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Impact of Gabapentin on Postoperative Hypotension in Enhanced Recovery after Surgery Protocols for Microvascular Breast Reconstruction

Corbin E. Muetterties, MD*
Jeremiah M. Taylor, BS*
Diana E. Kaeding, MSN*
Ricardo Rosales Morales, BS*
Anissa V. Nguyen, MPH*†
Lorna Kwan, MPH*†
Charles Y. Tseng, MD*
Michael R. Delong, MD*
Jaco H. Festekjian, MD*

Background: Enhanced recovery after surgery (ERAS) protocols have been associated with hypotensive episodes after autologous breast reconstruction. Gabapentin (Gaba), a nonopioid analgesic used in ERAS, has been shown to attenuate postoperative hemodynamic responses. This study assesses ERAS's impact, with and without Gaba, on postoperative hypotension after microvascular breast reconstruction.
Methods: Three cohorts were studied: traditional pathway, ERAS + Gaba, and ERAS no-Gaba. We evaluated length of stay, inpatient narcotic use [morphine milligram equivalents (MME)], mean systolic blood pressure, hypotension incidence, and complications. The traditional cohort was retrospectively reviewed, whereas the ERAS groups were enrolled prospectively after the initiation of the protocol in April 2019 (inclusive of Gaba until October 2022).
Results: In total, 441 patients were analyzed. The three cohorts, in the order mentioned above, were similar in age and bilateral reconstruction rates (57% versus 61% versus 60%). The ERAS cohorts, both with and without Gaba, had shorter stays ($P < 0.01$). Inpatient MME was significantly less in the ERAS + Gaba cohort than the traditional or ERAS no-Gaba cohorts (medians: 112 versus 178 versus 158 MME, $P < 0.01$). ERAS + Gaba significantly increased postoperative hypotensive events on postoperative day (POD) 1 and 2, with notable reduction after Gaba removal ($P < 0.05$). Across PODs 0–2, mean systolic blood pressure was highest in the traditional cohort, followed by ERAS no-Gaba, then the ERAS + Gaba cohort ($P < 0.05$). Complication rates were similar across all cohorts.
Conclusions: Postmicrovascular breast reconstruction, ERAS + Gaba reduced overall inpatient narcotic usage, but increased hypotension incidence. Gaba removal from the ERAS protocol reduced postoperative hypotension incidence while maintaining similar stay lengths and complication rates. *(Plast Reconstr Surg Glob Open 2024; 12:e5732; doi: 10.1097/GOX.0000000000005732; Published online 15 April 2024.)*

INTRODUCTION

Enhanced recovery after surgery (ERAS) protocols are designed to optimize patient outcomes subsequent to surgical interventions. Originating as a fast-track recovery method in 1994 to improve coronary artery bypass surgery outcomes through the bundling of perioperative treatments,[1–3] ERAS was found to reduce the length of intensive care unit stays by approximately 20%.[1] Subsequent investigations further validated ERAS's efficacy in various surgical domains, including microvascular breast reconstruction,[4–16] leading to the establishment of the ERAS society. This group asserted that the quality of perioperative care is as consequential as the surgery itself in determining patient outcomes.[17] Today, ERAS has earned wide acceptance across numerous surgical subspecialties, and it is notably recognized for its ability to decrease length of stay (LOS) and inpatient narcotic use without any statistical difference in morbidity.[4–16] Thus, the ERAS protocol has become a cornerstone in delivering patient-centered, cost-effective care in contemporary surgical practice.

Disclosure statements are at the end of this article, following the correspondence information.

Despite ERAS's transformative nature on surgical outcomes and perioperative patient care, a potential area of concern is the increased rates of postoperative hypotension after microvascular breast reconstruction.[18] This adverse effect may negatively impact wound healing and reconstructive outcomes. Central to this issue is gabapentin (Gaba), an antiepileptic drug repurposed as a nonopioid analgesic in the ERAS protocol. This drug has demonstrated capabilities in attenuating the hemodynamic response.[19–26] Some studies have reported the superiority of Gaba over known antihypertensives, such as clonidine, in mitigating hemodynamic responses.[26] However, a comprehensive understanding of Gaba's role within the ERAS protocol and its correlation with postoperative hypotension remains unclear. Therefore, we designed a comparative study with three cohorts to understand the effect of Gaba within the ERAS protocol. The traditional cohort underwent surgery without the ERAS pathway; the ERAS + Gaba cohort followed the standard ERAS protocol, inclusive of Gaba; and the ERAS no-Gaba cohort followed the ERAS protocol exclusive of Gaba. By segregating our participants into these three cohorts, we sought to evaluate differences in postoperative outcomes, with a primary focus on hypotensive episodes, and mean systolic blood pressure (SBP).

