Original Article

Gastrointestinal bleeding risk factors in type A aortic dissection post-aortic arch replacement

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Background: Gastrointestinal bleeding (GIB) is a notable complication in patients diagnosed with aortic dissection (AD). We evaluated the outcomes and identified the risk factors associated with GIB in patients with AD.

Methods: A retrospective case-control study was conducted on patients diagnosed with type A aortic dissection (TAAD) who underwent total aortic arch replacement (TAAR) at our institution from July 2021 to July 2023. Comprehensive clinical data, laboratory findings, and imaging results were meticulously gathered and analyzed to identify potential risk factors linked to GIB in this patient cohort.

Results: Of the 198 AD patients who underwent TAAR, 38 (19.2%) developed postoperative GIB (GIB group), with a median interval of 7 days between surgery and bleeding onset. The GIB group exhibited significantly higher mortality (26.3% *vs.* 3.1%, P<0.001), prolonged intensive care unit (ICU) stay {15 [interquartile range (IQR), 8–25] *vs.* 7 (IQR, 5–12) days, P<0.001}, and extended duration of ventilation [168 (IQR, 120–372) *vs.* 71 (IQR, 34–148) hours, P<0.001] compared to the control group (n=160, 80.8%). Logistic regression analysis identified age >54 years [odds ratio (OR): 3.529], intraoperative red blood cell (RBC) transfusion >600 mL (OR: 3.865), and concomitant celiac trunk and superior mesenteric artery (SMA) hypoperfusion (OR: 15.974) as independent risk factors for GIB in AD patients.

Conclusions: GIB subsequent to TAAR in AD patients is linked to adverse prognosis. Factors such as advanced age, extensive intraoperative transfusion, and gastrointestinal (GI) perfusion abnormalities may heighten the risk of GIB in this patient population.

Keywords: Type A aortic dissection (TAAD); gastrointestinal bleeding (GIB); perioperative period; retrospective analysis

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Introduction

Aortic dissection (AD), a life-threatening cardiovascular pathology characterized by the dissection of the aortic wall, constitutes a significant 58–62% of all aortic conditions, with a staggering preoperative mortality rate of up to 30% (1,2). Surgical intervention is the primary treatment for Stanford type A aortic dissection (TAAD). The optimal approach to managing the aortic arch varies significantly and should be individualized based on the patient's clinical presentation, arch anatomy, and distal aortic characteristics. Options may include standard hemiarch replacement, total aortic arch replacement (TAAR), and hybrid procedure (3). Despite advancements in surgical interventions, patients are still confronted with substantial perioperative complications, underscoring the critical and intricate nature of this pervasive disease (4,5).

Gastrointestinal bleeding (GIB) can occur as a complication after cardiovascular surgery, with an occurrence ranging from 0.4% to 1.4% and a linked mortality rate of 18% (6-8). Standford TAAD affects multiple organs, and cardiopulmonary bypass (CPB) can trigger a systemic inflammatory response and lead to gastrointestinal (GI) ischemia and hypoxia (9), thereby exacerbating the risk and complexity of GIB after TAAD. Malperfusion syndrome (MPS) is a significant factor associated with increased mortality in TAAD and may also be a crucial contributor to postoperative GIB (10). Consequently, the incidence and hazard of GIB following TAAD surgery exceed those associated with routine cardiac procedures. Indeed, there is a significant gap in the existing literature concerning the incidence, mortality rate, and risk factors of GIB following TAAD. Our study aims to delineate the disease characteristics and risk factors associated with GIB in the context of TAAD, with a view to enhancing and streamlining the perioperative management of this condition. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1752/rc).

Highlight box

Key findings

- Advanced age, extensive intraoperative transfusion, and gastrointestinal perfusion abnormalities may heighten the risk of post-operative gastrointestinal bleeding (GIB) in patients with aortic dissection.

What is known and what is new?

- GIB refers to any bleeding that starts in the gastrointestinal tract from the pharynx to the rectum, and is a frequent gastrointestinal complication following cardiovascular surgery.
- Factors such as advanced age, extensive intraoperative transfusion, and gastrointestinal perfusion abnormalities may heighten the risk of GIB in this patient population.

What is the implication, and what should change now?

- The risk of GIB is significantly heightened in patients with concomitant celiac trunk and superior mesenteric artery hypoperfusion. For these individuals, vigilant observation of abdominal symptoms is essential, with a specific focus on maintaining sufficient gastrointestinal perfusion and avoiding iatrogenic factors that could intensify gastrointestinal ischemia.

Methods

Study design and ethical review

We conducted a retrospective case-control study at Guangdong Provincial People's Hospital in Guangzhou, China. The study protocol was thoroughly reviewed and approved by the Ethics Committee of Guangdong Provincial People's Hospital (No. KY2023-580-01), and informed consent was waived due to the retrospective nature of the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Patients and groups

Total aortic arch replacement (TAAR) serves a treatment modality for TAAD. To maintain uniformity and mitigate potential confounding effects arising from surgical procedure variations, our study exclusively included TAAD patients who underwent TAAR.

Adult patients with AD who received TAAR at our hospital between July 2021 and July 2023 were enrolled. To be eligible for the study, participants had to be over 18 years of age.

Exclusion criteria were set as follows: (I) patients with a prior history of peptic ulcer disease; (II) patients with a documented history of chronic liver disease; (III) patients who had experienced GIB within 3 months before hospitalization; (IV) patients with injuries attributable to procedures such as intubation, echocardiography, or gastric tube insertion.

Patients exhibiting typical GIB symptoms (black stool, haematemesis or vomiting blood, presence of blood in the stool, and coffee-colored or bloody gastric juice) and testing positive in faecal or gastric occult blood tests were included in the GIB group. Conversely, patients who did not experience GIB during the same period were included in the control group.

