 d)	No significant difference in postoperative nausea between cohorts	No significant difference in morphine equivalents between total cohorts†	No significant difference [POD1 average pain scores 1.83 in PVB vs 1.89 in non-PVB)	Not performed
Coopey et al[32]	0.5% bupivacaine injection at T1	Significantly less in PVB cohort (42 vs 47 hrs)*	Incidence of nausea was reduced in the PVB cohort (42.8% vs 54.7%)	Time of conversion from intravenous to oral opioids was shorter in the PVB cohort (15 vs 20 hrs)	N/A	Not performed
Fahy et al[31] †	0.25%–0.5% bupivacaine injection at T1, T3, T5	HLOS <36 hrs significantly higher in PVB cohort (55.2% vs 42.2%)‡	Antiemetic use was significantly lower in the PVB cohort (38.8% vs 56.8%)	Opioid use was significantly lower in the PVB cohort (40.1 ± 15.2 vs 47.6 ± 17.7)	†No statistical difference in pain scores on POD0 (4.9 ± 2.2 vs 4.9 ± 2.4)	Controlling for procedure year, age, and surgery: HLOS was no longer significantly different; differences in antiemetic and opioid use persisted

Significant implies $P < 0.05$.
*Persisted on subgroup analysis of tissue expander recipients and direct-to-implant patients.
†Data reported for overall cohort. Discussion of reconstruction subgroup analysis in-text.
‡No statistical difference observed between cohorts with respect to time spent within the PACU.

Strazisar et al[39] also evaluated local infusion in AlBR, randomizing 30 patients to subpectoral 0.25% levobupivacaine IP compared to 30 controls receiving continuous IV infusion containing 30 mg piritramide, 20 mg metoclopramide, and 2.5 g metamizole. Patients were transitioned to PO diclofenac or paracetamol/tramadol after 24 hours. The IP cohort used significantly fewer opioids (9.8 versus 29.4 mg piritramide) and had reduced incidence of nausea (measured through metoclopramide use, 11.0 versus 24.3 mg) within the first 24 hours. There were no significant differences in tramadol/paracetamol and diclofenac use or complication rates. Strazisar et al[39] did not disclose the HLOS for each cohort. However, they noted that the combined mean HLOS was 5.3 days, and that HLOS did not vary when the two cohorts were compared.

DISCUSSION

AlBR is frequently performed following mastectomy in the immediate setting. The previous literature has demonstrated considerable postoperative pain and prolonged hospitalization, which may worsen postreconstruction quality of life.[35,41] Opioid treatment falls short with questionable efficacy and significant side-effects. Our systematic review aimed to identify opioid-sparing strategies in AlBR. To systematically review each article, we have divided our discussion into an evaluation of individual studies and summary statements for six opioid-sparing strategies.

ERAS Protocols

Implementation of ERAS protocols in AlBR (Table 2) offers patients a transition to outpatient care through multimodal analgesia. Chiu et al[27] demonstrated reduced postoperative opioid consumption, whereas Dumestre et al[28] demonstrated improved postoperative satisfaction. Despite commendable studies, limitations exist. Chiu et al reported reduced protocol adherence, evidenced by only moderate increases in total IV anesthesia (8% pre-ERAS, to 33% ERAS) and dexamethasone administration (18% pre-ERAS, to 53% ERAS). Moreover, analgesic characteristics of pre-ERAS patients (ie, PRN versus around-the-clock administration) were not documented and preclude judicious comparison. Comparatively, Dumestre et al's study is limited by exclusion of patients with ASA class greater than 2, limited demographic information, and neither denoting nor controlling for prior opioid use or chronic pain syndromes (CPS). The study does not report total

Table 4. Randomized Control Trial Standardized Medication Profile[36]

	Administration Time Points		
Therapy	Preoperative	Intraoperative	Postoperative
Anesthesia		GA; 50 mL 0.5% lidocaine infused into breasts before mastectomy	
Paracetamol	1000 mg PO, 1 hr before surgery		1000 mg PO, every 8 hrs
Opioids		Fentanyl (and sevoflurane) for anesthesia maintenance	Intravenous PCA delivering morphine or ketobemidone
Thromboprophylaxis	Low molecular weight heparin, 1 hr before surgery		
Diclofenac	Randomization; 50 mg diclofenac every 8 hrs. Treatment starts 1 hr before surgery and continues for a total of 3 d.		