Our study aimed to evaluate the impact of ERAS, with and without Gaba, on postoperative hypotension and outcomes after autologous breast reconstruction at our institution. We hypothesized that by omitting Gaba from our ERAS protocol, patients would see a reduction in postoperative hypotension occurrence when compared with an ERAS+Gaba cohort. Additionally, we hypothesized that both ERAS cohorts would demonstrate a shorter LOS and lesser inpatient narcotic use compared with a traditional cohort, without increasing rates of postoperative morbidity.

METHODS

This IRB-approved study (approval no.: 23-000595) examined postoperative hypotension and perioperative outcomes after autologous breast reconstruction.

STUDY DESIGN AND PARTICIPANTS

We conducted a longitudinal, comparative analysis from April 4, 2019, to April 26, 2023, on patients undergoing deep inferior epigastric perforator or muscle-sparing transverse rectus abdominis myocutaneous (MS-TRAM) breast reconstructions, the predominant flap procedures at our institution. We excluded all other flaps as they constitute a negligible portion of our practice. Due to the low volume of the other flaps, it is unlikely that their exclusion influenced the results of this study.

The study was segmented into three periods, reflecting different care pathways:

- Traditional cohort (April 2019 to February 2021): Patients managed under a pre-ERAS care pathway, with data collected retrospectively.

Takeaways

Question: Does the inclusion of gabapentin in Enhanced recovery after surgery (ERAS) protocols increase postoperative hypotension occurrence in patients undergoing microvascular breast reconstruction?

Findings: Gabapentin within ERAS protocols reduced narcotic use but was associated with an increase in postoperative hypotension. Gabapentin's removal from the protocol decreased hypotension rates while maintaining low narcotic usage and a shorter hospital stay.

Meaning: Removing gabapentin from ERAS protocols may be beneficial in reducing the risk of postoperative hypotension in microvascular breast reconstruction.

- ERAS + Gaba cohort (April 2019 to October 2022): Managed under the initial ERAS protocol, including Gaba, with data gathered prospectively.
- ERAS no-Gaba cohort (October 2022 to April 2023): Managed under a revised ERAS protocol that excluded Gaba, with prospective data collection.

The ERAS protocol's implementation began in April 2019 and achieved full departmental adoption by February 2021. Postoperative hypotension observations prompted Gaba investigation, leading to its exclusion from the protocol on October 5, 2022, with full departmental adoption by October 26, 2022. Data such as age, bilateral reconstruction rates, body mass index (BMI), LOS, inpatient narcotic use, postoperative hypotensive episodes, Foley catheter removal, return to customary diet, and complication rates were collected for each cohort.

MILLIGRAM MORPHINE EQUIVALENTS CALCULATION

Each administered narcotic was translated into its respective oral equivalent dosage. The resulting value was multiplied by the dosage frequency, yielding a certain product, and then transformed into milligram morphine equivalents (MMEs) using the appropriate CONSORT classification conversion factor (Table 1).[27] After converting each medication into its MME, the total MME was calculated as the sum of the MMEs for all medications a patient received during their LOS.

Table 1. MME Conversion Factors

Medication	Conversion Factor
Codeine	0.150
Fentanyl (transmucosal)	0.125
Hydrocodone	1.000
Hydromorphone	4.000
Morphine	1.000
Oxycodone	1.500
Tramadol	0.100

Example: For a patient that received six, 5-mg PO oxycodone doses during their inpatient stay: $(6 \times 5) \times 1.5 = 45$ MME

PAIN SCORE CALCULATION

To assess patient pain levels, our medical staff utilized a visual analog scale. Each patient self-assessed their current pain severity on a scale from 0, implying no pain, to 10, denoting the utmost possible pain. These assessments were recorded before the scheduled administration of each analgesic dose, with the results subsequently incorporated into the patient's medical record. The daily frequency of these assessments was subject to variation due to patient-related elements such as sleep schedule and willingness to participate. To accommodate this variability, we computed a mean pain score for each patient on each postoperative day (POD). Each cohort then had their daily average calculated.

ERAS PROTOCOL AND KEY CHANGES

Several distinctive modifications pertaining to preoperative counseling, intraoperative and postoperative pain management, and postoperative care were introduced in the ERAS cohorts in contrast to the traditional pathway (Table 2).

PREOPERATIVE COUNSELING AND PAIN CONTROL

Detailed preoperative counseling was conducted for both ERAS cohorts with their supervising surgeon. The focus was on understanding the objectives of the ERAS pathway, preparing for anticipated postoperative discomfort, and emphasizing the strategy to decrease postoperative narcotic utilization via multimodal analgesia.

