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Effects of Perioperative Beta-Blockers on Postoperative Major Adverse Cardiovascular and Cerebrovascular Events in Patients with Colorectal Cancer : a propensity score matching analysis

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Abstract

Background

Patients with colorectal cancer (CRC) undergoing surgical resection face a high risk of perioperative adverse events, and the relationship between perioperative use of beta-blockers and major adverse cardiovascular and cerebrovascular events (MACCE) after surgery remains unelucidated.

Methods

Consecutive patients newly received radical surgery for CRC between 1 September 2019 and 30 September 2021 were identified through the research database and electronic medical records of the Union Hospital of Fujian Medical University. Patients were categorized into two groups based on the use of perioperative beta-blockers, and a 1:2 propensity-score matching (PSM) analysis was conducted to balance confounding factors. The primary outcome was the incidence of MACCE within 30 days postoperatively.

Results

A total of 1859 patients with complete medical records were included in the study. Among these, 80 patients developed MACCE, resulting in an overall incidence rate of 4.3%. Prior to PSM, the MACCE incidence was significantly higher in the beta-blockers group compared to the non-beta-blockers group (12.7% vs. 3.8%, OR 3.72, 95% CI 2.02 to 6.86, P < 0.001). After 1:2 PSM, MACCE incidence which 108 patients in the beta-blockers group and 216 patients in the non-beta-blockers group were included, remained higher in the beta-blockers group (13.0% vs. 4.6%, OR 3.07,95% CI 1.32 to 7.16, P = 0.007). There was no significant difference in total morbidity between the groups (38.9% vs.44.4%, OR 1.26, 95% CI 0.79 to 2.01, P = 0.34). Sensitivity analyses further supported these findings.

Conclusions

Perioperative use of beta-blockers in patients with CRC is independently associated with an increased risk of postoperative MACCE; however, this association may not be purely causal but rather reflects the generally poorer overall health status and higher invasiveness of surgery in the group of patients receiving these medications.

Introduction

Colorectal cancer (CRC) ranks as the fourth most commonly diagnosed malignancy and the third leading cause of cancer-related mortality worldwide, posing a persistently substantial disease burden [1]. Surgical resection remains the cornerstone of curative treatment for non-metastatic CRC, with over 95% of patients potentially deriving survival benefit from surgical intervention [2]. Nevertheless, the occurrence of major adverse cardiovascular and cerebrovascular events (MACCE) during the perioperative period—encompassing postoperative mortality, myocardial injury, non-fatal cardiac arrest, congestive heart failure, ischemic stroke, and acute myocardial infarction [3]—critically jeopardizes both short- and long-term patient outcomes. MACCE not only constitutes a predominant contributor to perioperative morbidity and mortality [4] but also significantly escalates prolonged hospitalization risk and associated healthcare expenditure [5, 6].

Previous investigations have established multiple patient-related risk factors for postoperative MACCE, including advanced age, obesity, hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease, and anemia [3]. Additionally, intraoperative blood loss, hypotension, and tachycardia have been identified as precipitating factors for adverse cardiovascular sequelae in the non-cardiac surgery setting [7, 8]. These hemodynamic perturbations may be particularly deleterious in CRC surgery, wherein gut microbiota dysbiosis and systemic metabolic derangements potentially compound

the baseline cardiovascular risk profile [9]. Despite these insights, the specific risk factors predisposing to MACCE following radical CRC resection remain inadequately elucidated. Moreover, extant literature has largely centered on the American Society of Anesthesiologists (ASA) physical status classification [10], with insufficient systematic evaluation of modifiable perioperative elements such as anesthetic modality, intraoperative pharmacotherapy, and hemodynamic management protocols. Consequently, the optimization of perioperative pharmacological interventions to mitigate cardiovascular risk has emerged as a pivotal concern in anesthesiology and perioperative medicine.

Beta-blockers, through their established mechanisms of heart rate reduction, myocardial oxygen consumption diminution, and coronary plaque stabilization, have secured a definitive therapeutic role in the management of heart failure and myocardial infarction. However, their perioperative application remains a subject of vigorous debate. While accumulating evidence suggests that perioperative beta-blockade may confer favorable long-term cardiac outcomes in non-cardiac surgical patients—potentially mediated by attenuation of catecholamine-induced excitotoxicity [11]—this perspective has been challenged by landmark randomized controlled trials since the PeriOperative ISchemic Evaluation (POISE) trial in 2008. The POISE study and subsequent large-scale RCTs have demonstrated that although beta-blocker therapy reduces non-fatal myocardial infarction, it concurrently engenders a significant increase in severe hypotension, bradycardia, stroke, and all-cause mortality [12]. This apparent paradox likely arises from substantial heterogeneity across studies in patient selection, timing of drug initiation, dosing strategies, and perioperative hemodynamic stewardship. Furthermore, the generalizability of many RCT findings is constrained by the exclusion of high-risk, elderly, or hemodynamically unstable patients, as well as the diversity of surgical procedures, underscoring the pressing need for real-world evidence derived from large-scale populations.

