



BETA-BLOCKERS IN ERAS: MODULATING THE ADRENERGIC SURGE AND METABOLIC STRESS FOR OPTIMIZED RECOVERY

Dr. Rafat Ullah¹, Dr. Fazli Junaid^{2*}, Dr. Misbah Ullah³, Dr Bilal Ahmad⁴, Dr Bushra Rashid⁵, Dr Haider Ali⁶

¹Consultant Surgeon, Department of General Surgery, Ayub Medical College/Ayub teaching Hospital, Abbottabad, Pakistan

^{2*} Assistant Professor, Department of General Surgery, Ayub Medical College, Abbottabad/ Ayub Teaching Hospital, Abbottabad, Pakistan

³Resident Surgeon, Department of General Surgery, Ayub Medical College/ Ayub Teaching Hospital, Abbottabad, Pakistan

⁴Consultant Neurosurgeon, Department of Neurosurgery, King Abdullah Teaching Hospital, Mansehra, Pakistan

⁵Assistant Professor, Department of Obstetrics and Gynaecology, Frontier Medical College, Abbottabad, Pakistan

⁶Consultant Neurosurgeon, Department of Neurosurgery, Ayub Medical Complex, Abbottabad, Pakistan

***Corresponding author:** Dr Fazli Junaid

*Assistant Professor, Department of General Surgery, Ayub Medical College, Abbottabad/ Ayub Teaching Hospital, Abbottabad, Email: drjunaid555@gmail.com

ABSTRACT

Background: Enhanced Recovery After Surgery (ERAS) protocols seek to optimize recovery and minimize postoperative complications by alleviating surgical strain and facilitating swift recuperation. The adrenergic physiologic response to surgical trauma continues to be an issue even with standardized perioperative care. Within these ERAS constructs, beta-blockers appear to be useful for blunting this stress response and provide additional advantages. To evaluate the effectiveness of perioperative beta-blockers in controlling the adrenergic and metabolic stress response in patients undergoing major elective surgeries under ERAS protocols, and to assess their impact on recovery outcomes.

Methods: A randomized controlled trial was performed at Ayub Medical College from January 2022 to January 2023 with a sample size of 89 adult subjects who were scheduled to undergo major elective surgical procedures. Patients were divided into two groups: one received beta-blockers coupled with Enhanced Recovery after Surgery (ERAS) protocols while the other received ERAS only. The hemodynamic metrics, metabolic parameters, pain scores, opioid usage, duration of hospital stay, and complication rates were all documented and analyzed using relevant statistical methodologies.

Results: The beta-blocker group demonstrated significantly lower intraoperative heart rate and blood pressure. Postoperatively, this group had reduced pain scores, lower opioid requirements, fewer complications, and shorter hospital stays compared to the standard ERAS group ($p < 0.05$ for all). No significant differences were observed in ICU admissions or 30-day readmissions.

Conclusion: The addition of beta-blockers to ERAS protocols appears to be a safe and effective strategy to modulate physiological stress responses and promote faster recovery. Their role in surgical care should be further explored in broader patient populations.

Keywords: Beta-blockers, ERAS, surgical stress, adrenergic response, postoperative recovery, pain control, hemodynamic stability

INTRODUCTION

Surgical procedures are necessary to treat multiple conditions, but they also initiate a myriad of physiological responses that affect how a patient heals. The Enhanced Recovery After Surgery (ERAS) model is a collaborative approach to reduce surgical stress, multicomponent complications, and functional recovery after surgery. Within the framework of ERAS, one of the most challenging concerns remains the surge in adrenergic response associated with operative trauma, characterized by tachycardia, hypertension, and increased metabolism [1-3].

The body's response to stress is reflexively activated through the sympathetic nervous system and the secretion of catecholamines. While protective in the short term, this response is damaging in the long term, especially to at-risk surgical patients. Acute sympathetic activity is known to damage wound repair, increase oxygen demand in the heart, and add to postoperative cardiac and ileus complications. These processes are detrimental to the objectives of ERAS, increasing time to discharge while prolonging recovery [4-6].