On the day of surgery, the ERAS + Gaba cohort received a combination of preoperative analgesics that included acetaminophen, celecoxib, Gaba, and ondansetron. The ERAS no-Gaba cohort was administered a similar analgesic regimen; however, Gaba was excluded. In contrast, the traditional cohort did not participate in preoperative counseling, nor were they given preoperative analgesics.

Table 2. Traditional versus ERAS pathway protocols

Traditional Pathway	ERAS + Gaba	ERAS No-Gaba
Preoperative	**Preoperative (day of surgery)**	**Preoperative (day of surgery)**
None	Acetaminophen 1000 mg PO, celecoxib 400 mg PO, gabapentin 300 mg PO, ondansetron 4 mg IV	Acetaminophen 1000 mg PO, celecoxib 400 mg PO, ondansetron 4 mg IV
Intraoperative	**Intraoperative**	**Intraoperative**
Discretion of anesthesia team	IV acetaminophen 1000 mg	IV acetaminophen 1000 mg
No nerve block	Intraoperative TAP block and pectoralis block with 0.25% bupivacaine with epinephrine	Intraoperative TAP block and pectoralis block with 0.25% bupivacaine with epinephrine
POD 0	**POD 0**	**POD 0**
NPO, bedrest, maintenance IV Fluids 135cc/hr	Clear liquid diet, bedrest, maintenance IVF 135 cc/h	Clear liquid diet, bedrest, maintenance IVF 135 cc/h
Hydromorphone PCA	Toradol 15 mg IV (PACU), oxycodone 5/10/15 mg PO prn, acetaminophen 1000 mg q8h PO, celecoxib 200 mg PO q8h, gabapentin 300 mg PO q8h	Toradol 15 mg IV (PACU), oxycodone 5/10/15 mg PO prn, acetaminophen 1000 mg q8h PO, celecoxib 200 mg PO q8h
POD 1	**POD 1**	**POD 1**
Clear liquid diet, bedrest, continue IV fluids, q1h flap checks	Customary diet, saline lock IV, movement—out of bed—walk down hall, q1h flap checks	Customary diet, saline lock IV, movement—out of bed—walk down hall, q1h flap checks
Hydromorphone PCA	Oxycodone—acetaminophen—celecoxib—gabapentin regimen same as POD 0	Oxycodone—acetaminophen—celecoxib regimen same as POD 0
POD 2	**POD 2**	**POD 2**
Customary diet, continue IV Fluids, q2h flap checks, sliding scale oxycodone [5/10/15 mg, dependent on mild (0–3)/moderate (4–6)/severe pain (7–10)], NO NSAIDs	Customary diet, discontinue Foley catheter, q2h flap checks, oxycodone—acetaminophen—celecoxib—gabapentin regimen same as POD 0	Customary diet, discontinue Foley catheter, q2h flap checks, oxycodone—acetaminophen—celecoxib regimen same as POD 0
Movement—out of bed—walk down hall	Movement—out of bed—walk down hall	Movement—out of bed—walk down hall
POD 3	**POD 3**	**POD 3**
Saline lock IV, discontinue Foley catheter, q4h flap checks, sliding scale oxycodone	Discharge to home	Discharge to home
POD 4		
Discharge to home		
Discharge medications: oxycodone 5 mg (45–60 tablets), ondansetron 4 mg PO prn, Colace, senna, miralax	Discharge medications: acetaminophen 1000 mg q8h, ibuprofen 400 mg q6h, gabapentin 300 mg q8h, ondansetron 4 mg PO q6h prn, oxycodone 5 mg (20 tablets) or tramadol 50 mg (20 tablets) prn, Colace, senna, miralax	Discharge medications: acetaminophen 1000 mg q8h, ibuprofen 400 mg q6h, ondansetron 4 mg po q6h prn, oxycodone 5 mg (20 tablets) or tramadol 50 mg (20 tablets) prn, Colace, senna, miralax

INTRAOPERATIVE PAIN CONTROL

Modifications in intraoperative pain management for both ERAS cohorts involved the provision of IV acetaminophen and the targeted application of transversus abdominis plane and pectoralis blocks using 0.25% bupivacaine with epinephrine. In the case of the traditional pathway, the approach to intraoperative analgesia was flexible, being largely determined by the anesthesiology team's judgement and devoid of any prespecified nerve block.

POSTOPERATIVE CARE

Postoperative adjustments in both ERAS pathways involved a variety of key measures, including alterations in narcotic use, introduction of multimodal analgesia, prompt return to customary diet, Foley catheter removal timepoint and discharge. These elements deviated from the practices in the traditional pathway, wherein most of these protocols were either not implemented or were carried out at later stages of postoperative recovery. The ERAS cohorts differed only in Gaba administration (Table 2).

