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Article

Risk Factors for Bleeding Events After One-Stop Hybrid Coronary Revascularization

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Abstract

Background: Gastrointestinal bleeding events represent a serious complication after coronary revascularization. In recent years, hybrid coronary revascularization (HCR) has gradually become one of the main surgical methods for multivessel coronary artery disease. This study aimed to identify risk factors for gastrointestinal bleeding following one-stop HCR. **Method**: This single-center retrospective study included 231 patients with coronary artery disease who underwent one-stop HCR between April 2018 and April 2023. Baseline conditions and perioperative parameters of patients were collected from electronic medical records; gastrointestinal bleeding events were documented, and retrospective statistical analyses were performed. **Results**: Among the 231 patients, 12 experienced gastrointestinal bleeding events, yielding an incidence rate of 5.2%; three patients died due to gastrointestinal bleeding, corresponding to a mortality rate of 25.0% among patients with bleeding events. Compared with patients without bleeding events, those with gastrointestinal bleeding had significantly higher rates of prior cerebrovascular disease (50.0% vs. 21.0%), preoperative creatinine (defined as the last serum creatinine measured within 24 h before surgery) (78.5 vs. 67.7 µmol/L), perioperative total blood transfusion volume during the period (600 vs. 0 mL), perioperative blood transfusion >5 units (33.3% vs. 8.7%), intraoperative bleeding volume (400 vs. 200 mL), total postoperative drainage volume (1453 vs. 1160 mL), mechanical ventilation time (18.0 vs. 16.0 h), and mortality (25.0% vs. 3.2%) (all $p < 0.05$). Single-factor and multi-factor regression analyses identified prior cerebrovascular disease (CVD) as an independent risk factor for gastrointestinal bleeding (odds ratio (OR) = 3.754, 95% confidence interval (CI) = 1.202–11.724; $p = 0.023$). Mortality was significantly higher in the gastrointestinal bleeding group than in the control group. **Conclusion**: Previous cerebrovascular disease is a risk factor for gastrointestinal bleeding after one-stop HCR. In such patients, antiplatelet strategies should be appropriately adjusted to prevent and reduce gastrointestinal bleeding. However, the number of events in our study was limited, and future studies should incorporate larger sample sizes to validate these findings.

Keywords: gastrointestinal bleeding; hybrid coronary revascularization; risk factor; dual antiplatelet therapy; cerebrovascular disease

1. Introduction

The occurrence of gastrointestinal bleeding after coronary revascularization represents a serious complication of cardiac surgery, associated with high mortality and disability rates [1]. Several retrospective studies have reported various bleeding-related complications after coronary revascularization [1,2]. However, to our knowledge, no studies have specifically evaluated the risk factors for upper gastrointestinal bleeding after hybrid coronary revascularization (HCR), a combination of stent percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), primarily used to revascularize multivessel coronary artery disease [3]. HCR combines the minimally invasive features of PCI with the long-term patency of CABG grafts, effectively reducing the occurrence of postoperative major adverse cardiovascular and cerebrovascular events (MACCEs). HCR also shortens intensive care unit (ICU) and overall hospital stays, reduces ventilation time, lowers the perioperative period, decreases the need for blood transfusions, and reduces the incidence of atrial fibrillation; thus, HCR has become one of the main revascularization methods currently used to treat multivessel coronary artery disease [4]. As the clinical application of HCR increases, the safety of the associated perioperative management has attracted more attention, especially the balance between antithrombotic therapy and bleeding risk. Dual antiplatelet therapy (DAPT) is recommended after both CABG and PCI [5]. Similarly, antiplatelet therapy is commonly prescribed after percutaneous (transcatheter) heart valve replacement (*i.e.*, transcatheter aortic valve replacement/implantation, TAVR/TAVI) to reduce thrombotic events and recurrent ischemic complications, with the choice between single and DAPT based on patient-specific ischemic and bleeding risk as well as current evidence and guidelines [6]. However, this increases the risk of bleeding-related complications after cardiac surgery. Although gastrointestinal bleeding after general coronary revascularization has been of concern, upper gastrointestinal bleeding, as a specific subtype characterized by more rapid progression and poorer prognosis, has not been specifically stud-

ied in the HCR population. Existing studies on bleeding complications after HCR have primarily focused on cardiovascular-related bleeding, such as mediastinal and wound bleeding, with limited systematic exploration of upper gastrointestinal bleeding. Consequently, the incidence rates, risk factors, and clinical impact of upper gastrointestinal bleeding in HCR patients remain unclear. Therefore, identifying the risk factors associated with upper gastrointestinal bleeding is necessary. Thus, this study aimed to review and collect relevant preoperative, intraoperative, and postoperative data from patients to identify risk factors for upper gastrointestinal bleeding after HCR, thereby helping surgeons identify high-risk patients early and implement timely, effective interventions to improve survival rates and quality of life.