GA, general anesthesia.

opioid consumption, but interestingly included standing administration of preoperative oxycodone with postoperative administration of up to 12 PRN oxycodone tablets (no dosing or administration reported) and subsequent PRN tramadol-acetaminophen (no dosing noted, 1–2 tablets every 3–4 hours). Such oxycodone reporting does not provide clarity in opioid administration and detracts from study evaluation. The reporting per-breast complications and subjective stratification of complication categories, without reporting aggregate complications, may skew outcomes. Last, recovery surveys were not provided to pre-ERAS controls.

Summary Statement

Although high-quality evidence evaluating ERAS protocols in AlBR is limited, ERAS appears to reduce postoperative opioid use and pain with improved recovery quality. Emphasis should be applied to multimodal use of preoperative and postoperative acetaminophen, gabapentin, and/or nonsteroidal anti-inflammatory drugs (NSAIDS). These agents reduce pain and opioid use in breast and plastic surgery procedures.[42–50] As recommended by the Clinical Practice Guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council (Recommendation 10), prophylactic preoperative opioids should not be prescribed given the lack of clear benefit derived from preoperative narcotics.[51] Additional agents employed via ERAS pathways (ie, avoidance of prolonged fasting, scopolamine patches, etc.) are not intended to spare opioids, but are thought to improve overall patient outcomes. Intraoperative local analgesia recommendations are described below.

Paravertebral Blocks

Despite the randomized control study design, Wolf et al's[30] analysis may be skewed by a surgical population extending beyond immediate AlBR, incorporating delayed AlBR in addition to a large percentage (54.05%) of second stage expander-to-implant procedures with concurrent symmetrizing surgeries. Although this improves external generalizability, it introduces confounding variables.

Several salient limitations are present in the additional retrospective studies evaluated. Each lacked consistent time-point recordings of pain scores. Notably, Coopey et al[32] attempted to control for this by reporting conversion to oral opioids, a surrogate of transitioning to less severe pain. Unfortunately, they do not report mean morphine consumption. Moreover, with the exception of Aufforth et al,[33] studies did not quantify opioid-naivety, CPS, and axillary procedures. Aufforth et al's study is limited by small subgroup analyses required to identify differences in reconstructive patients' opioid use and was confounded by a greater number of axillary procedures in the PVB cohort and lumpectomies in the non-PVB cohort. Moreover, NSAID use was uncontrolled. Finally, some studies lacked perioperative medication standardization.[28,33]

Summary Statement

Level 1 evidence provided by Wolf et al, in conjunction with limited level 3 evidence, suggests that paravertebral blocks should be employed in AlBR to reduce opioid use. PVBs reduce pain scores in AlBR, but do not decrease nausea/antiemetic use. In nonreconstructive breast procedures, PVBs reduce pain and opioid consumption[52–55] with reported postoperative pain relief ranging from 0.5 to 12 hours.[32,53–55] PVBs should be considered a component of multimodal ERAS protocols.

Intercostal Blocks

Both ICB studies reduce confounding by excluding patients with CPS or chronic opioid use and employing standardized postoperative opioid regimens, yet limitations remain. One study is confounded by botulinum toxin pectoralis injections, which may underpower findings and prevents pure interpretation of ICBs.[12] Furthermore, the unilateral nonblock cohort was somewhat underrepresented (n = 12 compared to n = 43) and the study should transparently report opioid consumption among all patients as mean morphine equivalents without laterality subgroup analysis. Lanier et al[29] uniquely noted that 16 of 34 patients experienced significant axillary pain during recovery which suggests technical inadequacy of ICBs. A prior assessment by Blanco et al[56] notes the importance of anesthetizing the long thoracic and thoracodorsal nerves for axillary anesthesia. Lanier et al[29]additionally performed pectoral blocks, but noted a lack of medial pectoral nerve visualization during infusion.

Summary Statement

Conflicting outcomes exist in the studies evaluating ICBs in AlBR. The absence of higher-quality prospective studies supporting ICBs precludes recommendation to implement ICBs in favor of PVBs. Although ICBs tend to be more rapidly employed than PVBs,[12] their opioid-sparing affect seems marginal, in part due to axillary pain.

Liposomal Bupivacaine

Results of LB appear somewhat heterogenous. Motakef et al's[35] randomized trial is somewhat constrained by a small sample size but is otherwise devoid of major flaws. Abdelsattar et al[34] identified improved pain control with LB, yet did not demonstrate a difference in opioid consumption and lacked consistent time-point pain score recordings, particularly beyond 36 hours, an optimal time to elucidate the effects of LB. They did not quantify opioid naive patients and had cohort discrepancies in submuscular versus subglandular TE placement. Despite having a larger sample size, Butz et al's[36] study is limited as a portion of the control arm received local anesthesia, which obscured the immediate postoperative impact of LB at 0.5 and 2 hours postoperatively. Last, Butz et al neither analyze nor characterize patients with prior opioid use or CPS. Despite reporting a statistical difference in the same-day discharge, this study appears to be somewhat underpowered as HLOS, measured in hours or days, is not statistically different.