BLOOD PRESSURE MEASUREMENTS AND HYPOTENSION EVALUATION

The nursing staff collected blood pressure measurements approximately every 4 hours during the inpatient LOS. It is important to note that the exact number of these assessments varied daily, influenced by factors such as the timing of the surgery during the operative day, and the patient's comorbidities. Patients that manifested hypotensive episodes were subjected to more intensive surveillance, with blood pressure readings being obtained on an hourly basis until the resolution of the hypotensive event. To accommodate for the variability in the frequency of these measurements, we calculated two metrics for each cohort on every POD: the percentage of patients experiencing at least one episode of SBP below 90, and the average SBP for each cohort.

STATISTICAL ANALYSIS

Statistical comparisons among the three cohorts were performed using ANOVA or Kruskal-Wallis for continuous variables, and chi-square or Fisher exact tests for categorical variables, using a significance level of P less than 0.05. All statistical analyses were conducted in SAS 9.4 (SAS Institute, Cary, N.C.).

RESULTS

We examined 441 patients stratified into three cohorts: traditional (n = 94), ERAS + Gaba (n = 275), and ERAS no-Gaba (n = 72). Overall, the cohorts were similar across recorded patient and surgical demographics (Table 3). The median age across cohorts was similar, with 53.0, 51.0, and 53.0 years for traditional, ERAS + Gaba, and ERAS no-Gaba, respectively. There were no significant differences in bilateral reconstruction rates (traditional: 57.4%, ERAS + Gaba: 61.1%, ERAS no-Gaba: 59.7%; $P = 0.8217$). The flap type was consistent across cohorts, with 94.7% of traditional, 97.5% of ERAS + Gaba, and 95.8% of ERAS no-Gaba patients undergoing a deep inferior epigastric perforator flap. The remaining patients underwent an MS-TRAM flap. Median operative time (in minutes) was also comparable (traditional: 461.0, ERAS + Gaba: 499.0, ERAS no-Gaba: 490.0; $P = 0.1994$). BMI did not differ between the cohorts, with most patients having a BMI greater than 25.0 ($P = 0.3698$).

The ERAS cohorts demonstrated a significant reduction in median inpatient narcotic consumption (traditional: 178.0 MME, ERAS + Gaba: 112.0 MME, ERAS no-Gaba: 158.0 MME; $P < 0.0001$). Although only POD 0 and 1 were statistically significant, mean pain scores were consistently lowest in the ERAS + Gaba cohort; pain scores in the other two cohorts were approximately equal. Both ERAS cohorts achieved earlier discharge milestones, such as return to diet and Foley removal, than the traditional cohort. Moreover, a statistically significant decrease in the LOS was observed in both ERAS cohorts, with 86.5% of ERAS + Gaba and 93.1%

Table 3. Patient Demographics and Surgical Characteristics

	Total (N = 441)	Group			P
		Traditional (N = 94)	ERAS + Gaba (N = 275)	ERAS No-Gaba (N = 72)	
Age, median (IQR)	52.0 (45.0, 59.0)	53.0 (44.0, 59.0)	51.0 (44.0, 59.0)	53.0 (47.5, 60.0)	0.4234*
BMI, n (%)					0.3698†
Underweight (≤18.5)	5 (1.1%)	2 (2.1%)	2 (0.7%)	1 (1.4%)	
Normal (18.5–24.9)	135 (30.6%)	21 (22.3%)	91 (33.1%)	23 (31.9%)	
Overweight (25.0–29.9)	192 (43.5%)	48 (51.1%)	114 (41.5%)	30 (41.7%)	
Obese (≥30)	109 (24.7%)	23 (24.5%)	68 (24.7%)	18 (25.0%)	
Operative time (min), median (IQR)	488.0 (396.0– 561.0)	460.5 (367.0– 549.0)	499.0 (408.0–566.0)	490.0 (394.5–551.5)	0.1994*
Flap Type, n (%)					0.3274†
DIEP	426 (96.6%)	89 (94.7%)	268 (97.5%)	69 (95.8%)	
MS-TRAM	15 (3.4%)	5 (5.3%)	7 (2.5%)	3 (4.2%)	
Laterality, n (%)					0.8217‡
Bilateral	265 (60.1%)	54 (57.4%)	168 (61.1%)	43 (59.7%)	
Unilateral	176 (39.9%)	40 (42.6%)	107 (38.9%)	29 (40.3%)	

*Kruskal-Wallis P value.
†Fisher exact P value.
‡Chi-square P value.

of ERAS no-Gaba discharged on POD 3 or earlier, compared with only 2.1% in the traditional cohort (Table 4). Rates of complications (ie, operating room takebacks, flap necrosis, constipation/ileus, emergency department readmission, wound infection, and donor site dehiscence) were similar across cohorts (all $P > 0.05$).