2. Materials and Methods

2.1 Study Design and Patient Population

This single-center retrospective study included 163 men and 68 women who underwent one-stop HCR at Beijing Chaoyang Hospital, affiliated with Capital Medical University, from April 2018 to April 2023. HCR is suitable for patients with multivessel disease involving the left main coronary artery (LMCA) and/or the proximal left anterior descending artery (LAD), in whom CABG and PCI are high-risk or difficult, or when a single method cannot achieve the best outcome. A total of 231 patients were included in the study: 12 (5.2%) experienced gastrointestinal bleeding and 219 (94.8%) did not. According to the follow-up protocol, discharged patients were required to attend the outpatient clinic for re-examination at 6 weeks and 6 months after discharge, and then annually. In addition to routine follow-up visits, researchers contacted all discharged patients by telephone again before October 2023. For patients who experienced gastrointestinal bleeding and were admitted to the hospital, the emergency and inpatient medical records from that visit were reviewed. If the patient had been treated at another hospital, the patient was asked about their medical records to clarify the diagnosis of gastrointestinal bleeding. Since this was a retrospective study, the requirement for informed consent was waived.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion Criteria

(1) Patient selection: adults (age $\geq$18 years) who underwent one-stop HCR.

(2) Coronary anatomy: multivessel coronary artery disease ($\geq$2 major coronary arteries with stenosis $\geq$70%), involving the LMCA and/or the proximal LAD.

(3) Surgical indications: patients deemed high-risk candidates for conventional CABG or PCI by a multidisciplinary heart team.

(4) Data completeness: availability of complete perioperative records, including antiplatelet/anticoagulant regimens, bleeding events, and imaging data.

(5) Baseline stability: no evidence of active gastrointestinal bleeding, coagulopathy, or other uncontrolled bleeding risks preoperatively.

2.2.2 Exclusion Criteria

(1) Preoperative bleeding risk: active gastrointestinal bleeding or a history of gastrointestinal bleeding within the preceding 6 months, including a history of peptic ulcer disease, prior upper gastrointestinal bleeding, or gastric ulcer.

(2) Organ dysfunction: severe hepatic insufficiency (Child–Pugh class C) or renal insufficiency (estimated glomerular filtration rate (eGFR) $<$30 mL/min/1.73 m^2).

(3) Anticoagulant use: long-term use of oral anticoagulants (e.g., warfarin, direct oral anticoagulants) that cannot be temporarily discontinued perioperatively.

(4) Missing data: incomplete records (e.g., undocumented antiplatelet strategies, loss to follow-up, or failure to complete at least one postoperative outpatient visit).

(5) Intraoperative conversion: patients requiring intraoperative conversion to conventional CABG or emergency PCI due to technical failure.

(6) Malignancy: active malignancy or life expectancy $<$1 year (Fig. 1).

(7) High baseline gastrointestinal (GI)-bleeding risk: During screening, 9 patients who met one or more of the above exclusion criteria (mainly criterion 1, and in some cases criteria 2 and/or 3) were excluded because recent or active GI bleeding, severe renal dysfunction (eGFR $<$30 mL/min/1.73 m^2), and/or non-discontinuable oral anticoagulation are recognized high bleeding-risk features and could introduce substantial confounding when identifying perioperative predictors of new-onset postoperative GI bleeding after one-stop HCR.

2.3 Intervention

In HCR surgery, minimally invasive direct CABG (MIDCABG) and PCI are performed simultaneously in a hybrid operating room. Generally, MIDCABG is performed first, followed by PCI. To maintain the integrity of the sternum, the left internal mammary artery (LIMA) is harvested under direct vision through a small 5–7 cm incision on the anterolateral side of the fourth and fifth intercostal spaces, with the heart kept beating at normal temperature. The LIMA–LAD anastomosis is completed. After the anastomosis is completed, transit-time flow measurement (TTFM) is used to evaluate the graft flow and anastomosis quality [7]. PCI is performed on other non-anterior descending diseased vessels. A drug-eluting stent (DES) is generally selected. In selected cases, a drug-coated balloon (DCB) strategy may be considered after adequate lesion preparation, provided the final angiographic result shows Thrombolysis in Myocardial Infarction (TIMI) 3 flow, no flow-limiting dissection, and $\leq$30% residual stenosis; otherwise, DES (bailout stenting) is performed.