Data collection

Clinical parameters, including baseline characteristics, surgical details, perioperative treatments, prognosis, and preoperative echocardiography and computed tomography angiography (CTA) findings, were extracted from medical records. In this study, hypoperfusion was defined based on CTA findings, specifically the presence of false lumen blood supply or severe stenosis (>70%) in the celiac trunk/superior mesenteric artery (SMA). Notably, these criteria were applied even in the absence of clinical manifestations of ischemia, such as abdominal pain or intestinal ischemia. Additional data for the GIB group included bleeding volume, occurrence time, treatment, and endoscopic results. The GIB group was categorized based on clinical manifestations and bleeding severity according to guidelines (11,12): (I) mild: black stools, no bloody gastric juice/stools, no significant hemoglobin (Hb)/hematocrit (HCT) decline, estimated bleeding volume 50–250 mL; (II) moderate: coffee-colored/bloody gastric contents exceeding 250 mL, hematemesis/bloody stools, estimated bleeding volume 250–400 mL; (III) severe: persistent hematemesis/bloody stools, cold/clammy extremities, heart rate >100 beats/min, systolic blood pressure <90 mmHg, Hb <70g/L, estimated bleeding volume >400 mL.

Upon the occurrence of GIB in patients, clinicians collaborate with gastroenterologists to assess the extent and severity of the bleeding. Depending on the clinical scenario, interventions, such as implementing dietary restrictions, gastric acid suppression, and administering coagulation factors and red blood cells (RBCs), are initiated. Gastroenterologists evaluate the potential benefits and risks of urgent endoscopic examination. In cases of severe bleeding where conservative medical management fails to demonstrate significant improvement or when hemodynamic instability persists despite active resuscitation, emergency endoscopic examination is administered to the patient.

Statistical analysis

Statistical analyses were conducted using SPSS 23.0.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as counts and percentages, and continuous variables as mean ± standard deviation (SD) or median with interquartile ranges (IQR), depending on data distribution. Chi-squared or Fisher's exact tests were used for categorical comparisons, and Student's *t*-test or Mann-Whitney *U* test for continuous variables, based on data normality. For multivariate analysis, the cut-off value of count data was determined using Youden's index following receiver operating characteristic (ROC) curve analysis. Multivariate analysis incorporated factors potentially influencing postoperative GIB, with a P value <0.05 deemed statistically significant.

Results

Comparison of baseline clinical information between the GIB and control groups

Table 1 presents the baseline clinical characteristics of the study population. The study encompassed 198 patients (mean age 54±11 years, 83.3% male, over all range 37–77 years) (*Figure 1*). Of these, 38 patients (19.2%) were categorized into the GIB group, while the remaining 160 patients (80.8%) constituted the control group. The mean age of patients in the GIB group (age range, 30–73 years) was significantly elevated compared to the control group (age range, 27–77 years) (58±11 *vs.* 52±11, P=0.003). No significant disparities were observed between the two groups in terms of gender distribution, age, weight, height, smoking history, hypertension history, diabetes history, hyperlipidemia history, prior surgical history and the interval between the onset of symptoms and surgery (P>0.05) (*Table 1*).

Analysis of patient characteristics in 38 cases of GIB

Thirty-eight patients developed GIB post-TAAR, with a median onset of 7 days. The GIB group had higher mortality (26.3% *vs.* 3.1%, P<0.001), reintubation rates (34.2% *vs.* 7.5%, P<0.001), intensive care unit (ICU) stay [15 (IQR, 8–25) *vs.* 7 (IQR, 5–12) days, P<0.001], and ventilation duration [168 (IQR, 120–372) *vs.* 71 (IQR, 34–148) hours, P<0.001]. In the GIB group, there were 10 fatalities, with 7 cases attributed to multiple organ dysfunction syndrome (MODS) induced by infection, 1 case to hemorrhagic shock, and 2 cases to non-infectious MODS. In the control group, 5 fatalities occurred, all due to MODS resulting from infection. No significant difference was found in pre-bleeding ICU stay duration (P>0.05).

Table 1 Baseline clinical characteristics of 198 patients

Variable	Total (N=198)	GIB group (N=38)	Control group (N=160)	t/χ^2	P
Female, n (%)	33 (16.7)	5 (13.2)	28 (17.5)	0.417	0.51
Age (years), mean (SD)	54 (11.0)	58 (11.0)	52 (11.0)	−2.976	0.003
Weight (kg), mean (SD)	71.8 (14.3)	72.6 (16.7)	71.7 (13.8)	−0.356	0.72
Height (cm), mean (SD)	168.6 (8.2)	169.5 (7.9)	167.9 (8.5)	−0.827	0.41
Smoking, n (%)	31 (15.7)	7 (18.4)	24 (15.0)	0.272	0.60
Hypertension, n (%)	111 (56.1)	25 (65.8)	86 (53.8)	1.807	0.17
Diabetes, n (%)	4 (2.0)	1 (2.6)	3 (1.9)	0.089	0.76
Hyperlipidemia, n (%)	33 (16.7)	7 (18.4)	26 (16.3)	0.270	0.60
Previous surgery, n (%)	16 (8.1)	5 (13.2)	11 (6.9)	1.632	0.20
Time from symptom onset to surgery (days), mean (SD)	1.1 (2.0)	1.3 (2.3)	1.1 (1.9)	−0.603	0.54

GIB, gastrointestinal bleeding; SD, standard deviation.