Our examination of postoperative hypotension revealed distinct trends among the three cohorts studied. In the ERAS + Gaba cohort, we observed a statistically significant increase in hypotensive episodes on POD 1 and 2 (Fig. 1). Additionally, there was a statistically significant decrease in mean SBP on POD 1–3, compared with the ERAS no-Gaba and traditional cohorts (Fig. 2).

DISCUSSION

ERAS protocols have been recognized for their ability to decrease LOS and postoperative narcotic consumption in autologous reconstruction.[9–13,15,16] Despite these advantages, recent literature has connected ERAS protocols with a higher occurrence of postoperative hypotension, possibly due to a blunted sympathetic stress response.[18]

Table 4. Perioperative Outcomes

		Group			
	Total (N = 441)	Traditional (N = 94)	ERAS + Gaba (N = 275)	ERAS No-Gaba (N = 72)	P
Return to Diet (POD), n (%)					<0.0001*
1	346 (78.5%)	0 (0.0%)	275 (100.0%)	71 (98.6%)	
2	95 (21.5%)	94 (100.0%)	0 (0.0%)	1 (1.4%)	
Foley Removal (POD), n (%)					<0.0001*
1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
2	346 (78.5%)	0 (0.0%)	274 (99.6%)	72 (100.0%)	
3+	95 (21.5%)	94 (100.0%)	1 (0.4%)	0 (0.0%)	
Length of Stay (d), n (%)					<0.0001†
1	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
2	2 (0.5%)	0 (0.0%)	0 (0.0%)	2 (2.8%)	
3	305 (69.2%)	2 (2.1%)	238 (86.5%)	65 (90.3%)	
4	122 (27.7%)	85 (90.4%)	32 (11.6%)	5 (6.9%)	
5+	12 (2.7%)	7 (7.4%)	5 (1.8%)	0 (0.0%)	
Inpatient MME (POD), Median (IQR)					
Total Stay	136.0 (67.0, 221.0)	178.0 (104.0, 285.0)	112.0 (57.0, 201.0)	158.0 (74.0, 253.0)	<0.0001‡
Narcotics on POD 0–3	131.0 (67.0, 210.0)	158.0 (97.0, 250.0)	112.0 (53.0, 194.0)	155.0 (74.0, 253.0)	0.0002‡
0	37.0 (14.0, 74.0)	12.0 (8.0, 24.0)	45.0 (18.0, 81.0)	58.0 (33.0, 96.0)	<0.0001‡
1	30.0 (11.0, 61.0)	41.0 (22.0, 89.0)	23.0 (8.0, 53.0)	45.0 (23.0, 75.0)	<0.0001‡
2	26.0 (8.0, 60.0)	55.0 (26.0, 74.0)	15.0 (0.0, 45.0)	30.0 (10.0, 60.0)	<0.0001‡
3	15.0 (0.0, 38.0)	45.0 (15.0, 75.0)	7.5 (0.0, 30.0)	10.0 (0.0, 30.0)	<.0001‡
Systolic Blood Pressure (POD), Mean (SD)					
0	119.5 (14.9)	122.3 (14.5)	118.7 (15.2)	119.0 (14.2)	0.1308§
1	106.9 (13.6)	113.6 (14.7)	104.3 (12.0)	107.8 (14.7)	<0.0001§
2	113.3 (14.1)	118.8 (15.9)	111.1 (12.8)	114.7 (14.3)	<0.0001§
3	117.2 (14.4)	121.0 (14.5)	115.3 13.5)	119.6 (16.5)	0.0011§
Hypotensive Events (POD), n (%)					
0	45 (10.3%)	5 (5.3%)	34 (12.5%)	6 (8.3%)	0.1216*
1	132 (30.1%)	18 (19.2%)	94 (34.4%)	20 (27.8%)	0.0185*
2	49 (11.2%)	8 (8.5%)	38 (13.9%)	3 (4.2%)	0.0426*
3	12 (2.8%)	5 (5.3%)	6 (2.2%)	1 (1.5%)	0.2742†
Pain (POD), Mean (SD)					
0	1.3 (1.7)	1.6 (1.9)	1.1 (1.5)	1.5 (1.8)	0.0168§
1	2.5 (2.1)	2.5 (2.1)	2.3 (2.0)	3.1 (2.3)	0.0178§
2	2.5 (2.1)	2.7 (1.9)	2.4 (2.0)	2.8 (2.3)	0.2395§
3	2.5 (2.2)	2.7 (1.9)	2.3 (2.2)	2.8 (2.4)	0.1371§
Complications, n (%)					
OR takebacks (microvascular)	17 (3.9%)	6 (6.4%)	9 (3.3%)	2 (2.8%)	0.3959†
Flap necrosis	7 (1.6%)	1 (1.1%)	5 (1.8%)	1 (1.4%)	0.9999†
Constipation/ileus	2 (0.5%)	2 (2.1%)	0 (0.0%)	0 (0.0%)	0.0714†
ED readmission	5 (1.1%)	1 (1.1%)	3 (1.1%)	1 (1.4%)	0.9999†
Wound infection	17 (3.9%)	4 (4.3%)	10 (3.6%)	3 (4.2%)	0.8817†
Donor site dehiscence	6 (1.4%)	1 (1.1%)	5 (1.8%)	0 (0.0%)	0.840†