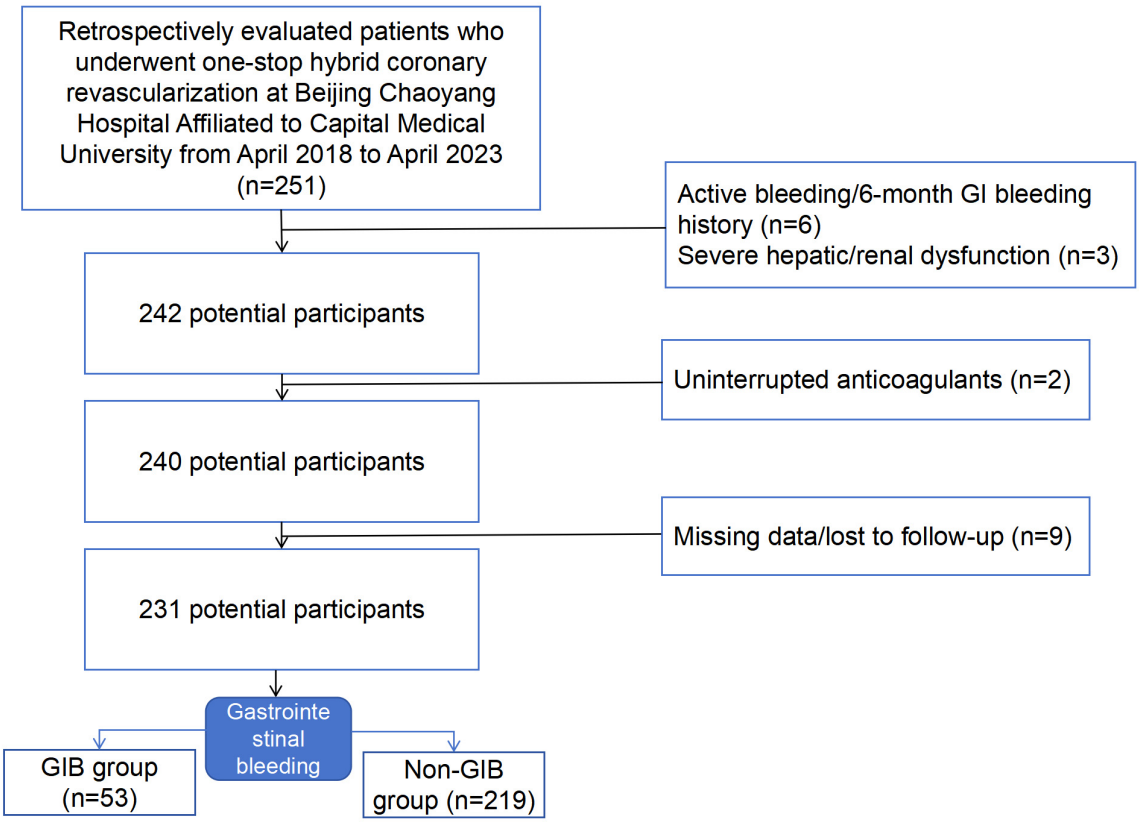

Fig. 1. Inclusion and exclusion criteria flowchart. GIB, gastrointestinal bleeding.

2.4 Perioperative Antithrombotic Strategies for HCR

From 2018 to 2023, the detailed perioperative antithrombotic therapies with potential impacts on bleeding risk were as follows: (1) Preoperative medication: All patients continued oral aspirin (100 mg/day) until the morning of surgery to maintain baseline antiplatelet activity. Clopidogrel was discontinued 5–7 days preoperatively to reduce intraoperative bleeding risk while avoiding excessive attenuation of antiplatelet effects; (2) intraoperative anticoagulants and antiplatelet agents: During surgery, unfractionated heparin was administered at a dose of 100–120 IU/kg body weight to maintain an activated coagulation time (ACT) >300 s, ensuring adequate anticoagulation during MIDCABG and PCI. After completion of the LIMA–LAD anastomosis, protamine sulfate was administered intravenously to neutralize residual heparin, minimizing the risk of postoperative bleeding. Before PCI initiation, a loading dose of clopidogrel (300 mg) was delivered via nasogastric tube to achieve rapid platelet inhibition. If the intraoperative activated clotting time (ACT) was <200 s, an additional dose of unfractionated heparin (100 IU/kg body weight) was supplemented to ensure the safety and effectiveness of PCI; (3) postoperative DAPT: Patients received clopidogrel (75 mg/day) postoperatively for 12 months. Aspirin was administered at 300 mg/day for the first 30 days postoperatively, and then adjusted to 100 mg/day for lifelong maintenance to balance the prevention of thrombotic events and reduction of bleeding risk [8].