Summary Statement

Commercially available LB, Exparel (Pacira Pharmaceuticals; Parsippany, N.J.), is indicated for postsurgical local analgesia or for interscalene brachial plexus nerve blocks.[57] Abdelsattar et al has previously defined an injection technique for AlBR.[40] A 2016 systematic review reports safe outcomes with generally improved analgesia in several surgical procedures.[58] Local intraoperative infiltration of LB is recommended as a component of ERAS pathways.

Diclofenac

The randomized study design and standardized perioperative medication regimen employed by Legeby et al is highly commendable with some limitations.[36] The authors do not identify patients with CPS or prior opioid use. Additionally, the authors state that they adjust for unilateral versus bilateral cases; however, it is unclear if they account for the symmetrizing procedures that occurred in unilateral cases. The authors perform multivariable regression to analyze blood loss, but do not report odds ratios or factors within the regression model. Last, a 3-day stay for immediate AlBR is uncommon in the years since publication.

Summary Statement

Although diclofenac use reduced early opioid consumption in AlBR, it was not shown to be effective during early mobilization suggesting inefficiency as a standalone modality for pain control. Although increased perioperative bleeding was observed, meta-analyses in plastic surgery have not consistently demonstrated this risk of NSAIDs.[50,59] NSAIDs remain a recommended component of AlBR ERAS pathways.

Local Anesthesia

Both articles evaluating LA have noted limitations. Lu and Fine[38] do not describe patient histories of prior opioid use, appears to lack standardized antiemetic protocols, and does not specify patient criteria for transition from IV Dilaudid to oral hydrocodone/acetaminophen.[37] Additionally, pain scores were only tracked within the PACU, limiting findings. Last, lack of conversion to mean morphine equivalents impairs opioid consumption quantification. Comparatively, Strazisar et al's analysis is strengthened by standardized anesthesia, scheduled pain measurements, and patient exclusion for prior chronic opioid consumption.[38] However, the study is significantly confounded by postoperative pain regimens. Although 3-mg rescue doses of intravenous piritramide were available to both cohorts, the control cohort received a continuous infusion of piritramide (30 mg) over 24 hours. Their subsequent mean piritramide use was 29.4 mg in 24 hours, compared to 9.8 mg in the study cohort. The control group may not have needed 29.4 mg of piritramide, but the continuous administration was predicated on study design. Subsequent comparisons are confounded. Moreover, the 5.3-day HLOS is notable.

Summary Statement

Although LA infusions reduced opioid consumption, the studies identified have limited and confounded methodology and outcomes. The absence of quality prospective studies supporting LA infusions precludes their recommendation in ERAS pathways. Our findings preferentially suggest PVBs and/or LB field blocks over LA infusions.

This systematic review is not without limitations. The notable paucity of patients undergoing prepectoral AlBR in this literature limits our review. Prepectoral AlBR prevents chest wall dissection, preserves the pectoralis muscle, and potentially reduces pain.[60–62] Copeland-Halperin et al[63] recently demonstrated that patients undergoing prepectoral AlBR required fewer days and refills of opioid medications than their counterparts undergoing subpectoral AlBR. Future studies assessing AlBR pain management must consider prepectoral approaches. Additionally, these recommendations are made through limited level 1 and 3 evidence. There is considerable need for additional level 1 randomized trials with appropriately designed placebo-controlled cohorts undergoing standardized perioperative management. Moreover, article bias was assessed and reported as aggregate qualitative findings by a single reviewer and the GRADE certainty of evidence was not applied, which is a deviation of our original PROSPERO protocol. Last, meta-analysis could not be performed due to outcomes heterogeneity. Future trials should adhere to uniform outcomes, particularly unadjusted mean morphine equivalent consumption.

CONCLUSIONS

Considerable pain accompanies AlBR. Multimodal analgesia should be provided via ERAS pathways to spare opioid use. Acetaminophen, NSAIDs, gabapentin, PVBs, and LB are essential components to ERAS protocols. Additional prospective, randomized trials are necessary to further delineate efficacy. Due to the limited quality of current literature, future trials need consistent endpoints (mean morphine equivalents utilized at specific postoperative time points), clear documentation of pain medication provided (dose and frequency), and patient demographics (including cohort exposure to radiation and history of prior opioid/narcotic use).

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