*Chi-square *P* value.
†Fisher exact *P* value.
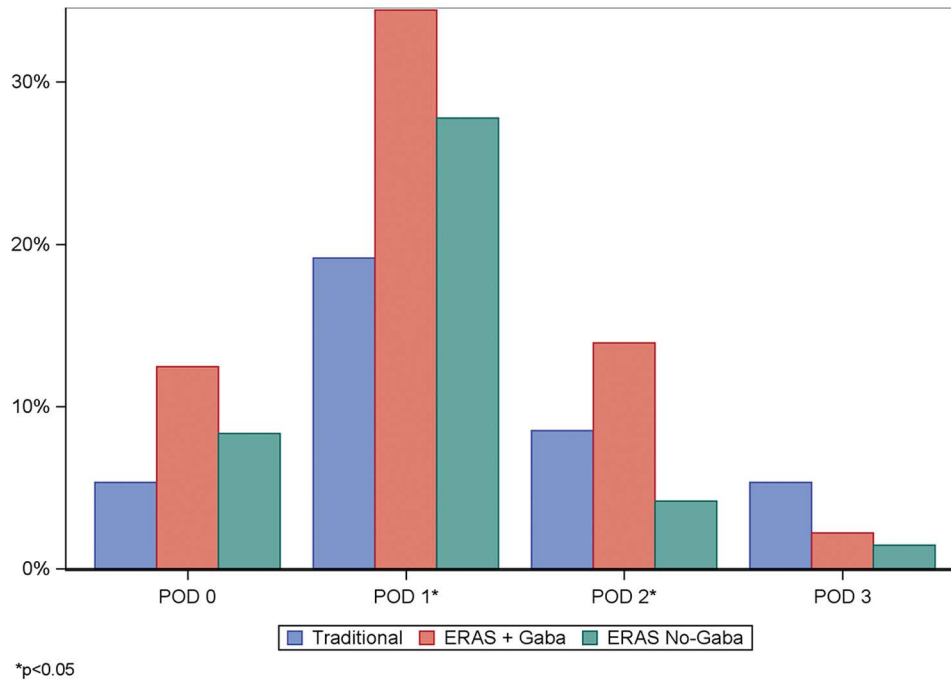‡Kruskal-Wallis *P* value.
§ANOVA F-test *P* value.

Fig. 1. Incidence of postoperative hypotension across different perioperative protocols. The graph compares the traditional protocol, ERAS + Gaba, and ERAS no-Gaba cohorts, with significant increases in hypotensive events on POD 1 and 2 for the ERAS + Gaba cohort.
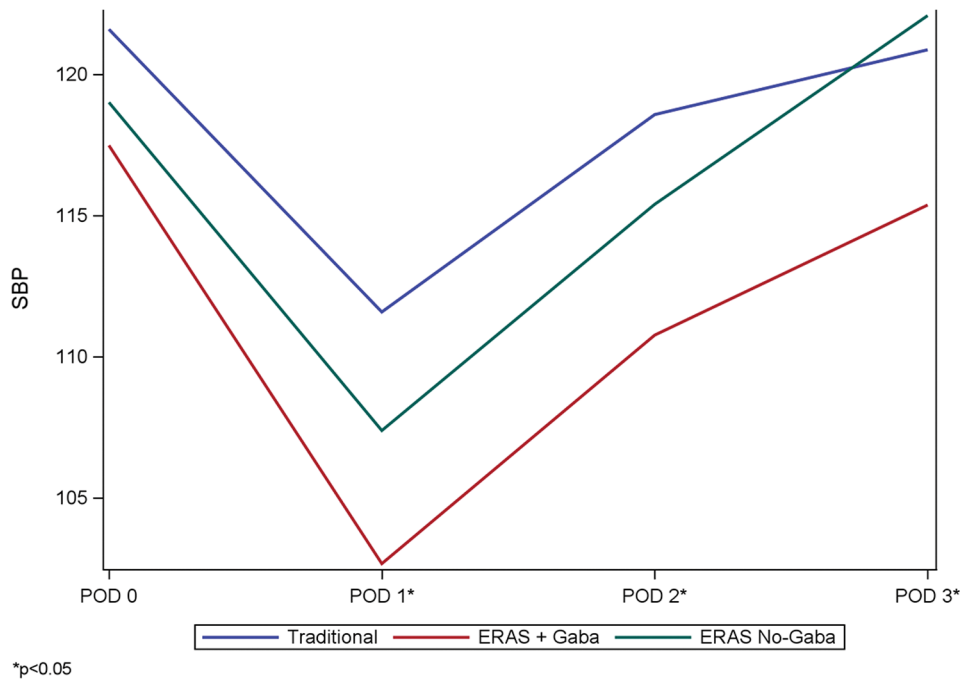