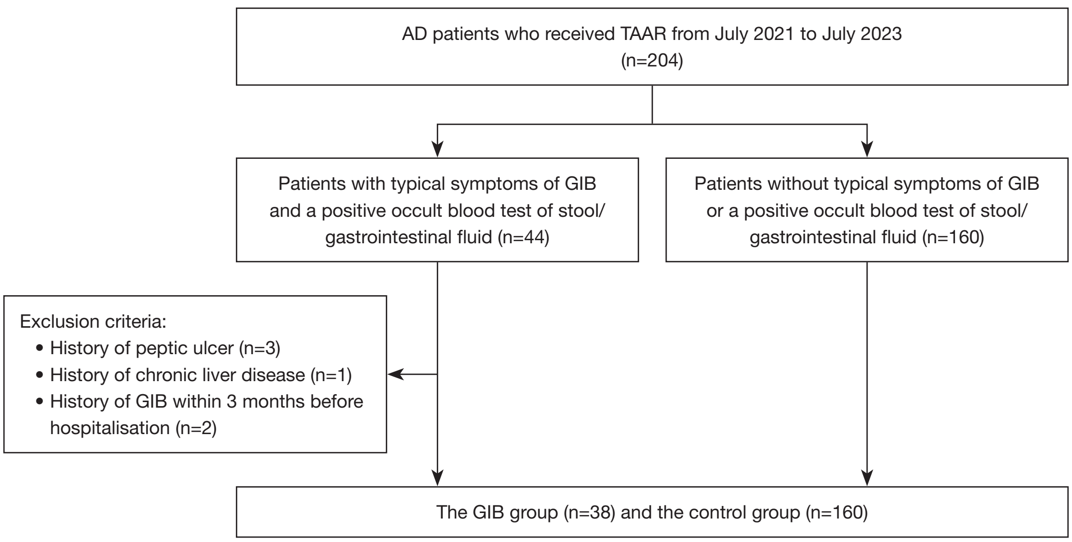

Figure 1 Flowchart illustrating the selection process of the study population. AD, aortic dissection; TAAR, total aortic arch replacement; GIB, gastrointestinal bleeding.

Postoperatively, hospital stay duration and pulmonary infection incidence were similar (P>0.05), but the GIB group had higher bloodstream infection incidence (10.5% *vs.* 1.9%, P=0.009), Kidney Disease: Improving Global Outcomes (KDIGO) stage 3 acute kidney injury (57.9% *vs.* 11.3%, P<0.001), and continuous renal replacement therapy (CRRT) requirement (50.0% *vs.* 9.4%, P<0.001) (*Table 2*). Among the GIB patients, 34% (N=13) had mild/moderate bleeding, and 32% (N=12) had severe bleeding (*Figure 2A*). Two patients with mild/moderate bleeding and eight with severe bleeding died. Thirty-one patients (82%) were treated medically [high dose intravenous proton pump inhibitors (PPIs), fasting, and hemostatic drugs, etc.] and did not require endoscopy (*Figure 2B*). Seven patients (18%) underwent emergency endoscopy due to massive bleeding and ineffective medication. Of these, one failed interventional hemostasis and three required surgical treatment. Endoscopy revealed gastric/duodenal ulcers and

Table 2 Morbidity and mortality of 198 patients

Variable	Total (N=198)	GIB group (N=38)	Control group (N=160)	t/χ^2	P
Mortality, n (%)	15 (7.6)	10 (26.3)	5 (3.1)	23.586	<0.001
Hospital stays (days)*	22 [17–33]	25 [17–37]	22 [17–32]	–	0.21
ICU stay (days)*	8 [5–14]	15 [8–25]	7 [5–12]	–	<0.001
Ventilation duration (h)*	96 [39–168]	168 [120–372]	71 [34–148]	–	<0.001
Reintubation, n (%)	25 (12.6)	13 (34.2)	12 (7.5)	19.859	<0.001
Pulmonary infection, n (%)	76 (38.4)	19 (50.0)	57 (35.6)	2.683	0.10
Bloodstream infection, n (%)	7 (3.5)	4 (10.5)	3 (1.9)	6.739	0.009
AKI-KDIGO grade, n (%)				42.099	<0.001
None	87 (43.9)	7 (18.4)	80 (50.0)	12.431	<0.001
Grade 1	36 (18.2)	4 (10.5)	32 (20.0)	1.853	0.17
Grade 2	35 (17.7)	5 (13.2)	30 (18.8)	0.660	0.41
Grade 3	40 (20.2)	22 (57.9)	18 (11.3)	41.444	<0.001
CRRT, n (%)	34 (17.2)	19 (50.0)	15 (9.4)	35.631	<0.001

*, continuous variables are presented as median with interquartile ranges [IQR] for data with large SD or non-normal distributions. GIB, gastrointestinal bleeding; ICU, intensive care unit; AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes; CRRT, continuous renal replacement therapy; SD, standard deviation.

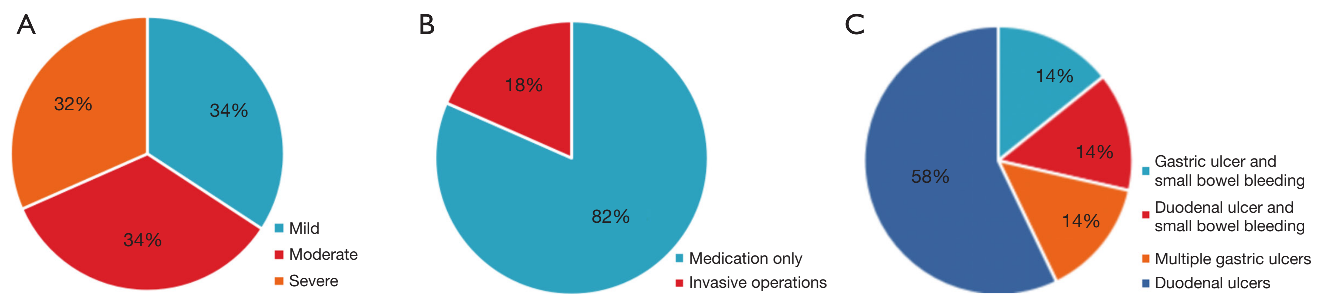

Figure 2 Characteristics of patients in the gastrointestinal bleeding group. (A) Among the 38 patients in the bleeding group, 13 (34%) had mild bleeding, 13 (34%) had moderate bleeding, and 12 (32%) had severe bleeding. (B) Out of the 38 patients with gastrointestinal bleeding, 31 (82%) showed improvement with medication, while 7 (18%) (all with severe bleeding) required invasive procedures such as emergency endoscopy, interventional hemostasis, and surgical treatment (bowel resection). (C) Endoscopy clearly identified 7 patients, with 1 (14%) having gastric ulcer combined with small bowel bleeding, 1 (14%) having duodenal ulcer combined with small bowel bleeding, 1 (14%) having multiple gastric ulcers bleeding alone, and 4 (58%) having duodenal ulcers bleeding.

small intestinal bleeding (*Figure 2C* and *Figure 3A-3F*).