Propensity score matching (PSM), as a method that emulates the randomization process, enables effective equilibration of measurable confounders between exposure and non-exposure groups, thereby affording more robust estimates of causal treatment effects. Accordingly, the present study leverages PSM in a retrospective cohort of patients undergoing radical CRC resection to determine whether perioperative beta-blocker use influences the 30-day postoperative MACCE risk. By doing so, we aim to furnish evidence-based insights grounded in real-world clinical anesthesia management data, thereby informing the individualized perioperative application of beta-blockers.

Materials and Methods

2.1 Study Setting and Participants

This single-center retrospective cohort study consecutively enrolled patients who underwent radical resection for CRC at Fujian Medical University Union Hospital between September 1, 2019, and September 30, 2021, which approved by the Institutional Review Board of Fujian Medical University Union Hospital (Approval No. 2024KY223) and registered with the Chinese Clinical Trial Registry (ChiCTR2400091355). Written informed consent was waived due to the retrospective design. All clinical data were extracted from the institutional research database and electronic medical records, with strict patient confidentiality maintained. Diagnosis of CRC was histopathologically confirmed. Postoperative MACCE was ascertained using ICD-9 codes, covering coronary artery disease, heart failure, transient ischemic attack, and stroke.

Inclusion criteria were: (1) radical CRC resection under general anesthesia; (2) histopathologically confirmed colorectal malignancy; and (3) complete clinical data. Exclusion criteria were: benign tumors, non-curative resection, preoperative intensive care unit (ICU) admission, incomplete clinical data, indeterminate TNM staging, pre-existing atrial fibrillation, and second-degree or higher atrioventricular block (requiring temporary pacemaker insertion).

2.2 Definitions and Perioperative Beta-Blocker Administration

The perioperative period was defined as 24 hours preoperatively to discharge from the post-anesthesia care unit (PACU) [13]. Colorectal cancer procedures comprised left hemicolectomy, right hemicolectomy, subtotal colectomy, total colectomy, transverse colectomy, low anterior resection, and abdominoperineal resection. Cardiovascular comorbidities included

hypertension, ischemic heart disease, atrial fibrillation, pulmonary hypertension, implantable cardioverter-defibrillator, prior valve repair/replacement, pacemaker implantation, heart failure, cardiomyopathy, prior percutaneous coronary intervention, and prior coronary artery bypass grafting. Pulmonary diseases included asthma, chronic obstructive pulmonary disease, bronchiectasis, and emphysema. Beta-blocker types included metoprolol, esmolol, bisoprolol, and arotinolol.

2.3 Outcome Variables

The primary outcome was the incidence of MACCE within 30 days postoperatively. Secondary outcomes included overall postoperative complications, surgical complications, pulmonary complications, urinary tract infection, length of hospital stay, unplanned reoperation, and ICU admission rate. Overall complications were defined as the presence of at least one of the following: surgical site infection (superficial/deep incisional, organ/space)[14], anastomotic bleeding[15], anastomotic leakage[16], chylous leakage[17], ileus[18], bloodstream infection (sepsis/bacteremia)[14], myocardial infarction[19], congestive heart failure[19], stroke/transient ischemic attack[20], urinary tract infection[21], pulmonary embolism[19], and pneumonia[22]. Surgical complications were defined as at least one of: surgical site infection[14], anastomotic bleeding[15], anastomotic leakage[16], chylous leakage[17], ileus[18], and bloodstream infection[14]. All postoperative complications were recorded during hospitalization.

2.4 Sample Size Calculation

Based on a prior estimated MACCE incidence of 3% in the beta-blocker group, a minimum of 1,520 CRC patients was required to provide 85% power to detect an odds ratio (OR) ≥ 3.0 between beta-blocker users and non-users. Our final cohort of 1,859 patients met this requirement. In logistic regression modeling, we adhered to the "10 events per variable" rule to ensure regression coefficient stability and accuracy.