Fig. 2. Mean SBP trends from POD 0 to POD 3 among the three cohorts. This line graph illustrates the differences in SBP with the ERAS + Gaba cohort maintaining the lowest SBP over the period.

This phenomenon may be further influenced by Gaba, a third-generation antiepileptic drug, as it is known to attenuate hemodynamic responses and is often used as a nonopiate adjunct in ERAS protocols.[19–26] In this study, we sought to examine the effect of ERAS implementation and Gaba use on postoperative hypotension and outcomes following microvascular breast reconstruction. Our findings revealed that the inclusion of Gaba in an ERAS protocol

facilitated an increase in postoperative hypotension rates and decrease in mean SBP during the inpatient postoperative period. This work contributes to the ongoing refinement of ERAS protocols, aiming to fully exploit its benefits while mitigating potential adverse effects.

Hypotension, as it is associated with ERAS protocols, is a new finding in the field of autologous breast reconstruction. This phenomenon was reported by Anolik et al, who posited that ERAS protocol implementation may engender a unique blunted sympathetic stress response.[18] Despite this insight, existing research has not probed into the specific elements within ERAS that may contribute to this occurrence. Our analysis indicates that Gaba could be instrumental in this regard, as its incorporation into an ERAS protocol correlated with an escalated incidence of postoperative hypotension and a decrease in average SBP. These results bear clinical relevance, given that vascular compromise continues to be the primary cause of flap failure.[28–33] Adding to this concern is the synchronicity between the peak of Gaba-associated hypotension and the most common failure timepoint for free flaps—within POD 1. While our study did not uncover a statistical divergence in microvascular takebacks and complications between the ERAS cohorts, this does not entirely nullify the clinical significance. Other studies have noted an anecdotal increase in patient complaints of dizziness and lightheadedness following ERAS implementation.[18] This could detrimentally impact patients' ability to achieve postoperative ambulation and dietary returns, subsequently prolonging LOS. In light of these observations, further research is warranted to fully understand the nuances of Gaba's impact following autologous breast reconstruction. Such knowledge may guide surgeons in further tailoring ERAS protocols, and potentially facilitate the selection of alternative nonopiate analgesics.

The pathophysiologic cause for this hypotensive phenomenon is not fully understood. Initial insights from in vitro studies have indicated that Gaba may inhibit the release of catecholamines from adrenal chromaffin cells, and clinical findings have further demonstrated reduced cortisol and catecholamine levels following presurgical Gaba administration.[34,35] Another significant mechanism may involve Gaba's inhibition of the alpha 2-delta subunit of presynaptic voltage-gated calcium channels.[36] This proposal gains prominence given that other institutions have cited the use of pregabalin, a drug with a quicker onset of action, higher bioavailability, and increased binding affinity for the alpha 2-delta subunit,[37,38] in their ERAS protocols in lieu of Gaba.[18] If the blunted postoperative hemodynamic response is indeed correlated with the alpha 2-delta subunit, it may provide additional impetus for surgeons to exercise caution with this entire drug class following these procedures. As this mechanism becomes more defined, it can potentially aid surgeons in striking a careful balance between achieving optimal pain management and minimizing undesirable hemodynamic effects.

During the opioid crisis, the incidence of chronic opioid use postsurgery was one in 16 patients, with the risk escalating at higher postoperative dosages.[39–44] In this context, ERAS protocols were adopted as an efficacious countermeasure. Our study substantiates this approach, revealing that ERAS no-Gaba and ERAS + Gaba cohorts had lower median opioid consumptions of 158.0 and 112.0 MME, respectively, compared with 178.0 MME in the traditional cohort during the complete inpatient period. To account for both ERAS cohorts' reduced LOS, we also assessed narcotic consumption throughout PODs 0–3. Here, the ERAS + Gaba group recorded a significantly lower median opioid use of 112.0 MME, compared with 155.0 and 158.0 MME for the ERAS no-Gaba and traditional cohorts, respectively. Additionally, mean pain scores were consistently the lowest in the ERAS + Gaba cohort, reaching statistical significance on POD 0 and 1. Concurrently, these results introduce a complex decision-making element for surgeons considering Gaba as a nonopioid analgesic. The question arises: Is the opioid-sparing effect of Gaba an adequate trade-off for the risk of postoperative hypotension? Notably, our group decided poststudy to reintegrate Gaba into our ERAS protocol. However, as our analysis simply omitted Gaba, while maintaining consistent levels of other nonopioid analgesics (Table 2) across both ERAS cohorts, it lays the groundwork for further inquiry. Future research should investigate whether a safe increase in this set of "other" nonopioid analgesics or the introduction of a nonopioid, non-Gaba alternative may allow for similar postoperative MME levels in ERAS cohorts without inducing Gaba-related hypotension.