Analysis of blood tests, CTA scan, surgical and perioperative treatment

The GIB group demonstrated significantly elevated preoperative leukocyte levels ($12.9\pm3.8\times10^9$/L *vs.* $10.7\pm4.0\times10^9$/L, P=0.008), preoperative D-dimer levels (13,410.6±7,559.6 *vs.* 8,209.3±7,524.6 ng/mL, P<0.001), and preoperative creatinine levels (140.5±131.3 *vs.* 104.2 ±89.9 ng/mL, P=0.04) compared to the control group. However, there were no significant differences observed in preoperative Hb levels, preoperative platelet levels, preoperative alanine transaminase (ALT) levels, preoperative prothrombin time (PT), preoperative activated partial thromboplastin time (APTT), total bilirubin and

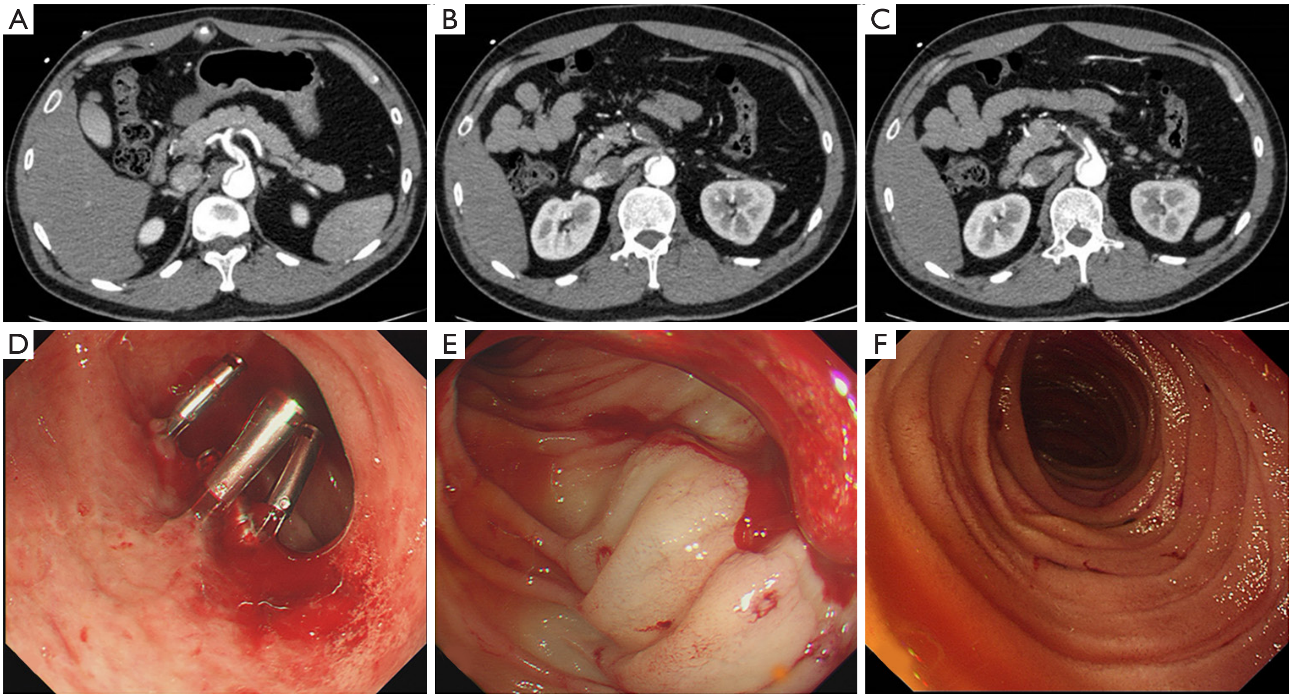

Figure 3 Demonstration of aortic CTA and emergency gastroscopy in a patient with severe gastrointestinal bleeding. The patient, a 33-year-old man, exhibited abnormal blood supply to the celiac trunk (A) and superior mesenteric artery (B,C) on preoperative aortic CTA. Upper gastrointestinal bleeding with multiple ulcers in the bulb (D) and descending (E,F) segments occurred, and recurrent bleeding was observed 1 day after total aortic arch replacement. CTA, computed tomography angiography.

preoperative lactate levels. Preoperative left ventricular ejection fraction (LVEF), as assessed by echocardiography, did not exhibit significant differences between the GIB group and the control group. According to preoperative CTA examination of the aorta, the incidence of concomitant celiac trunk and SMA hypoperfusion (including false lumen blood supply or severe stenosis) was significantly higher in GIB patients compared to the control group (34.2% *vs.* 5.6%, P<0.001). The duration of CPB, aortic cross clamp (ACC), and deep hypothermic circulatory arrest (DHCA) did not differ significantly between the two groups. The intraoperative RBC transfusion volume in the GIB group was significantly greater than that in the control group (734±409 *vs.* 501±400 mL, P=0.002), while there was no significant difference in platelet transfusion volume between the two groups. In the GIB group, 32 cases utilized a transesophageal echocardiography (TEE)-guided aortic arch cannulation, and 6 cases employed axillary artery cannulation. In the control group, 140 cases utilized TEE-guided aortic arch cannulation, and 20 cases employed axillary artery cannulation. There were no statistically significant differences between the two groups in terms of the type of aortic cannulation used (*Table 3*).

Binary logistic regression analysis

Based on baseline data and comparative results of blood tests and examination data, several factors were included in univariate and multivariate regression analyses. These factors comprised age, intraoperative RBC transfusion volume, preoperative leukocyte level, preoperative D-dimer level, preoperative creatinine level, and concomitant celiac trunk and SMA hypoperfusion.