2.6 Statistical Analysis

Continuous variables are presented as medians (interquartile ranges), and categorical variables as frequencies (percentages). Normally distributed continuous variables were compared using the independent-samples t-test; otherwise, the Mann–Whitney U test was applied. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test. Patients were stratified by perioperative beta-blocker exposure, and propensity score matching (PSM) with a caliper of 0.02 and a 1:2 ratio was employed to balance confounders. Primary and secondary outcomes were compared before and after matching using chi-square, continuity-corrected chi-square, or Fisher's exact tests. Sensitivity analysis was conducted in the pre-match cohort (n = 1,859) to validate the robustness of the primary findings. All analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

3.1 Patient Recruitment

Among 2,000 initially screened patients, 141 were excluded, yielding 1,859 patients with complete data for the pre-match cohort. Patients with pre-existing atrial fibrillation—a significant and clinically irreversible MACCE predictor[23]—were deliberately excluded. Perioperative beta-blockers were administered to 110 patients (5.9%, 110/1,859), while 1,749 (94.1%, 1,749/1,859) were non-users. After 1:2 PSM, 108 beta-blocker users and 216 non-users were successfully matched, resulting in a final analytical cohort of 324 patients (Fig. 1).

3.2 Patient Characteristics Before and After Matching

Prior to matching, beta-blocker users were older, had poorer overall health status (higher ASA and TNM stages), higher proportions of abdominal surgery history, preoperative chemotherapy, malignancy history, and anemia, as well as a greater burden of hypertension, diabetes, chronic pulmonary disease, and cardiovascular disease. Additionally, beta-blocker users

experienced greater intraoperative fluid infusion and blood loss. Following PSM, all covariates achieved satisfactory balance (SMD < 0.1) between groups (Table 1, Fig. 2).

Table 1
Clinical variables between no beta-blocker group and beta-blocker group, before and after propensity-score matching

Varlables	Before after Propensity-score matching *N* = 1859			After propensity-score matching *N* = 324		
	No beta-blocker	**Beta-blocker**	**SMD**	**No beta-blocker**	**beta-blocker**	**SMD[a]**
	N = 1749	**N = 110**		**N = 216**	**N = 108**	
Age(yr), median [IQR]	61(53, 69)	67(57, 73)	0.38	66(57,70)	68(57,70)	0.01
Female, n/group N (%)	696(39.8%)	40(36.4%)	0.07	116 (35.2%)	43(36.8%)	0.06
BMI,kg·m^2, median [IQR]	22.9(20.9, 25.2)	23.7(21.3, 25.2)	0.21	24 (22,28)	24 (21,28)	0.04
ASA status, n/group N (%)			0.47			<0.001
I-II	1492(85.3%)	73(66.4%)		219(66.4%)	76(65%)	
III-IV	257(14.7%)	37(33.6%)		111(33.6%)	41(35%)	
TNM stages, n/group N (%)			0.001			<0.001
0[d]-II	987(56.4%)	62(56.4%)		186(56.4%)	66(56.4%)	
III-IV	762(43.6%)	48(43.6%)		144(43.6%)	51(43.6%)	
History of laparotomy, n/group N (%)	284(16.2%)	21(19.1%)	0.07	52(15.8%)	22(18.8%)	0.01
History of maliganancy, n/group N (%)	87(5.0%)	6(5.5%)	0.02	17(5.2%)	6(5.1%)	0.06
Hypertention, n/group N (%)	494(28.2%)	76(69.1%)	0.88	221(67.0%)	79(67.5%)	0.01
Diabetes,n/group N (%)	242(13.8%)	27(24.5%)	0.25	74(22.4%)	28(23.9%)	0.08
Cardiovascular comorbidities[b], n/group N (%)	72(4.1%)	23(20.9%)	0.08	60(19.1%)	30(25.6%)	0.04
Pulmonary comorbidities[c],n/group N (%)	323(18.5%)	29(26.4%)	0.42	79(23.9%)	31(26.5%)	0.07
ALB(g/L),median [IQR]	42.7(40.2,46.8)	42.6(39.2,44.6)	0.16	41.8(39.5,44.4)	42.6(39.3,44.7)	0.06

SMD = standardized mean difference; IQR = interquartile range; BMI = body mass index; ASA = American society of anesthesiologists; TNM = tumor node metastasis

[a] SMD ≤ 0.1 were considered to be balanced between the two groups

[b] Cardiovascular Comorbidity includes ischemic heart disease, automated implantable cardioverter defibrillators insertion, cardiac valve replacement, pacemaker insertion, cardiomyopathy, percutaneous coronary intervention, coronary artery bypass graft, atrial fibrillation.