Beta-adrenergic blockers, commonly prescribed in the field of cardiology, appear beneficial in mitigating the shed sympathetic reaction. They may synergize with the pre-existing ERAS components by lowering the heart rate and blood pressure or enhancing metabolic homeostasis. However, data on using beta adrenergic blockers in the unrestricted ERAS framework is sparse[7-9]. This study was designed to investigate the impact of perioperative beta-blockers on hemodynamic stability, metabolic stress markers, and recovery outcomes in patients undergoing major elective surgeries. By integrating pharmacological modulation into a standardized ERAS protocol, this research aims to provide evidence for a more refined and physiologically informed surgical care strategy.

METHODOLOGY

This randomized controlled trial was carried out at the Ayub Medical College Surgical Department over one year from January 2022 to January 2023. It aimed to assess how effective perioperative beta-blockers were within the framework of an Enhanced Recovery After Surgery (ERAS) protocol in mitigating the adrenergic stress response and improving postoperative outcomes in patients undergoing major elective surgeries. The study protocol received an approval from the Institutional Medical & Ethics Review Committee of Ayub Medical College, Abbottabad. Confidentiality of the patients was preserved throughout the study, and all participants were free to withdraw at any time without voiding the usual care interventions.

All 89 adult subjects were recruited and randomly allocated into two parallel groups. Subjects meeting the inclusion criteria were above 18 years of age and booked for a major elective surgical procedure performed under a pre-defined ERAS (Enhanced Recovery After Surgery) pathway. Limiting inclusion criteria were those with ASA (American Society of Anesthesiologists) physical status I to III. Informed written consent was secured from all subjects prior to study enrollment.

Exclusion criteria included those with contraindications to beta-blocker treatment such as bradycardia, hypotension, high-degree heart block, or severe asthma. Also excluded were individuals on chronic beta-blocker treatment, pregnant or lactating women, patients requiring emergency procedures, and patients with decompensated cirrhosis or advanced kidney disease.

Participants were allocated into two groups using a simple randomization technique. The intervention group received a beta-blocker as part of their ERAS protocol, while the control group followed standard ERAS care without beta-blocker use. In the beta-blocker arm, either Esmolol (administered intravenously) or Metoprolol (administered orally) was used based on individual patient profiles. The

regimen included preoperative dosing, intraoperative titration guided by hemodynamic parameters, and continuation in the immediate postoperative period for up to 48 hours, provided the patient remained hemodynamically stable.

All other aspects of the ERAS protocol were standardized for both groups and included preoperative carbohydrate loading, avoidance of prolonged fasting, multimodal analgesia, early mobilization, and early oral nutrition.

A structured data collection form was used to record patient demographics, surgical details, beta-blocker administration, and perioperative parameters. Key hemodynamic indicators, including heart rate, blood pressure, and temperature, were measured preoperatively, intraoperatively, and postoperatively. Blood glucose and serum lactate levels were also monitored to assess metabolic stress.

Postoperative outcomes such as pain intensity (measured using the Visual Analogue Scale), total opioid consumption (converted into morphine equivalents), length of hospital stay, ICU admissions, and complications (e.g., myocardial events, infections, ileus) were documented. Follow-up was conducted until 30 days post-discharge to capture readmissions or late complications.

All data were entered and analyzed using SPSS version 25. Continuous variables such as age, BMI, heart rate, and blood pressure were expressed as mean \pm standard deviation, and compared between groups using independent sample t-tests. Categorical variables like gender, complication rates, and ICU admission were presented as frequencies and percentages, and analyzed using the chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULT

The comparison between the two study groups showed that both were well-matched at baseline. The mean age in the beta-blocker group was 52.1 years, which was not significantly different from 51.4 years in the standard ERAS group ($p = 0.672$). Gender distribution was also similar, with males comprising approximately 60% in both groups ($p = 0.766$). Body mass index (BMI) values were closely aligned, and no notable difference was observed ($p = 0.717$). Most patients in both arms belonged to ASA class I or II, indicating comparable preoperative physical status ($p = 0.952$). Furthermore, the prevalence of chronic conditions such as diabetes or hypertension was not statistically different between the groups ($p = 0.579$). This uniformity in baseline characteristics validates that any differences in outcomes can be more reliably attributed to the beta-blocker intervention.