2.5 Data Definition

Perioperative baseline variables are shown in Table 1. Preoperative, intraoperative, and postoperative parameters included age, gender, body mass index (BMI), smoking and drinking history, hypertension, diabetes history, hyperlipidemia history, peripheral vascular disease, previous cerebrovascular disease, previous myocardial infarction (MI), previous PCI, left main disease, preoperative left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVED), history of bleeding disorders, any previous digestive tract disease, history of malignant tumors, number of diseased coronary arteries, preoperative D-dimer, preoperative hemoglobin, preoperative platelet count, preoperative Cr, total perioperative blood transfusion, intraoperative heparin dosage, length of hospital stay, mechanical ventilation time, ICU length of stay, drainage volume within 24 hours after surgery, total postoperative drainage volume, mortality, postoperative MI, and repeat revascularization. The above data were obtained from the electronic medical records of Chaoyang Hospital by designated personnel who were not involved in this study to minimize bias and ensure data authenticity and reliability.

Table 1. Baseline characteristics of patients in the gastrointestinal bleeding and the non-gastrointestinal bleeding groups.

Variables	All patients (n = 231)	GIB group (n = 12)	Non-GIB group (n = 219)	*p*-value
Age (years)	65.0 ± 9.9	68.8 ± 7.9	64.8 ± 10.0	0.181
Male	163 (70.6%)	10 (83.3%)	153 (69.9%)	0.502
BMI (kg/m^2)	25.6 ± 3.1	24.5 ± 2.8	25.6 ± 3.1	0.220
Previous smoking	117 (50.6%)	8 (66.7%)	109 (49.8%)	0.254
Previous alcohol drinking	80 (34.8%)	6 (50.0%)	74 (33.9%)	0.409
Hypertension	167 (72.3%)	9 (75.0%)	158 (72.1%)	1.000
Diabetes mellitus	142 (61.5%)	7 (58.3%)	135 (61.6%)	1.000
Hyperlipidemia	91 (39.4%)	5 (41.7%)	86 (39.3%)	1.000
CRD	10 (4.3%)	1 (8.3%)	9 (4.1%)	0.420
PVD	18 (7.8%)	2 (16.7%)	16 (7.3%)	0.238
CVD	52 (22.5%)	6 (50.0%)	46 (21.0%)	0.047
Previous MI	48 (20.8%)	5 (41.7%)	43 (19.6%)	0.143
Previous PCI	62 (26.8%)	4 (33.3%)	58 (26.5%)	0.852
Left main disease	89 (38.5%)	6 (50.0%)	83 (37.9%)	0.593
LVEF (%)	65.0 (60.0, 70.0)	65.0 (56.8, 69.3)	65.0 (60.0, 70.0)	0.782
LVED	48.1 ± 5.5	47.5 ± 5.9	48.1 ± 5.5	0.731
Bleeding events	5 (2.2%)	0 (0.0%)	5 (2.3%)	1.000
Any GID	50 (21.7%)	4 (33.3%)	46 (21.0%)	0.522
Malignant	9 (3.9%)	2 (16.7%)	7 (3.2%)	0.073
Diseased branches	3 (3, 3)	3 (3, 3)	3 (3, 3)	0.657
Preoperative D-dimer	0.29 (0.19, 0.51)	0.30 (0.14, 0.83)	0.29 (0.19, 0.51)	0.748
Preoperative HGB	133.7 ± 17.0	132.5 ± 19.2	133.8 ± 16.7	0.820
Preoperative PLT	204 (172, 241)	176 (157, 215)	204 (174, 242)	0.082
Preoperative Cr	68.5 (58.6, 81.5)	78.5 (76.1, 95.0)	67.7 (58.4, 81.2)	0.011
Transfusion	103 (44.6%)	7 (58.3%)	96 (43.8%)	0.079
Total transfusion (mL)	0 (0, 400)	600 (50, 1350)	0 (0, 400)	0.009
Transfusion >5 units	23 (10.0%)	4 (33.3%)	19 (8.7%)	0.022
Heparin dosage	120 (100, 150)	130 (115, 150)	120 (100, 150)	0.569
Bleeding volume (mL)	200 (200, 350)	400 (300, 650)	200 (200, 300)	0.001
Operation time (min)	300 (255, 330)	300 (240, 390)	300 (263, 330)	0.421
Reoperation for bleeding	7 (3.0%)	1 (8.3%)	6 (2.7%)	0.315
Hospital days (d)	20.0 (16.0, 24.0)	20.5 (15.0, 27.3)	20.0 (17.0, 24.0)	0.666
Ventilator time (h)	16.0 (15.0, 18.0)	18.0 (17.0, 37.5)	16.0 (15.0, 17.0)	0.012
ICU days (d)	4.0 (2.0, 6.0)	4.0 (3.3, 6.8)	3.0 (2.0, 6.0)	0.243
Drainage, 24 h	845.0 (625, 1090)	980.0 (871, 1218)	825.0 (610, 1070)	0.095
Total drainage (mL)	1170 (805, 1540)	1453 (1363, 1565)	1160 (800, 1535)	0.028
Mortality	10 (4.3%)	3 (25.0%)	7 (3.2%)	0.011
Postoperative MI	10 (4.3%)	2 (16.7%)	8 (3.7%)	0.088
Repeat revascularization	19 (8.2%)	1 (8.3%)	18 (8.2%)	1.000