The optimal cut-off values were determined as follows: age >54 years (*Figure 4A*), intraoperative RBC transfusion volume >600 mL (*Figure 4B*), preoperative leukocyte level >11.23×10^9/L (*Figure 4C*), preoperative D-dimer level >4,680 ng/mL (*Figure 4D*) and preoperative creatinine >88.73 µmol/L (*Figure 4E*). These values were included as categorical variables in the regression analysis.

The six factors in the GIB and control groups were analyzed using one-way logistic regression analysis (*Table 4*). When these factors were included in the multifactorial

Table 3 Analysis of blood tests, CTA scan, surgical and perioperative treatment of 198 patients

Variable	Total (N=198)	GIB group (N=38)	Control group (N=160)	t/χ^2	P
Preoperative leukocyte (×10^9/L)	11.5 (4.1)	12.9 (3.8)	10.7 (4.0)	–2.717	0.008
Preoperative hemoglobin (g/L)	126 (18.0)	122 (20.0)	127 (18.0)	1.469	0.14
Preoperative platelet (×10^9/L)	192.8 (77.7)	187.1 (87.2)	196.2 (72.0)	0.553	0.58
Preoperative PT (s)	14.7 (1.2)	14.6 (1.2)	14.7 (1.2)	0.422	0.67
Preoperative APTT (s)	39.4 (8.6)	41.7 (12.0)	38.0 (5.4)	–1.979	0.05
Preoperative D-dimer (ng/mL)	9,137.1 (7,771.1)	13,410.6 (7,559.6)	8,209.3 (7,524.6)	–3.596	<0.001
Preoperative creatinine (μmol/L)	110.9 (99.5)	140.5 (131.3)	104.2 (89.9)	–1.990	0.04
Preoperative total bilirubin (μmol/L)	17.4 (9.0)	17.5 (8.0)	17.4 (9.7)	–0.051	0.96
Preoperative ALT (U/L)	49.9 (99.5)	41.7 (44.6)	54.9 (121.6)	0.626	0.53
Preoperative lactate (mmol/L)	1.4 (0.6)	1.4 (0.8)	1.4 (0.5)	–0.105	0.91
Preoperative LVEF*	63 (7.0)	62 (5.0)	64 (7.0)	1.021	0.30
Concomitant celiac trunk and superior mesenteric artery hypoperfusion	22 (11.1)	13 (34.2)	9 (5.6)	25.405	<0.001
Extracorporeal (min)					
CPB	244.6 (65.6)	251.7 (80.6)	243.0 (61.7)	–0.731	0.46
ACC	129.4 (42.2)	129.5 (42.2)	129.3 (42.3)	–0.019	0.98
DHCA	19.2 (10.8)	19.9 (18.1)	19.1 (8.3)	–0.379	0.70
Intraoperative RBC transfusion (mL)	546 (411.0)	734 (409.0)	501 (400.0)	–3.213	0.002
Intraoperative PLT transfusion (unit)	1.1 (0.7)	0.9 (0.5)	1.1 (0.7)	1.636	0.10
Type of aortic cannulation, n (%)				0.291	0.58
TEE guided aortic arch cannulation	172 (86.9)	32 (84.2)	140 (87.5)		
Axillary artery cannulation	26 (13.1)	6 (15.8)	20 (12.5)		

Data are presented as mean (SD) unless otherwise specified. *, LVEF from the preoperative echocardiography. CTA, computed tomography angiography; GIB, gastrointestinal bleeding; PT, prothrombin time; APTT, activated partial thromboplastin time; ALT, alanine transaminase; LVEF, left ventricular ejection fraction; CPB, cardiopulmonary bypass; ACC, aortic cross clamp; DHCA, deep hypothermic circulatory arrest; RBC, red blood cell; PLT, platelet; TEE, transesophageal echocardiography; SD, standard deviation.

logistic regression equation, the results indicated that age >54 years [P=0.02, odds ratio (OR): 3.529, 95% confidence interval (CI): 1.216–10.239], intraoperative RBC transfusion volume >600 mL (P=0.01, OR: 3.865, 95% CI: 1.326–11.269), and concomitant celiac trunk and SMA hypoperfusion (P<0.001, OR: 15.974, 95% CI: 3.428–74.441) were independent risk factors for concurrent GIB after TAAR for TAAD (*Table 4*).

Discussion

This retrospective study analyzed 198 patients with TAAD who underwent TAAR. The findings are as follows: (I) among the 38 patients with bleeding, 31 patients were effectively treated with medication therapy, while 7 patients required more invasive interventions such as endoscopy, interventional procedures, or even surgical hemostasis. (II) Logistic regression analysis identified age >54 years (OR: 3.529), intraoperative RBC transfusion >600 mL (OR: 3.865), and concomitant celiac trunk and SMA hypoperfusion (OR: 15.974) as independent risk factors for GIB following TAAR in AD patients.

TAAD is widely recognized for its elevated rates of mortality and morbidity. Selecting the most suitable surgical approach is crucial for achieving favorable outcomes in type A dissection; however, determining the optimal procedure

