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RESEARCH ARTICLE

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Bleeding is associated with severely impaired outcomes in surgery for acute type a aortic dissection

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ABSTRACT

Background. Surgery for acute type A aortic dissection confers a risk for significant bleeding. We analyzed the impact of massive bleeding on complications after surgery for acute type A aortic dissection. *Methods*. Patients undergoing surgery for acute type A aortic dissection from the retrospective multicenter Nordic Consortium for Acute Type A Aortic Dissection (NORCAAD) database 2005–2014 were eligible. Massive bleeding was defined according to the Universal Definition of Perioperative Bleeding. The primary outcome measure was early mortality and secondary outcome measures were perioperative stroke, mechanical ventilation more than 48 h, new-onset dialysis, and intensive care unit stay. Propensity score matching was performed to adjust for differences in covariates. *Results*. Nine hundred ninety-seven patients were included, of whom 403 (40.4%) had massive bleeding. In the propensity score-matched cohort (344 pairs), patients with massive bleeding had higher 30-day mortality (17.2 versus 7.6%, $p < .001$), mechanical ventilation more than 48 h (52.8 versus 22.6%, $p < .001$), perioperative stroke (24.3 versus 14.8%, $p = .002$), new-onset dialysis (22.5 versus 4.9%, $p < .001$), and longer intensive care unit stay (6 versus 3 days, $p < .001$), compared with patients without massive bleeding. Risk factors for massive bleeding were previous cardiac surgery, preoperative clopidogrel or ticagrelor therapy, DeBakey type I dissection, and localized or generalized malperfusion. *Conclusions*. Massive bleeding in surgery for acute type A aortic dissection is associated with a markedly increased risk for severe complications as well as early death. Further improvement of surgical technique and pharmacological optimization of coagulation is paramount to possibly improve outcomes in acute type A aortic dissection repair.

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Type A aortic dissection; bleeding complications; mortality

Introduction

Acute type A aortic dissection (ATAAD) is a life-threatening condition that necessitates immediate surgical repair [1]. Outcomes after ATAAD surgery are affected by comorbidity burden and preoperative state of the patient, particularly the extent of the dissection and the presence of malperfusion [2,3]. It has been shown that ATAAD is associated with impairment of the coagulation system and surgical repair for ATAAD is generally considered to be associated with high risk for bleeding [4–6]. There are several factors contributing to the coagulopathic state in ATAAD. The contact between blood and tissue factor and collagen in the subendothelial tissue of the aortic wall causes consumption of coagulation factors and increased fibrinolysis [4,7]. Specific surgical techniques may potentiate coagulopathy. For instance, the use of extracorporeal circulation causes hemodilution, platelet activation, a decrease in platelet count, and in the concentration of fibrinogen and numerous other coagulation factors, while at the same time promoting fibrinolysis [8,9]. Also, induced hypothermia and acidosis during ATAAD repair further impairs the coagulation system by increasing platelet consumption [10,11].

Studies on the impact of bleeding on postoperative outcomes after ATAAD surgery are scarce and generally

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relatively small single-center investigations [12–14]. Risk factors for bleeding in ATAAD repair are poorly defined [12]. With data from the multicenter Nordic Consortium for Acute Type A Aortic Dissection (NORCAAD) database, our group has previously shown that preoperative treatment with antiplatelet drugs increase the risk for severe bleeding [15]. In that study, patients with major bleeding had an increased risk for major adverse events. In the current study, we further analyze the associations between massive bleeding and early mortality and major complications in patients undergoing surgery for ATAAD included in the NORCAAD database.

Methods

This is a study from the NORCAAD database; a retrospective observational, multicenter registry including patients who underwent ATAAD surgery between January 2005 and December 2014. The detailed study protocol has been published previously [16].

Ethical statement

The study was approved by the Swedish Ethical Review Authority (No. 2019-02087, 2019-04-29), waiving the need to obtain individual written informed consent.

Study population

Data were collected consecutively from eight cardiac surgery centers in four Nordic countries (Denmark, Finland, Iceland, and Sweden). Adult patients who underwent ATAAD surgery from January 2005 to December 2014 were eligible. The operation had to occur within 2 weeks of diagnosis or occurrence of symptoms. Patients who underwent repair of a chronic dissection were excluded. Intraoperative death was an exclusion criterion, since postoperative bleeding severity was not possible to classify according to the current bleeding classification in these patients. Data were collected by medical chart review.