Note: Continuous and normally distributed variables between the two groups were analyzed using an independent-samples *t*-test. A signed-rank test was applied to such data with a non-normal distribution. GIB, gastrointestinal bleeding; CRD, chronic respiratory disease; PVD, peripheral vascular disease; CVD, cerebrovascular disease; LVEF, left ventricular ejection fraction; LVED, left ventricular end diastolic diameter; GID, gastrointestinal disease; HGB, hemoglobin; PLT, platelets; ICU, intensive care unit; MI, myocardial infarction; Cr, creatinine; PCI, percutaneous coronary intervention; BMI, body mass index.

2.6 Statistical Analysis

Continuous variables are expressed as the mean ± standard deviation (SD) when normally distributed, and as the median with interquartile range, M (P25, P75), when not normally distributed; categorical variables are expressed as rates or percentages. Power analysis was conducted using G*Power software (version 3.1, Heinrich Heine University, Düsseldorf, Germany), with effect size, alpha level (α = 0.05, two-tailed), and expected power (1 – β = 0.8) as parameters to confirm adequate statistical power; the final

Table 2. Univariate logistic regression of patients in the gastrointestinal bleeding and the non-gastrointestinal bleeding groups.

Variables	Regression coefficient	SEM	Wald	OR	95% CI	*p*-value
CVD	1.341	0.560	5.730	3.822	1.275–11.458	0.017
Preoperative Cr	0.000	0.017	0.000	1.000	0.968–1.033	0.986
Ventilator time (h)	0.001	0.002	0.111	1.001	0.997–1.005	0.739
ICU length of stay (d)	0.061	0.025	5.819	1.062	1.011–1.116	0.016
Operation time	0.011	0.005	4.594	1.011	1.001–1.021	0.032
Pre-D-dimer	0.502	0.253	3.922	1.652	1.005–2.715	0.048
Transfusion >5 units	1.402	0.639	4.820	4.063	1.162–14.205	0.028
Bleeding volume	0.002	0.001	6.000	1.002	1.000–1.004	0.014
Total drainage	0.001	0.000	4.752	1.001	1.000–1.001	0.029
Total transfusion	0.001	0.000	7.042	1.001	1.000–1.002	0.008

Note: SEM, standard error of the mean; CVD, cerebrovascular disease; OR, odds ratio; CI, confidence interval; ICU, intensive care unit; Cr, creatinine.

Table 3. Multivariate logistic regression of patients in the gastrointestinal bleeding and the non-gastrointestinal bleeding groups.

Variables	Regression coefficient	SEM	Wald	OR	95% CI	*p*-value
CVD	1.323	0.581	5.185	3.754	1.202–11.724	0.023
Total drainage	0.001	0.000	5.714	1.001	1.000–1.001	0.017

Note: SEM, standard error of the mean; CVD, cerebrovascular disease; OR, odds ratio; CI, confidence interval.

sample size was subsequently set at n = 231. For continuous variables that conformed to a normal distribution, univariate analysis was performed using the two-independent-samples *t*-test; for variables that did not conform to a normal distribution, the Wilcoxon–Mann–Whitney U test was used. For the analysis of categorical variables, the chi-square test was used; however, when the expected frequency was less than 5, Fisher's test was used for a more accurate assessment. Single-factor logistic regression was used to analyze risk factors for gastrointestinal bleeding, and multivariable logistic regression was used to identify independent risk factors. A forward selection method was used to build the model; p-values < 0.05 indicate that the model was successfully built. Odds ratio (OR) and 95% confidence intervals (CIs) were calculated, and p-values < 0.05 were considered statistically significant. All analyses were performed using SPSS software (version 26.0, IBM Corp., Armonk, NY, USA).