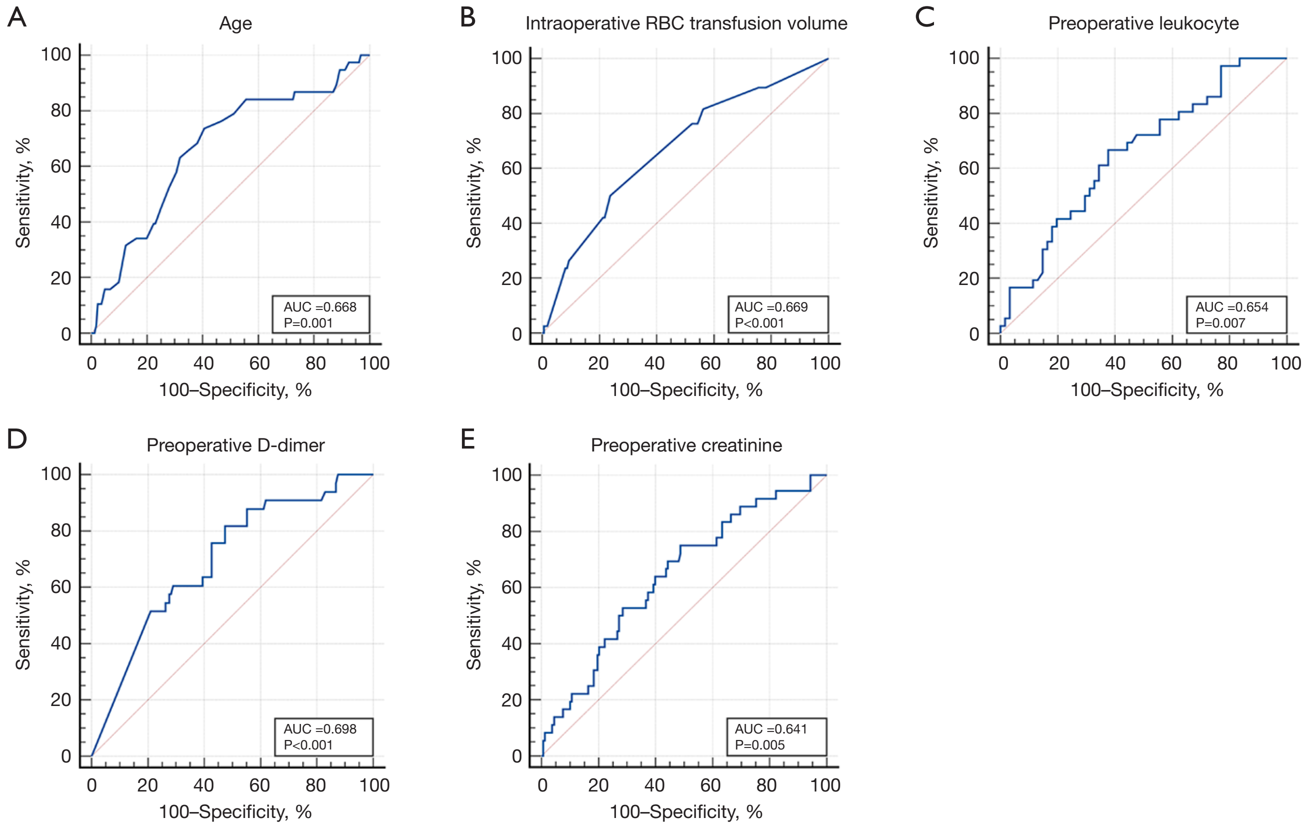

Figure 4 Optimal cut-off values for selected test results in 198 patients. ROC curve analysis revealed that the optimal cut-off values for age (A), intraoperative RBC transfusion volume (B), preoperative leukocyte level (C), D-dimer level (D), and creatinine level (E) were age >54 years, intraoperative RBC transfusion volume >600 mL, preoperative leukocyte level >11.23×10^9/L, preoperative D-dimer level >4,680 ng/mL and preoperative creatinine >88.73 µmol/L. The corresponding areas under the curve are indicated in the figure. AUC, area under the curve; ROC, receiver operating characteristic; RBC, red blood cell.

Table 4 Binary logistics regression analysis

Variable	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Age >54 years	4.092	1.861–8.999	<0.001	3.529	1.216–10.239	0.02
Intraoperative red blood cell transfusion >600 mL	3.211	1.543–6.681	0.002	3.865	1.326–11.269	0.01
Preoperative leukocyte >11.23×10^9/L	0.943	0.407–2.183	0.89	1.229	0.423–3.575	0.70
Preoperative D-dimer >4,680 ng/mL	3.000	1.393–6.461	0.005	2.419	0.824–7.104	0.10
Preoperative creatinine >88.73 µmol/L	2.646	1.229–5.695	0.01	1.710	0.581–5.035	0.33
Concomitant celiac trunk and superior mesenteric artery hypoperfusion	8.724	3.376–22.546	<0.001	15.974	3.428–74.441	<0.001

CI, confidence interval.

remains a matter of controversy. For patients with a tear localized to the ascending aorta who have a normal caliber aortic arch without distal malperfusion, the standard surgical repair involves hemiarch replacement with an open distal anastomosis under circulatory arrest. Standard indications for total arch replacement in acute dissection include the presence of an extensive intimal tear throughout the arch and arch vessels not amenable to primary resection and dilatation of the arch (3). Sun *et al.* found that the in-hospital mortality was 4.7% (7 of 148) and 6.1% (4 of 66) in the patients treated by stented elephant trunk (SET) implantation and conventional surgical repair (CSR) groups, respectively. Total arch replacement combined with an SET implantation demonstrated the superiority of the combined surgical and interventional approach, effectively addressing the weaknesses associated with individual methods (13).

A comprehensive review by Rodriguez *et al.* incorporated data from 35 papers, covering 151,652 cardiac surgery patients over the past 30 years (14). The review found that GI complications occurred, on average, in 1.21% of cardiac surgery cases, with an associated mortality rate of 32% (14). GIB is the most common complication, accounting for 33% of all GI complications (14). However, the underlying causes of GI complications after TAAD remain incompletely understood. Several factors contribute to these complications during CPB: (I) loss of physiological pulsatile blood flow and compromised regulation of visceral blood flow; (II) systemic inflammatory response triggered by contact between blood and abiotic tubules; and (III) haemodilution, resulting in decreased visceral blood flow and intestinal mucosal ischemia due to lower Hb concentration and reduced oxygen carrying capacity (14-16). CPB also induces microthrombosis, production of free radicals after ischemia-reperfusion injury, visceral hypoxia, and CPB-related mesenteric vasoconstriction (17-19). Prolonged CPB duration may contribute to oxidative stress and systemic inflammatory, which is a potential significant factor in the development of GIB. However, our study data showed no significant difference in the duration of CPB between the GIB group and the control group, suggesting that the occurrence of CPB-related GI complications may be related to the patient's own vascular condition.