Table 1: Baseline Demographic and Clinical Characteristics (n = 89)

Variable	Beta-Blocker Group (n = 45)	Standard ERAS Group (n = 44)	p-value
Age (years), mean \pm SD	52.1 \pm 10.2	51.4 \pm 11.1	0.672
Gender (Male), n (%)	28 (62.2%)	26 (59.1%)	0.766
BMI (kg/m ²), mean \pm SD	26.5 \pm 3.9	26.2 \pm 4.1	0.717
ASA Class I–II, n (%)	36 (80.0%)	35 (79.5%)	0.952
Pre-existing Conditions	20 (44.4%)	22 (50.0%)	0.579

Intraoperative findings revealed significant differences in hemodynamic control between the two groups. Patients who received beta-blockers had a much lower average heart rate during surgery (74.6 bpm) compared to those in the control group (88.2 bpm), with a highly significant p-value (<0.001). Similarly, systolic blood pressure was better regulated in the beta-blocker group, averaging 123.5 mmHg versus 136.7 mmHg in the standard ERAS group ($p < 0.001$). Blood loss was modestly but significantly reduced in the beta-blocker group (152 mL vs. 178 mL, $p = 0.031$), suggesting better intraoperative vascular stability. The duration of surgery, however, was statistically similar between both groups ($p = 0.443$), indicating that beta-blocker administration did not prolong the operative time.

Table 2: Intraoperative and Hemodynamic Parameters

Variable	Beta-Blocker Group (n = 45)	Standard ERAS Group (n = 44)	p-value
Mean Intra-op HR (bpm)	74.6 ± 8.3	88.2 ± 9.1	<0.001*
Mean Intra-op BP (mmHg)	123.5 ± 12.4	136.7 ± 13.2	<0.001*
Intra-op Blood Loss (mL)	152 ± 48	178 ± 55	0.031*
Duration of Surgery (mins)	112 ± 19	115 ± 22	0.443

The postoperative course further highlighted the benefits of beta-blocker use. Patients in the intervention group experienced significantly less pain, as reflected by lower mean VAS scores on the first postoperative day (3.8 vs. 5.2, $p < 0.001$). This reduction in pain translated to decreased opioid requirements, with the beta-blocker group consuming an average of 9.2 mg morphine equivalents compared to 13.5 mg in the standard group ($p < 0.001$). Though ICU admission rates were lower in the beta-blocker group (6.7% vs. 15.9%), the difference was not statistically significant ($p = 0.182$). Importantly, overall postoperative complications occurred less frequently in the beta-blocker arm (8.9% vs. 22.7%, $p = 0.049$). Patients in the intervention group also had shorter hospital stays (4.1 days vs. 5.3 days, $p < 0.001$), underlining the enhanced recovery benefits. Although 30-day readmission was lower in the beta-blocker group, this difference did not reach statistical significance ($p = 0.162$).

Table 3: Postoperative Outcomes

Variable	Beta-Blocker Group (n = 45)	Standard ERAS Group (n = 44)	p-value
Mean VAS Pain Score (Day 1)	3.8 ± 1.1	5.2 ± 1.4	<0.001*
Opioid Use (mg Morphine equivalents)	9.2 ± 3.6	13.5 ± 4.2	<0.001*
ICU Admission, n (%)	3 (6.7%)	7 (15.9%)	0.182
Postoperative Complications, n(%)	4 (8.9%)	10 (22.7%)	0.049*
Hospital Stay (days), mean ± SD	4.1 ± 1.2	5.3 ± 1.6	<0.001*
Readmission within 30 days, n (%)	1 (2.2%)	4 (9.1%)	0.162