[c] Pulmonary Comorbidity includes asthma, chronic obstructive pulmonary disease, bronchiectasis, emphysema.

[d] TNF 0 stage that pathologic complete response (ypCR).

Varlables	Before after Propensity-score matching *N* = 1859			After propensity-score matching *N* = 324		
	No beta-blocker	**Beta-blocker**	**SMD**	**No beta-blocker**	**beta-blocker**	**SMD[a]**
Preoperative anemia,n/group N (%)	684(39.0%)	53(48.2%)	0.18	92(42.6%)	51(47.2%)	0.09
Preoperative chemoradiotherapy, n/group N (%)	487(27.8%)	31(28.2%)	0.01	55(25.5%)	31(28.7%)	0.07
Surgical approachs, n/group N (%)			0.07			0.04
laparoscopic	1697(95.9%)	112(92.6%)		303(91.8%)	109(93.2%)	
open	72(4.1%)	9(5.2%)		27(8.2%)	8(6.8%)	
Duration of surgery(min), median[IQR]	215(178, 260)	223(193, 265)	0.104	211(178, 265)	223(192, 264)	0.09
Dexmedetomidine,n/group N (%)	1015(58.0%)	58(52.7%)	0.11	119(55.1%)	57(52.8%)	0.04
Infusion(100ml), median [IQR]	15(11, 16)	15(15, 20)	0.21	15(14.5,19.3)	15(15,19)	0.04
Blood loss(ml), median [IQR]	50(30, 50)	50(30, 100)	0.09	50(30,100)	50(25,50)	0.06
Ostomy, n/group N (%)	454(26.0%)	23(20.9%)	0.12	85(25.8%)	26(22.2%)	0.04

SMD = standardized mean difference; IQR = interquartile range; BMI = body mass index; ASA = American society of anesthesiologists; TNM = tumor node metastasis

[a] SMD ≤ 0.1 were considered to be balanced between the two groups

[b] Cardiovascular Comorbidity includes ischemic heart disease, automated implantable cardioverter defibrillators insertion, cardiac valve replacement, pacemaker insertion, cardiomyopathy, percutaneous coronary intervention, coronary artery bypass graft, atrial fibrillation.

[c] Pulmonary Comorbidity includes asthma, chronic obstructive pulmonary disease, bronchiectasis, emphysema.

[d] TNF 0 stage that pathologic complete response (ypCR).

Table 2
Postoperative outcomes in cohort before propensity-score matching

Characteristics		No beta-blocker	Beta-blocker	OR	95%CI	*P*-value
		***N* = 1749**	***N* = 110**			
Primary Outcome	MACCE[a]	66 (3.8%)	14 (12.7%)	3.72	2.02–6.86	<0.001
Secondary Outcome	Total complications	60 (34.8%)	50 (45.5%)	1.56	1.06–2.31	0.02
	Surgical complications	366 (20.9%)	22 (20.0%)	0.95	0.58–1.52	0.82
	PPCs	208 (11.9%)	20 (18.2%)	1.65	0.99–2.73	0.05
	Urine infection	40(2.3%)	3(2.7%)	1.20	0.37–3.94	0.77
	ICU admission	84(4.85)	14(12.7%)	2.89	1.58–5.28	<0.001[d]
	Postoperative length of stay	8 (6,11)	9 (7,15)	-	-	0.04
	Postoperative Death	4 (0.2%)	0(0.0%)	-	-	-
	Unplanned Secondary Surgery	12(0.7%)	1(0.9%)	-	-	-

[a] MACCE major adverse cardiovascular and cerebrovascular events,includes postoperative mortality, myocardial injury, non-fatal cardiac arrest, congestive heart failure, ischemic stroke, acute myocardial infarction, and pulmonary embolism.