The GI tract is primarily perfused by the celiac trunk, SMA, and inferior mesenteric artery (IMA). The celiac trunk and its branches supply blood to the stomach, proximal duodenum, and spleen. The SMA supplies most of the small intestine and colon up to the level of the splenic flexure. The gastroduodenal and pancreaticoduodenal arteries serve as the main anastomotic connections between the SMA and celiac arteries, ensuring continuous blood supply through extensive collateral circulation even if one vessel is damaged. However, in cases of TAAD, the blood supply to the celiac trunk and mesenteric arteries is often simultaneously impaired due to false lumen supply (20,21). Consequently, reduced mucosal blood flow, ischemia, and reperfusion injury may contribute to the development of erosions and ulcers in the esophagus, stomach, and duodenum.

Ren *et al.* reported a case of TAAD combined with mesenteric artery malperfusion in a 60-year-old patient who experienced refractory postoperative GIB. The patient was successfully treated with a combination of pharmacological, interventional, and surgical hemostasis (22). A retrospective analysis based on GERAADA revealed that approximately 33.7% of patients with AD had combined organ malperfusion, with a high operative mortality rate of 43.4% for cases involving malperfusion of three organs. Furthermore, mesenteric artery malperfusion increased the mortality rate of acute AD by three to four times (23). In-hospital mortality was significantly higher in patients with preoperative combined GI malperfusion (63.2% *vs.* 23.8%, P<0.001), and visceral malperfusion remained an independent predictor of in-hospital mortality even after total arch replacement (OR: 3.0, P=0.003) (24). Our results revealed that, despite the absence of clinical manifestations of malperfusion such as abdominal pain or intestinal ischemia/necrosis, patients in the GIB group exhibited a significant elevation in preoperative creatinine levels compared to the control group. Previous study indicated that an elevated blood creatinine level is a manifestation of MPS (25). This suggests that some patients may have experienced acute mesenteric artery ischemia during the perioperative period, leading to the occurrence of GIB. Our study also found a heightened risk of GIB in patients with concomitant celiac trunk and SMA hypoperfusion, further supporting the association between visceral malperfusion and adverse outcomes.

Yang *et al.* conducted a retrospective study spanning from 1996 to 2017, involving 602 patients diagnosed with acute TAAD. The overall in-hospital mortality rate for patients with mesenteric MPS (mesMPS) was 39%. Post-endovascular fenestration/stenting, 20 mesMPS patients (24%) succumbed to organ failure, 11 patients (13%) experienced fatal aortic rupture before undergoing open aortic repair, 47 patients (58%) underwent aortic repair, and 4 patients (5%) survived without requiring open repair.

Notably, there were no significant differences in operative mortality (2.1% *vs.* 7.5%; P=0.50) or long-term survival between mesMPS patients undergoing open aortic repair after recovering from mesMPS and patients without MPS (26). In conclusion, a more aggressive management approach for MPS such as thoracic aortic endovascular repair (TEVAR) or SMA revascularization may improve the survival outcomes in these patients.

Our study data demonstrated that concomitant celiac trunk and SMA hypoperfusion significantly increased the risk of GIB. Besides, advanced age and excessive transfusion might attribute to active bleeding or coagulation abnormalities.

Therefore, it is crucial to be vigilant about the occurrence of postoperative GIB in elderly patients, especially those requiring a substantial intraoperative blood transfusion (defined as exceeding 600 mL in this study), and those with preoperative abnormal blood supply to the GI tract. Continuous vigilance over postoperative stool or gastric contents is paramount in these patients, necessitating frequent assessments, such as every 4 hours within the initial 24 hours, to ensure prompt identification of GIB occurrence. Hb levels and coagulation-related indicators should be meticulously monitored every 4–6 hours throughout the perioperative period. In terms of treatment, timely supplementation of coagulation factors should be administered while avoiding hypoperfusion caused by hypotension or thrombus formation, as well as minimizing the use of vasoconstrictor drugs.

According to expert consensus on GIB, the main treatment strategy involves actively managing the primary disease while utilizing supportive, pharmacological, endoscopic, and interventional therapeutic measures to control bleeding based on individual patient conditions. Pharmacological treatment primarily consists of H_2-receptor blockers and PPIs (27,28). Further research can be conducted to ascertain whether such high-risk populations should be administered higher doses of PPIs or combination therapy to prevent bleeding. In our study, 38 patients received blood transfusion and acid suppression (high dose PPIs), with two-thirds of the patients effectively treated with conservative medical therapy.

Limitations

This study has several limitations. Firstly, it is a single-centre retrospective analysis with a limited sample size of 38 cases in the GIB group, which restricts the generalizability of the findings to other aortic surgery centres. Secondly, the site of bleeding was identified by gastroscopy in only 7 cases, while in the remaining 31 patients, the specific site of bleeding was not clearly identified. Further research is needed to investigate the site and nature of GIB in patients with postoperative AD. Thirdly, although the patients included in the study denied a history of GI diseases or recent GIB within 3 months, it cannot be completely ruled out that some patients may have had a history of peptic ulcer disease or previous bleeding prior to surgery, as early symptoms of GI diseases can be insidious. The absence of endoscopy in a substantial portion of patients is a notable limitation that may affect the overall robustness of the study.

Conclusions

GIB is a notable complication following TAAR for TAAD, and it has been linked to elevated mortality rates, prolonged ICU stays, and unfavorable prognoses. Several factors, including advanced age, extensive intraoperative transfusion, and abnormalities in GI perfusion, have been identified as potential risk factors for GIB in this specific patient population.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1752/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics committee of Guangdong Provincial People's Hospital (No. KY2023-580-01) and individual consent was waived due to the retrospective nature of the study.