3. Results

3.1 Baseline Characteristics and Perioperative Outcomes

A total of 231 patients who underwent HCR were included in this study. The mean age was 65.0 ± 9.9 years, and 163 (70.6%) were male. A total of 12 (5.2%) patients developed gastrointestinal bleeding. Patients were divided into two groups based on the presence of gastrointestinal bleeding. The total mortality rate for all patients was 4.3%. Among patients with gastrointestinal bleeding, three (25.0%) died; the mortality rate of patients with gastrointestinal bleeding was statistically different compared with the control group. Patients with gastrointestinal bleeding did not significantly differ from controls in gender, age, smoking and alcohol history, history of hypertension, history of hyperlipidemia, history of malignant tumors, preoperative hemoglobin, preoperative platelets, preoperative D-dimer, intraoperative heparin dosage, and 24 h drainage volume. However, the differences in previous cerebrovascular diseases (50.0% vs. 21.0%; $p = 0.047$), preoperative Cr (78.5 vs. 67.7 µmol/L; $p = 0.011$), and total perioperative blood transfusion volume (600 vs. 0 mL; $p = 0.009$), perioperative blood transfusion >5 units (33.3% vs. 8.7%; $p = 0.022$), intraoperative blood loss (400 vs. 200 mL; $p = 0.001$), postoperative total drainage volume (1453 vs. 1160 mL: $p = 0.028$), mechanical ventilation time (18.0 vs. 16.0 hours; $p = 0.012$), and mortality rate (25.0% vs. 3.2%; $p = 0.011$) were statistically significant. Baseline characteristics and intraoperative and postoperative data results are shown in Table 1.

3.2 Univariate and Multivariate Logistic Regression Analyses of Risk Factors for Gastrointestinal Bleeding

All clinical factors related to gastrointestinal bleeding were included in a binary logistic regression analysis. Several statistically significant risk factors were identified in the univariate analysis, including prior cerebrovascular disease, ICU length of stay, total operation time, preoperative D-dimer level, perioperative blood transfusion >5 units, total intraoperative bleeding, total postoperative drainage, and total perioperative blood transfusion. Based on the univariate results, statistically significant variables were in-

cluded in the multivariate analysis. The variables screened by the stepwise forward method were previous cerebrovascular diseases (OR = 3.754, 95% CI = 1.202–11.724; p = 0.023) and total postoperative drainage (OR = 1.001, 95% CI = 1.000–1.001; p = 0.029). Variables that showed statistical differences between univariate and multivariate logistic regression analyses are presented in Tables 2,3.

4. Discussion

Gastrointestinal bleeding is defined as a reduction in hemoglobin of at least 2 g/dL, accompanied by hematemesis or black stool, and is diagnosed accordingly [9]. In this study, the incidence of gastrointestinal bleeding in patients undergoing HCR was 5.2%, and the mortality rate among those who exhibited gastrointestinal bleeding was 25.0%. There was a significant difference in mortality between patients with and without gastrointestinal bleeding (25.0% vs. 3.2%; p = 0.011). Previous studies have reported an incidence of gastrointestinal bleeding after CABG of 1.1% [10]. Meanwhile, the incidence of gastrointestinal bleeding in patients treated with PCI was 0.6%. Compared with patients without gastrointestinal bleeding, the mortality rate was higher in those with gastrointestinal bleeding (9.7% vs. 1.1%; p = 0.001), as well as a longer median hospital stay (5.8 vs. 1.6 days) [11]. The incidence and mortality of gastrointestinal bleeding in this study were higher than those previously reported after CABG and PCI, potentially because HCR differs from traditional surgery; thus, HCR patients will be administered oral aspirin before the operation. Furthermore, heparin will be used on the day of operation to maintain an ACT >300 s during CABG, and patients will receive a loading dose of clopidogrel before the start of PCI. Postoperative anticoagulation includes the use of anticoagulants such as aspirin and heparin, all of which can increase the risk of postoperative gastrointestinal bleeding in patients with HCR and long-term antiplatelet drugs before operation.