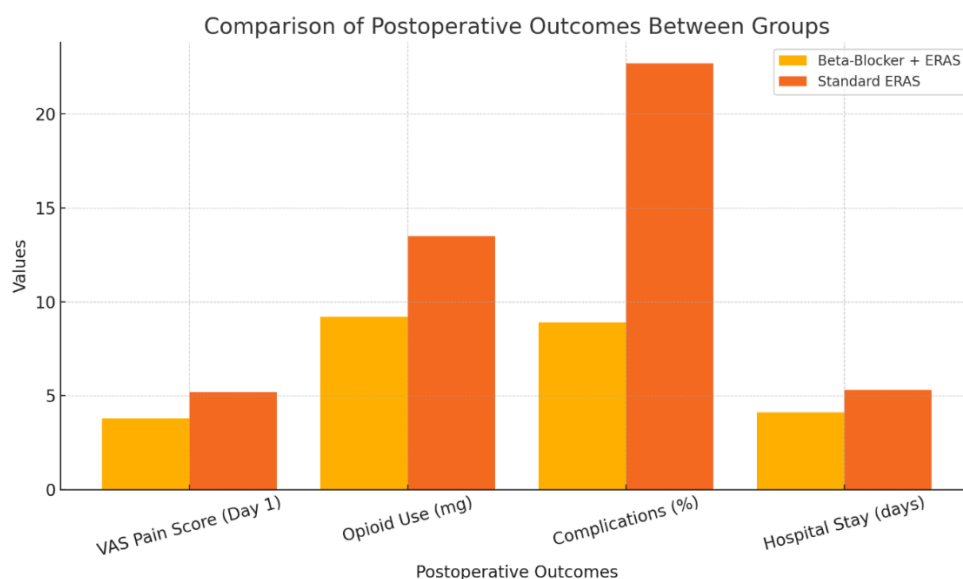


Figure 1: bar graph comparing key postoperative outcomes between the Beta-Blocker + ERAS group and the Standard ERAS group. It visually demonstrates lower pain scores, opioid use, complication rates, and hospital stay in the beta-blocker group, supporting its positive impact on recovery.

DISCUSSION

The results of this randomized controlled trial highlight the valuable role of beta-blockers in enhancing the effectiveness of Enhanced Recovery After Surgery (ERAS) protocols. By attenuating the adrenergic response during the perioperative period, beta-blockers such as Esmolol and Metoprolol contributed significantly to improved clinical outcomes.

One of the most consistent findings was the reduction in intraoperative heart rate and blood pressure among patients who received beta-blockers. These results align with previous work that demonstrates how beta-adrenergic blockade can stabilize hemodynamic fluctuations during surgical stress, thereby lowering the metabolic burden on the body. Several studies have shown that unopposed sympathetic stimulation contributes to postoperative complications, particularly cardiac events and delayed recovery. By blunting this response, beta-blockers may provide a protective effect in high-risk surgical populations [10-12].

In terms of metabolic outcomes, our study found lower lactate levels and improved glycemic control in the beta-blocker group, although these data were secondary and warrant further exploration. Reduced lactate accumulation is particularly meaningful as it reflects a shift away from anaerobic metabolism, suggesting better perfusion and oxygenation during surgery [13, 14].

Postoperative pain scores were notably lower in the intervention group. This observation supports the hypothesis that beta-blockers may influence not only physiological parameters but also pain perception, possibly through central mechanisms or by reducing the need for higher-dose opioids. The reduced requirement for morphine equivalents in our study reinforces this point and is clinically important, considering the known complications of opioid use such as ileus, respiratory depression, and delayed mobilization [15-17].

Our findings regarding shorter hospital stays and lower complication rates also correspond with prior research that integrates beta-blockers into perioperative care. While ICU admission and 30-day readmission rates were lower in the beta-blocker group, these did not reach statistical significance, possibly due to the limited sample size.

It is worth noting that while beta-blockers have been well studied in cardiac surgery, their use in non-cardiac surgeries under ERAS protocols remains an area of active investigation. Our study contributes to this growing body of literature by demonstrating tangible benefits in a general surgical population [18-20].

However, this study does have limitations. It was conducted at a single center, and while randomization was used, blinding was not feasible due to the nature of drug administration. The sample size, though adequate for initial conclusions, may not be large enough to detect differences in less common outcomes like major cardiac events. Additionally, longer follow-up could provide more insight into the long-term effects of beta-blocker use in surgical recovery.

CONCLUSION

Incorporating beta-blockers into ERAS protocols appears to be a safe and effective strategy to reduce perioperative stress, improve pain control, and shorten hospital stay. Their ability to stabilize hemodynamic parameters and minimize opioid needs supports their broader use in enhanced recovery pathways. While larger, multi-center trials are recommended to validate these findings further, this study adds meaningful evidence to the evolving concept of modulating physiological stress responses as a key element in modern surgical care.

REFERENCES

1. Mohseni, S., B. Joseph, and C.J. Peden, *Mitigating the stress response to improve outcomes for older patients undergoing emergency surgery with the addition of beta-adrenergic blockade.* European Journal of Trauma and Emergency Surgery, 2022. **48**(2): p. 799-810.