Table 3
Postoperative outcomes in cohort after propensity-score matching

Characteristics		No betablocker	Betablocker	OR	95%CI	*P*-value
		***N* = 1749**	***N* = 110**			
Primary Outcome	MACCE[a]	10 (4.6%)	14 (13.0%)	3.07	1.32–7.16	0.012
Secondary Outcome	Total complications	84 (38.9%)	48 (44.4%)	1.26	0.79–2.01	0.34
	Surgical complications	48 (22.2%)	21 (19.4%)	0.85	0.48–1.50	0.57
	PPCs	29 (13.4%)	18 (16.7%)	1.29	0.68–2.45	0.50
	Urine infection	10 (4.6%)	3 (2.8%)	0.59	0.16–2.18	0.55
	ICU admission	20 (9.3%)	14 (13.0%)	1.15	0.86–1.54	0.34
	Postoperative length of stay	9 (7,12)	9 (7,14.75)	-	-	0.69
	Postoperative Death	1 (0.5%)	0 (0.0%)	-	-	-
	Unplanned Secondary Surgery	3 (1.4%)	0 (0.0%)	-	-	-

[a] MACCE major adverse cardiovascular and cerebrovascular events,includes postoperative mortality, myocardial injury, non-fatal cardiac arrest, congestive heart failure, ischemic stroke, acute myocardial infarction, and pulmonary embolism.

3.3 Outcomes Before and After PSM

In the pre-match cohort, beta-blocker users exhibited a significantly higher MACCE incidence compared with non-users (12.7% vs. 3.8%; OR = 3.719, 95%CI: 2.016–6.860, P < 0.001). For secondary outcomes, overall complications were also more frequent in the beta-blocker group (45.5% vs. 34.8%; OR = 1.564, 95%CI: 1.061–2.305, P = 0.023). Postoperative mortality (4/1,749 vs. 0/110) and unplanned reoperation (12/1,749 vs. 1/110) were too infrequent for meaningful between-group comparisons. No significant differences were observed in other individual complications. The beta-blocker group had higher ICU admission rates (12.4% vs. 5.3%; OR = 2.552, 95%CI: 1.429–4.556, P < 0.001) and longer postoperative hospital stays (P = 0.045).

In the post-match cohort, the beta-blocker group still demonstrated a significantly elevated MACCE risk (13.0% vs. 4.6%; OR = 3.068, 95%CI: 1.315–7.159, P = 0.012). Overall complication rates no longer differed significantly between groups (OR = 1.257, 95%CI: 0.787–2.007, P = 0.337), nor did other secondary outcomes. Notably, between-group differences in ICU admission (OR = 1.149, 95%CI: 0.858–1.539, P = 0.338) and hospital stay (P = 0.686) were no longer statistically significant. Postoperative mortality and unplanned reoperation remained incomparable due to low event counts.

3.4 Sensitivity Analysis

Sensitivity analysis was performed on the entire pre-match cohort (n = 1,859) to validate the primary results. Univariate regression identified perioperative beta-blocker use as independently associated with MACCE. After adjusting for age, ASA grade, pTNM stage, operative duration, preoperative anemia, malignancy history, cardiovascular comorbidities, and hypertension, beta-blocker use remained significantly associated with MACCE (OR = 2.886, 95%CI: 1.486–5.606, P = 0.002), consistent with the PSM findings and demonstrating the robustness of our results (Fig. 3).

Discussion

The risk–benefit profile of perioperative beta-blocker therapy remains controversial in current clinical practice. In this single-center retrospective cohort of 1,859 colorectal cancer patients, the perioperative MACCE incidence was 4.3% (80/1,859), consistent with previous reports[3]. After adjusting for potential confounders via PSM, perioperative beta-blocker use was independently associated with increased MACCE incidence, with sensitivity analyses corroborating the reliability of this finding. In contrast to earlier studies suggesting protective effects, our results align more closely with recent safety concerns regarding perioperative beta-blocker administration, providing novel evidence specific to the colorectal surgery population.

The overall perioperative beta-blocker utilization rate was 5.9%, with indications potentially including preoperative comorbidities such as hypertension[24] or intraoperative tachyarrhythmias[25]. Consistent with prior studies[12], beta-blocker users in our cohort were older, had higher ASA grades, greater comorbidity burdens, and longer operative times. Consequently, beta-blocker administration in this context appears to reflect a responsive strategy to high-risk clinical scenarios rather than a prophylactic approach. Despite PSM adjustment, the independent positive association between beta-blocker use and MACCE persisted. However, PSM can only adjust for measured confounders; residual confounding remains inherent. Thus, whether beta-blockers constitute an independent causal risk factor or merely a marker of poor baseline health and advanced disease severity warrants further investigation. We are inclined toward the latter interpretation —that beta-blocker use primarily reflects accumulated baseline risk rather than a direct causal pharmacologic effect. Clinically, the timing, dosage, and target thresholds of heart rate and blood pressure for beta-blocker initiation warrant careful consideration, particularly avoiding high-dose acute perioperative administration without thorough hemodynamic reserve assessment.