Gastrointestinal bleeding after cardiac surgery is associated with increased mortality, prolonged ventilator use, pneumonia, wound infection, sepsis, acute renal injury, atrial fibrillation, MI, ICU treatment time, and prolonged hospital stay [12]. Previous studies have suggested several factors that increase the risk of bleeding during DAPT treatment, including a history of bleeding, oral anticoagulants, women, advanced age, low body weight, chronic renal insufficiency, diabetes, anemia, and long-term use of steroids or nonsteroidal anti-inflammatory drugs (NSAIDs) [11,13,14]. Intraoperative blood loss and postoperative total drainage may lead to gastrointestinal perfusion deficiency, vasoconstrictive catecholamine release, weakening of the mucus–bicarbonate barrier, gastric acid emptying, and other factors, such as gastrointestinal mucosal damage and gastrointestinal ulcers, which may lead to gastrointestinal bleeding in the later stage [15]. After multivariate analysis, prior cerebrovascular disease and total drainage were established as independent predictors of postoperative gastrointestinal hemorrhage in patients undergoing HCR. Cerebrovascular diseases included hemorrhagic stroke and ischemic stroke. In this study, 6 of 12 patients with gastrointestinal hemorrhage had a history of cerebral infarction and had been administering antiplatelet drugs for a long time. Therefore, it is considered that patients with previous cerebrovascular diseases may increase the risk of postoperative gastrointestinal bleeding due to long-term use of antiplatelet drugs before the operation. Indeed, long-term antiplatelet therapy (e.g., aspirin) may impair gastrointestinal mucosal repair and increase the risk of bleeding by disrupting the mucus–bicarbonate barrier and inhibiting platelet aggregation [16]. However, this mechanism must be considered alongside alternative explanations, such as generalized atherosclerosis, vascular frailty, and unmeasured confounders. Meanwhile, increased total drainage can also lead to a higher risk of postoperative gastrointestinal hemorrhage, primarily by inducing perioperative hypovolemia, which exacerbates gastrointestinal hypoperfusion, impairs mucosal barrier function, and promotes stress ulcer formation.

The results of this study are similar to those of previous studies, which have focused more on preoperative baseline data [17]. In contrast, this study includes many factors, such as intraoperative anticoagulant use and operation time, perioperative blood transfusion and postoperative drainage, and postoperative ICU length of stay. The results show that patients with previous cerebrovascular diseases have a relatively high risk of gastrointestinal bleeding after HCR. For these patients, attention should be paid to adjusting antiplatelet and prevention strategies to reduce the risk of gastrointestinal bleeding after the operation and discharge. Furthermore, caution is required in interpreting these findings. The wide CIs of the OR and the limitations of this study (small sample size, low event rate, unmeasured confounding factors) mean that the observed association cannot be definitively attributed solely to long-term antiplatelet therapy. Instead, these findings may reflect a combination of direct (mucosal damage caused by antiplatelet drugs) and indirect (systemic vascular dysfunction, unmeasured confounding factors) effects.

The use of dual antiplatelet drugs after coronary revascularization can reduce mortality and the incidence of ischemic events, but also increase the corresponding risk of bleeding [18]. DAPT generally uses aspirin and clopidogrel. Previous studies and guidelines recommend that aspirin be continued indefinitely after CABG, and that in patients with acute coronary syndrome (ACS) who are treated with DAPT and subsequently undergo CABG, P2Y12 inhibitor therapy be resumed after surgery to complete 12 months of DAPT following the ACS event. DAPT has been shown to reduce the risk of in-stent thrombosis by 0.4%, MI by 1.1%, and moderate-to-severe bleeding by 1.2% [13]. Since HCR combines CABG and PCI, balancing anticoag-

ulation and bleeding risk is a major challenge for both surgeons and anesthesiologists.

After coronary revascularization, the generally recommended antiplatelet strategy is DAPT, which can significantly reduce mortality and MACCEs. Common DAPT regimens include aspirin plus ticagrelor or clopidogrel. Aspirin plus ticagrelor is the best combination for reducing bridge restenosis, mortality, and MACCEs, but this combination is associated with increased risk of bleeding during use [19]. Aspirin directly acts on the phospholipid layer of gastric mucosa, destroys the hydrophobic protective barrier of gastric mucosa [20], promotes the release of cytotoxic substances such as leukotrienes, resulting in direct mucosal loss; meanwhile, aspirin also reduces prostaglandin synthesis, gastric mucosal blood flow, and mucosal protection by inhibiting mucosal cyclooxygenase (COX)-1 and COX-2 activity [21]. Clopidogrel noncompetitively inhibits adenosine diphosphate (ADP) receptors and platelet aggregation. However, it has been reported to delay gastrointestinal mucosal healing, which may contribute to an increased risk of gastrointestinal bleeding [22]. The AUGUSTUS trials have shown that aspirin use for 30 days or longer can seriously increase the risk of bleeding. After 30 days, continued aspirin therapy further increases the risk of bleeding without reducing the risk of ischemic events [23]. Almost all patients receiving antiplatelet therapy have varying degrees of gastrointestinal injury. The bleeding risk of aspirin or clopidogrel alone was lower than that of aspirin combined with clopidogrel (0.6% vs. 5.4%; $p < 0.001$) [24]. Indobufen is a reversible COX-1 inhibitor, with lower inhibition of prostacyclin, fewer gastrointestinal reactions, and a lower risk of hemorrhage. For patients with high risk of bleeding, the OPTION studies have shown that the incidences of cardiovascular death, non-fatal MI, ischemic stroke, and in-stent thrombosis were similar and low (1.40% vs. 1.51%; $p = 0.76$). The incidence of bleeding decreased significantly by 37% (2.97% vs. 4.71%; $p = 0.002$) when the indole buffer combined with clopidogrel is compared with aspirin combined with clopidogrel [25]. In addition, for patients at high risk of bleeding, the addition of a proton pump inhibitor (PPI), histamine-2 receptor antagonist (H2RA), or gastric mucosal protective agents is necessary to prevent gastrointestinal bleeding. PPIs can inhibit gastric acid secretion to a large extent, promote ulcer healing, and effectively prevent the gastrointestinal toxicity of antiplatelet drugs such as aspirin. PPI, as the first choice for the prevention and treatment of upper gastrointestinal bleeding, is superior to H2RAs in preventing gastrointestinal bleeding (OR = 2.102, 95% CI: 1.008–4.385) and ulcer formation (OR = 2.257, 95% CI: 1.277–3.989) [26].