In the field of microvascular reconstruction, the ERAS protocol has earned a reputation for decreasing postoperative LOS, thereby reducing costs, and enhancing patient satisfaction.[9–13,15,16,18] Our study lends further credence to this claim, as both ERAS cohorts displayed significant reductions in key postoperative milestones, including the timepoint of Foley catheter removal, postoperative return to a customary diet, and LOS. As both ERAS cohorts performed similarly across these three variables, Gaba's use did not seem to be associated with them. This consistency with previous literature affirms that even in the context of an adjustment to nonopioid pain management strategies, ERAS continues to achieve its core objectives.

Although this study provides valuable insights into a specific element within ERAS protocols that may contribute to postoperative hypotension, it is not without limitations. This study was conducted at a single institution; therefore, the distinct practices, resources, and patient populations treated could have influenced the outcomes. The study design, involving unequal cohort sizes and retrospective collection for the traditional cohort, may have introduced bias and affected the precision of comparisons. Variations in the quantity of pain score and blood pressure measurements may have also introduced an element of bias. Further, the assessment of complications after surgery was confined to the 30-day postoperative mark at our institution. Complications that could have occurred outside this period, or those addressed at other healthcare institutions, may not have been included. Our study's final limitation pertains to the reduction in LOS seen in both ERAS cohorts; this is not a universal finding in studies assessing ERAS in autologous breast reconstruction.[10] Clearance for patient discharge was based on

criteria such as oral diet tolerance, mobility, and Foley catheter removal, which were implemented and evaluated earlier for ERAS patients. This early assessment potentially introduced bias, as pre-ERAS patients often did not undergo this early evaluation to demonstrate discharge readiness, possibly affecting their perceived readiness and skewing the comparison. Despite these limitations, the study contributes essential knowledge, outlining areas for further exploration and refinement in the understanding of ERAS protocols in autologous breast reconstruction.

Critical Evaluation of Our Practice

Incorporating the insights from this study, we have meticulously reassessed the role of Gaba within our ERAS protocol. Although an increase in postoperative hypotension was associated with Gaba use, there was no significant rise in vascular-related complications. Moreover, when assessing PODs 0–3, our analysis revealed that the ERAS + Gaba cohort consumed 30% less narcotics compared with the traditional cohort. In contrast, the reduction in narcotic use for the ERAS no-Gaba cohort was less than 3% over the same timeframe. Given these outcomes, our practice has elected to reintroduce Gaba into the ERAS protocol as our standard, valuing the considerable opioid-sparing benefits over the hypotensive risks. Nevertheless, our commitment to patient-specific care remains unwavering. Thus, we advocate for a tailored approach, considering each patient's individual clinical profile. This patient-centered philosophy ensures that our practice not only observes the broad trends revealed by research but also respects the unique complexities of each surgical case.

CONCLUSIONS

This study provides critical insights into the relationship between ERAS protocols, Gaba use, and postoperative hypotension after microvascular breast reconstruction. Known for its ability to attenuate the hemodynamic response,[19–26] Gaba's inclusion in the ERAS protocol was found to be associated with a statistically significant increase in hypotensive episodes and decrease in mean SBP. Our findings support the beneficial aspects of ERAS protocols, both inclusive and exclusive of Gaba, as both cohorts demonstrated reduced total inpatient narcotic consumption and length of hospital stay without an increase in postoperative complications. Further research is needed to fully understand the underlying mechanisms responsible for the observed effects of Gaba in the immediate postoperative period. Overall, these insights contribute valuable perspectives to the ongoing refinement of ERAS protocols, aimed at maximizing benefits while minimizing potential adverse outcomes.

Jeremiah M. Taylor, BS
UCLA Medical School: University of California Los Angeles
David Geffen School of Medicine
Los Angeles, CA
E-mail: jeremiahtaylor@mednet.ucla.edu

Jaco H. Festekjian, MD
200 Medical Plaza Suite 460
Los Angeles, CA 90095
E-mail: JFestekjian@mednet.ucla.edu

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