Mechanistically, prior studies have suggested that beta-blockers may reduce perioperative complications by attenuating adrenergic receptor activation, thereby decreasing arrhythmias and preventing acute heart failure and sudden death[28], along with broader organ protection via inflammatory modulation[29]. However, these pharmacologic actions may translate into significant hemodynamic risks in patients with limited cardiac reserve or unstable volume status. The POISE-1 trial and subsequent RCTs have demonstrated that high-dose metoprolol initiated perioperatively reduces non-fatal myocardial infarction but concomitantly increases stroke and all-cause mortality[33]. Berger et al. further reported that short-term preoperative high-dose beta-blocker administration significantly elevated postoperative stroke (1.0% vs. 0.5%, P = 0.005) and mortality (3.1% vs. 2.3%, P = 0.03)[30], possibly related to increased preoperative arterial pressure thresholds[31]. Blessberger et al. systematically associated perioperative beta-blockers with hypotension and bradycardia[12, 32], and their negative inotropic effects may precipitate heart failure and cardiogenic shock in patients with pre-existing myocardial dysfunction[28]. Although the POISE-1 trial included a substantial proportion of abdominal surgeries, no subtype-specific effect was observed. In colorectal cancer patients, systemic inflammation triggered by gut microbiota translocation may exacerbate endothelial dysfunction and hemodynamic instability, rendering the negative hemodynamic consequences of beta-blockers more pronounced. The predominance of arrhythmias among MACCE events indirectly supports the notion that beta-blockers may fail to achieve adequate rhythm stabilization in this population and may even precipitate adverse events through excessive sympathetic suppression.

Of note, we did not identify independent associations between perioperative beta-blocker use and overall complications or specific non-cardiac complications (including surgical complications, pulmonary adverse events, and urinary tract infection), contrasting with findings by Ahl et al.[27]. This discrepancy may be attributable to heterogeneity in surgical types, sample sizes, and variations in complication definitions and inclusion criteria across studies. Different surgical procedures elicit varying degrees of stress and inflammatory responses, underscoring the need for future procedure-stratified analyses. Based on current evidence, our conclusions are restricted to patients undergoing CRC surgery.

Multivariable regression identified age, ASA grade, pTNM stage, operative duration, malignancy history, perioperative beta-blocker use, and anemia as independent risk factors for MACCE, consistent with previous reports[34, 35]. Beyond beta-

blockers, the remaining variables are well-established perioperative risk predictors, and their concurrent statistical significance further validates the internal quality of our cohort data and the robustness of our risk model. However, as a composite endpoint, overall complications have inherent limitations, as different definitions across studies[26, 28, 34] may yield discrepant results. Furthermore, given the low event incidence in our primary outcome, we did not perform reanalysis on each specific complication.

This study is methodologically innovative in employing PSM combined with logistic regression to systematically evaluate the association between perioperative beta-blocker use and postoperative MACCE and short-term outcomes in colorectal cancer patients. Nevertheless, several limitations should be acknowledged. First, the absence of detailed data on preoperative long-term beta-blocker use precludes differentiation between chronic users and perioperatively initiated users, potentially introducing indication bias. Second, the short observation window limited to hospitalization precluded assessment of long-term mortality and other extended outcomes. Third, the single-center retrospective design inherently risks selection and information biases. Future prospective studies incorporating patient-centered hemodynamic parameters —including blood pressure, heart rate, troponin, and RCRI scores—will enhance our understanding of the mechanisms and individualized application of perioperative beta-blocker therapy.

Conclusions

In patients undergoing radical CRC resection, perioperative beta-blocker use is independently associated with an increased risk of 30-day postoperative MACCE. However, this association may not represent a direct causal relationship but rather reflects the poorer baseline health status and greater surgical invasiveness in the treated population. Perioperative decision-making should carefully weigh the risks and benefits of beta-blocker initiation, with particular caution against high-dose acute administration without adequate hemodynamic reserve evaluation.

Abbreviations

CRC: colorectal cancer; MACCE: major adverse cardiovascular and cerebrovascular events; PSM: propensity score matching; ASA: American Society of Anesthesiologists; ICU: intensive care unit; PACU: post-anesthesia care unit.

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Fujian Medical University Union Hospital (Approval No. 2024KY223). The requirement for written informed consent was waived due to the retrospective nature of the study.