References

1. Harris KM, Nienaber CA, Peterson MD, et al. Early Mortality in Type A Acute Aortic Dissection: Insights From the International Registry of Acute Aortic Dissection. JAMA Cardiol 2022;7:1009-15.
2. Feng W, Li H, Wang Q, et al. Prognostic significance of neutrophil count on in-hospital mortality in patients with acute type A aortic dissection. Front Cardiovasc Med 2023;10:1095646.
3. El-Hamamsy I, Ouzounian M, Demers P, et al. State-of-the-Art Surgical Management of Acute Type A Aortic Dissection. Can J Cardiol 2016;32:100-9.
4. Teng Cai, Fei Z, Liu H, et al. Effect of pre-operative hypoxemia on the occurrence and outcomes of post-operative ARDS in Stanford type a aortic dissection patients. Respir Res 2023;24:161.
5. Fang M, Li J, Fang H, et al. Prediction of acute kidney injury after total aortic arch replacement with serum cystatin C and urine N-acetyl-β-d-glucosaminidase: A prospective observational study. Clin Chim Acta 2023;539:105-13.
6. Chaudhry R, Zaki J, Wegner R, et al. Gastrointestinal Complications After Cardiac Surgery: A Nationwide Population-Based Analysis of Morbidity and Mortality Predictors. J Cardiothorac Vasc Anesth 2017;31:1268-74.
7. Haywood N, Mehaffey JH, Hawkins RB, et al. Gastrointestinal Complications After Cardiac Surgery: Highly Morbid but Improving Over Time. J Surg Res 2020;254:306-13.
8. Hess NR, Seese LM, Hong Y, et al. Gastrointestinal complications after cardiac surgery: Incidence, predictors, and impact on outcomes. J Card Surg 2021;36:894-901.
9. Ma WG, Zheng J, Zhang W, et al. Frozen elephant trunk with total arch replacement for type A aortic dissections: Does acuity affect operative mortality? J Thorac Cardiovasc Surg 2014;148:963-70; discussion 970-2.
10. Igarashi T, Sato Y, Satokawa H, et al. The results of an entry-oriented strategy for acute type A aortic dissection in octogenarians: an 18-year experience. Eur J Cardiothorac Surg 2020;58:949-56.
11. Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015;47:a1-46.
12. Strate LL, Gralnek IM. ACG Clinical Guideline: Management of Patients With Acute Lower Gastrointestinal Bleeding. Am J Gastroenterol 2016;111:459-74.
13. Sun L, Qi R, Zhu J, et al. Total arch replacement combined with stented elephant trunk implantation: a new "standard" therapy for type a dissection involving repair of the aortic arch? Circulation 2011;123:971-8.
14. Rodriguez R, Robich MP, Plate JF, et al. Gastrointestinal complications following cardiac surgery: a comprehensive review. J Card Surg 2010;25:188-97.
15. Rosemurgy AS, McAllister E, Karl RC. The acute surgical abdomen after cardiac surgery involving extracorporeal circulation. Ann Surg 1988;207:323-6.
16. McSweeney ME, Garwood S, Levin J, et al. Adverse gastrointestinal complications after cardiopulmonary bypass: can outcome be predicted from preoperative risk factors? Anesth Analg 2004;98:1610-7.
17. Yilmaz AT, Arslan M, Demirkilç U, et al. Gastrointestinal complications after cardiac surgery. Eur J Cardiothorac Surg 1996;10:763-7.
18. Khan TA, Bianchi C, Ruel M, et al. Differential effects on the mesenteric microcirculatory response to vasopressin and phenylephrine after cardiopulmonary bypass. J Thorac Cardiovasc Surg 2007;133:682-8.
19. Velissaris T, Tang A, Murray M, et al. A prospective randomized study to evaluate splanchnic hypoxia during beating-heart and conventional coronary revascularization. Eur J Cardiothorac Surg 2003;23:917-24; discussion 924.
20. Morgan CE, Mansukhani NA, Eskandari MK, et al. Ten-

year review of isolated spontaneous mesenteric arterial dissections. J Vasc Surg 2018;67:1134-42.
21. Hashimoto O, Saito Y, Nakayama T, et al. Prognostic Impact of Branch Vessel Involvement on Computed Tomography versus Clinical Presentation of Malperfusion in Patients With Type a Acute Aortic Dissection. Am J Cardiol 2021;152:158-63.
22. Ren Y, Zhang J, Zhou H, et al. Experience in curing refractory gastrointestinal bleeding due to type A aortic dissection combined with mesenteric artery malperfusion: a case report. Ann Palliat Med 2021;10:10102-7.
23. Czerny M, Schoenhoff F, Etz C, et al. The Impact of Pre-Operative Malperfusion on Outcome in Acute Type A Aortic Dissection: Results From the GERAADA Registry. J Am Coll Cardiol 2015;65:2628-35.
24. Kamman AV, Yang B, Kim KM, et al. Visceral Malperfusion in Aortic Dissection: The Michigan Experience. Semin Thorac Cardiovasc Surg 2017;29:173-8.
25. Norton EL, Williams DM, Kim KM, et al. Management of acute type B aortic dissection with malperfusion via endovascular fenestration/stenting. J Thorac Cardiovasc Surg 2020;160:1151-1161.e1.
26. Yang B, Norton EL, Rosati CM, et al. Managing patients with acute type A aortic dissection and mesenteric malperfusion syndrome: A 20-year experience. J Thorac Cardiovasc Surg 2019;158:675-687.e4.
27. Rodrigues A, Carrilho A, Almeida N, et al. Interventional Algorithm in Gastrointestinal Bleeding-An Expert Consensus Multimodal Approach Based on a Multidisciplinary Team. Clin Appl Thromb Hemost 2020;26:1076029620931943.
28. Xu T, Yang Y, Zhan W, et al. Predictive value of clinical features for anti-reflux therapy response in suspected gastroesophageal reflux-induced chronic cough. J Thorac Dis 2023;15:2333-43.

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