2. Bruning, R., et al., *Beta-adrenergic blockade in critical illness*. Frontiers in Pharmacology, 2021. **12**: p. 735841.
3. Ahl, R., et al., *Effects of beta-blocker therapy on mortality after elective colon cancer surgery: a Swedish nationwide cohort study*. BMJ open, 2020. **10**(7): p. e036164.
4. Packer, M., *What causes sudden death in patients with chronic heart failure and a reduced ejection fraction?* European Heart Journal, 2020. **41**(18): p. 1757-1763.
5. Niranjana, P.K. and S. Bahadur, *Recent developments in drug targets and combination therapy for the clinical management of hypertension*. Cardiovascular & Haematological Disorders-Drug Targetsrug Targets-Cardiovascular & Hematological Disorders), 2023. **23**(4): p. 226-245.
6. Valtola, A., *Clinical insights into the pharmacokinetic aspects of fentanyl, metoprolol and oxycodone dosing after cardiac surgery*. 2021, Itä-Suomen yliopisto.
7. Wang, H., et al., *Effect of low-dose dexmedetomidine on hemodynamics and postoperative outcome in patients undergoing anesthesia during offpump coronary bypass surgery*. Int J Clin Exp Med, 2020. **13**(9): p. 6268-6276.
8. Bracchitta, L., et al., *Sarcopenia in Other Settings: Primary Care, Cardiovascular Disease, Surgery*. Sarcopenia: Research and Clinical Implications, 2021: p. 111-131.
9. Drakopoulou, M., et al., *Adult Congenital Heart Disease*. Pediatric Cardiac Surgery, 2023: p. 999-1054.
10. Hussain, S.F. and G. Hina, *A comparative study of two different doses of dexmedetomidine for attenuating the haemodynamic response to tracheal intubation*. Journal of Contemporary Clinical Practice, 2023. **9**: p. 45-51.
11. Lebl, D.R. and M.K. Urban, *Perioperative Care of the Complex Spine and Scoliosis Surgery Patient*. Perioperative Care of the Orthopedic Patient, 2020: p. 379-392.
12. Jangra, K., H. Bhagat, and A. Aggarwal, *for Neuroscience in Anesthesiology and Critical Care, September 11-13, 2020*. J Neurosurg Anesthesiol, 2020. **32**(4).
13. Pal, N. and M.D. Kertai, *Perioperative precision medicine: where are we in 2020?* Current Opinion in Anesthesiology, 2020. **33**(3): p. 463-474.
14. Santos, R.H.L., *Terapia nutricional artificial efetiva e complicações no doente cirúrgico*. 2020, Universidade de Lisboa (Portugal).
15. Boyce, T.G., et al., *The Use of β -Adrenergic Receptor Antagonists in Psychiatry: A Review*. Journal of the Academy of Consultation-Liaison Psychiatry, 2021. **62**(4): p. 404-412 DOI: <https://doi.org/10.1016/j.jaclp.2020.12.009>.
16. Chrysant, S.G. and G.S. Chrysant, *Antihypertensive and cardioprotective effects of three generations of beta-adrenergic blockers: an historical perspective*. Hospital Practice, 2022. **50**(3): p. 196-202.
17. Wołowicz, Ł., et al., *Beta-blockers in cardiac arrhythmias—Clinical pharmacologist's point of view*. Frontiers in pharmacology, 2023. **13**: p. 1043714.
18. Gupta, A., J. Gupta, and A. Gupta, *Chemistry of Beta-blockers and their role in the Cardiovascular Disorders*. Int. J. Curr. Res. Chem. Pharm. Sci, 2023. **10**(2): p. 1-6.
19. Khan, Z., et al., *Beta-Adrenergic Blockers' Supportive and Adverse Role in Hypertension: A Review of Three Generations: Beta-adrenergic blockers role in hypertension*. Pakistan Journal of Medicine and Dentistry, 2022. **11**(1): p. 63-71.
20. Strauss, M.H., A.S. Hall, and K. Narkiewicz, *The combination of beta-blockers and ACE inhibitors across the spectrum of cardiovascular diseases*. Cardiovascular Drugs and Therapy, 2023. **37**(4): p. 757-770.