Clinical trial number

not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Xiaoting Li, Qifa Guo, Fuyuan Li, Ting Yan, and Yaqi Huang contributed to the conception and design of the study. Xiaoting Li, Qifa Guo, Fuyuan Li, and Hongpeng Lin contributed to data acquisition. Xiaoting Li conducted the data analysis and interpretation. Qifa Guo and Fuyuan Li contributed to the drafting and revision of the manuscript and provided supervision. All authors reviewed and approved the final manuscript.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy and institutional restrictions but are available from the corresponding author on reasonable request.

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Figures

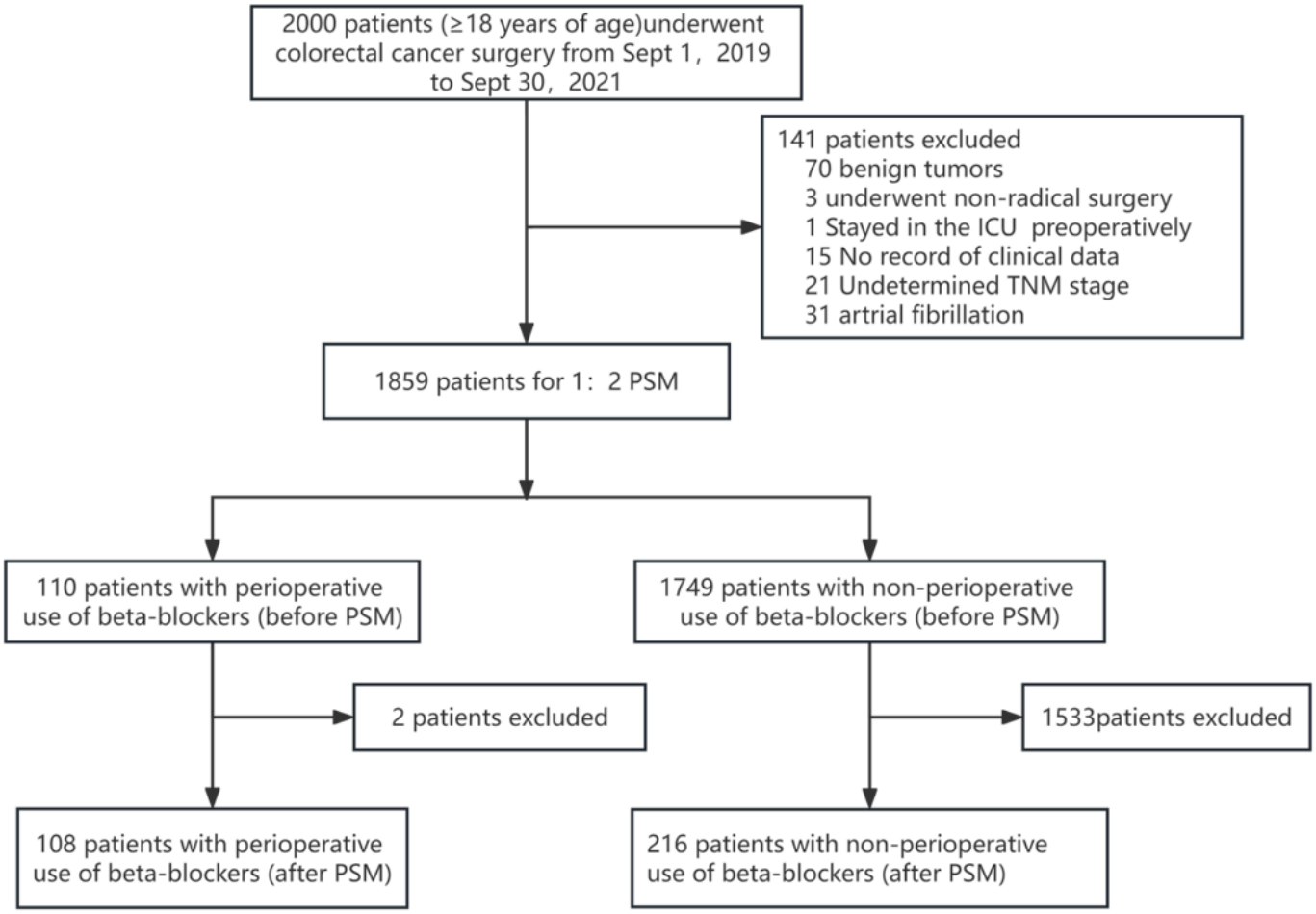


Figure 1

Flow chart of patient inclusion

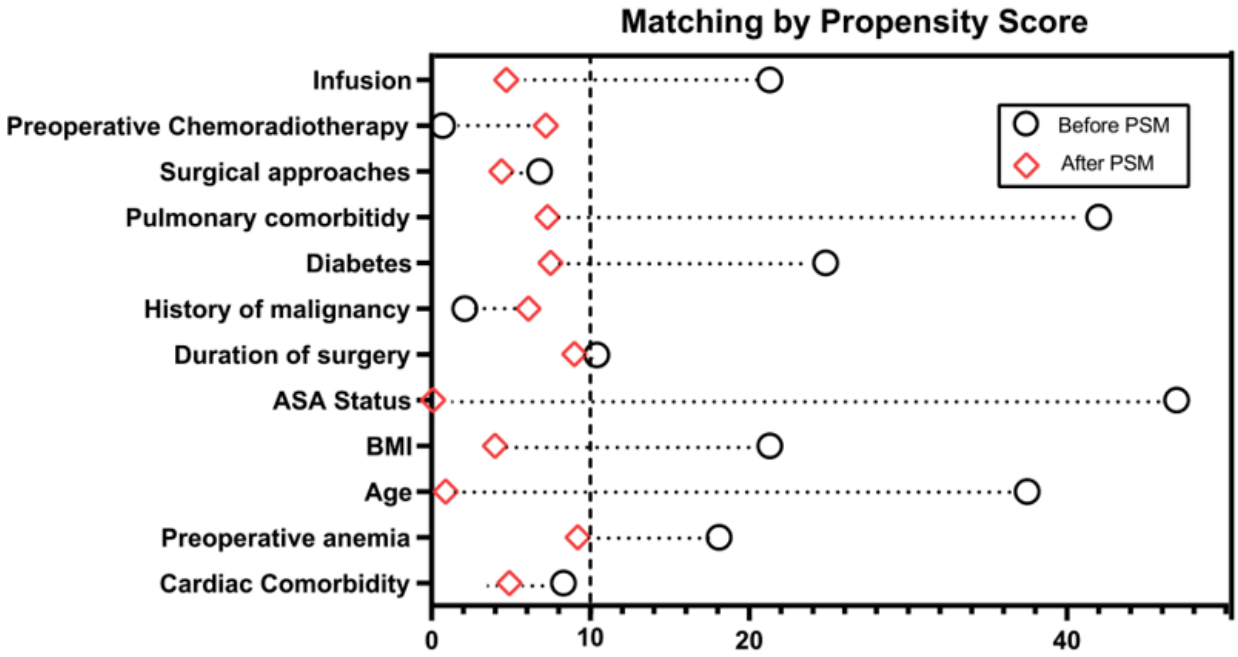


Figure 2

Standardized mean differences in variables before and after propensity-score matching