5. Conclusion

Among the patients undergoing HCR surgery, those with a history of cerebrovascular diseases exhibited a higher risk of postoperative gastrointestinal bleeding. For these patients, antithrombotic strategies should be adjusted, and appropriate preventive measures should be implemented to reduce the risk of gastrointestinal bleeding.

6. Innovation and Limitations

Most previous studies have focused on CABG and PCI; to our knowledge, there are currently no relevant studies on gastrointestinal bleeding after HCR. This study, as the first report analyzing risk factors for gastrointestinal bleeding after HCR, provides new insights and lays the foundation for future preventive strategies. However, this study has certain limitations. First, the critically low number of gastrointestinal bleeding events (n = 12) leads to insufficient statistical power for definitive analysis. The event-per-variable (EPV) ratio in the multivariable logistic regression model is only ~6, which is below the commonly recommended threshold of 10 EPVs. This may lead to model instability, potential overfitting, overestimated odds ratios, and wide confidence intervals, rendering the findings preliminary and unreliable for definitive conclusions. Second, this was a single-center retrospective study with a small overall sample size (n = 231). Moreover, patient selection and perioperative management may be specific to our institution, limiting the generalizability of the results. Third, due to the small number of events and sample size, we were unable to conduct subgroup analyses (e.g., differentiating types of cerebrovascular disease) or adjust for all potential confounders (e.g., severity of comorbidities, non-steroidal anti-inflammatory drug use, or gastrointestinal mucosal status). Additionally, the analysis of factors such as gender, age, and smoking history was inconsistent with previous studies, possibly due to insufficient statistical power required to detect true associations.

Abbreviations

ACT, Activated Clotting Time; CABG, Coronary Artery Bypass Grafting; CI, Confidence Interval; CRD, Chronic Respiratory Disease; CVD, Cerebrovascular Disease; DAPT, Dual Antiplatelet Therapy; DCB, Drug-Coated Balloon; DES, Drug-Eluting Stent; eGFR, estimated Glomerular Filtration Rate; GIB, Gastrointestinal Bleeding; HCR, Hybrid Coronary Revascularization; HGB, Hemoglobin; ICU, Intensive Care Unit; LAD, Left Anterior Descending Artery; LIMA, Left Internal Mammary Artery; LMCA, Left Main Coronary Artery; LVED, Left Ventricular End-Diastolic Diameter; LVEF, Left Ventricular Ejection Fraction; MACCEs, Major Adverse Cardiovascular and Cerebrovascular Events; MIDCABG, Minimally Invasive Direct Coronary Artery Bypass Grafting; OR, Odds Ratio; PCI, Percutaneous coronary intervention; PLT, Platelet Count; PPI, Proton Pump Inhibitor; PVD, Peripheral Vascular Disease; SD, Standard Deviation; SEM, Standard Error of the Mean; TTFM, Transit-Time Flow Measurement.

Availability of Data and Materials

The datasets used and analysed during the current study were available from the corresponding author on reasonable request.

Author Contributions

PS designed the study, secured funding, and oversaw the implementation of the project. ZF and YX managed the data. ZF collected demographic characteristics and wrote the initial draft, YX and PS revised it. All authors have accessed and verified the data and collectively decided to submit the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Beijing Chao-Yang Hospital, Capital Medical University (Approval No.: 2023-673). All methods were carried out in accordance with Declaration of Helsinki, and all of the participants provided signed informed consent.

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Conflict of Interest

The authors declare no conflict of interest.

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