Indicates the cut-off value of the standardized mean difference (SMD) used to assess group balance before (black) and after (red) propensity score matching.

Characteristics	Univariate analyses: OR(95%CI)	Univariate analyses: P-value	multivariate analyses: OR(95%CI)	multivariate analyses: P-value
Betablocker	3.72(2.02-6.86)	<0.001	2.89(1.49-5.61)	0.002
Age	1.03(1.01-1.05)	0.001	1.02(1.00-1.05)	0.02
ASA	1.70(1.00-2.89)	0.05	1.12(0.60-2.08)	0.73
pTNM	0.95(0.61-1.50)	0.84	0.95(0.59-1.52)	0.84
Hypertention	1.62(1.03-2.56)	0.04	1.05(0.61-1.79)	0.87
cirscular comorbidities	2.49(1.207-5.160)	0.01	1.35(0.59-3.08)	0.47
Duration of surgery	1.01(1.00-1.00)	<0.001	1.00(1.00-1.01)	<0.001
History of Malignancy	2.56(1.23-5.29)	0.01	2.14(1.01-4.55)	0.05
Preoperative Anemia	2.25(1.43-3.54)	<0.001	1.89(1.19-3.03)	0.01

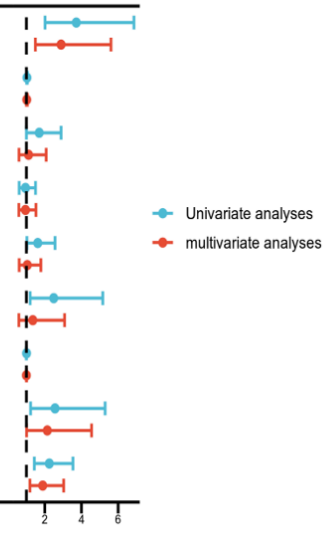


Figure 3

Univariate and multivariate analyses of MACCE in the entire cohort (n=1859)