Bleeding definition

Massive bleeding was defined according to the Universal Definition of Perioperative Bleeding (UDPB) in adult cardiac surgery [17]. UDPB has been validated in several studies and recommended for use as an outcome measure in clinical trials [18]. Although several definitions of bleeding in cardiac surgery have been suggested, the UDPB is one of the most studied [18]. The UDPB includes multiple parameters to classify perioperative bleeding, including transfusions and administration of hemostatic drugs, which differs this from other bleeding definitions. UDPB massive bleeding is defined as including one or more of the following criteria: postoperative blood loss more than 2000 ml within 12 h, 11 or more allogenic red blood cell (RBC) units transfused, 11 or more plasma units transfused, or the use of recombinant factor VIIa. UDPB severe bleeding is defined as postoperative blood loss 1000–2000 ml within 12 h, 5–10 RBC units transfused, 5–10 plasma units transfused, or resternotomy for bleeding. Moderate or less bleeding in UDPB is defined as postoperative blood loss less than 1000 ml within 12 h, no more than four RBC units transfused, or no more than four plasma units transfused.

Outcomes

The primary outcome was 30-day mortality. Secondary outcomes were perioperative stroke, mechanical ventilation more than 48 h, new-onset dialysis, and intensive care unit stay. All complications were recorded between surgical repair and hospital discharge.

Perioperative treatment

Generally, median sternotomy, extracorporeal circulation, cardioplegic arrest, and hypothermic circulatory arrest with or without cerebral perfusion were used. Perioperative strategy regarding cannulation, degree of hypothermia, cerebral perfusion and surgical technique were at the discretion of the responsible surgeons at each center. Transfusion protocols were implemented at all centers but the final decision to transfuse was a clinical decision made by the responsible physicians, as was the use of hemostatic drugs. There was no general protocol for timing of chest closure.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation or as median and interquartile range, in cases of skewed distributions. Categorical variables are expressed as frequencies and percentages. Missing data was not replaced. The variables history of smoking, body mass index, previous cardiac surgery, malperfusion, and lowest temperature had >5% missing data and for the remaining variables 1.4% ± 1.3% had missing values. In the overall cohort, outcomes were compared by independent samples *t*-test and χ^2 test for binary and categorical variables, and analysis of variance for continuous variables. To reduce selection bias, a propensity score was calculated with UDPB massive bleeding as the dependent variable. In the propensity score-matched cohort, outcomes were compared by univariate conditional logistic regression for binary and categorical variables and by paired samples *t*-test for continuous variables. The propensity score-matched cohort was constructed by nearest neighbour matching with a caliper of 0.2 and without replacement. The following variables were included as covariates: age, gender, previous cardiac surgery, chronic kidney disease, hypertension, preoperative treatment with acetylsalicylic acid, clopidogrel, ticagrelor, or warfarin, DeBakey type I dissection, organ malperfusion, Penn class, and type of distal and proximal surgical procedure. These covariates were chosen based on prior research regarding bleeding in ATAAD repair and other cardiac surgery, taking into consideration the variables available from the NORCAAD database, which was not designed with the primary aim to

assess bleeding complications. The variables age, gender, previous cardiac surgery, chronic kidney disease, hypertension, preoperative treatment with antiplatelet agents or warfarin, are all well-established risk factors for bleeding in cardiac surgery. The variables DeBakey type I dissection, organ malperfusion, Penn class, and type of distal and proximal surgical procedure has been associated with bleeding in previous studies in patients undergoing ATAAD repair [12–14]. We calculated standardized differences for variables to investigate post-match balance. A standardized difference <0.1 was considered to indicate adequate balance between variables of the cohorts. Long-term survival rates for all-cause mortality were estimated and graphed using the Kaplan–Meier method, and the log-rank test was used to compare differences between the curves. Logistic regression was performed to identify predictors for UDPB massive bleeding. All variables with $p < .2$ in univariable analysis (age, diabetes mellitus, chronic kidney disease, previous cardiac surgery, acetylsalicylic acid, ticagrelor or clopidogrel, warfarin, DeBakey type I, and localized or generalized malperfusion; Penn class) were included in the multivariable model. Odds ratios with 95% confidence intervals were reported. A two-sided p value of <.05 was considered to indicate statistical significance. Analyses were performed using Stata v.17.1 statistical software (StataCorp LP, College Station, Texas, USA).

Results

We included 997 patients who underwent surgery for acute type A aortic dissection, of whom 403 (40.4%) had massive bleeding. Operative risk assessed with EuroSCORE II was higher in the massive bleeding group (Table 1). Patients with massive bleeding had longer extracorporeal circulation duration (228 ± 86 vs. 186 ± 52; $p < .001$), aortic cross clamp duration (113 ± 61 vs. 97 ± 47; $p < .001$), and hypothermic circulatory arrest duration (31 ± 19 vs. 28 ± 16; $p = .023$). The total procedure duration was longer in the massive bleeding group (433 ± 146 vs. 317 ± 82; $p < .001$). The incidence of massive bleeding was higher in the early surgical era (2005–2009) versus the later era (2010–2015), 47.1% versus 37.5%; $p = .004$. In the propensity score-matched cohort (344 pairs), patient and procedural characteristics were well balanced (Figure 1).

Table 1. Patient characteristics and surgical procedure.

	Overall cohort			Propensity score-matched cohort		
	Massive bleeding $n = 403$	No massive bleeding $n = 594$	Standardized difference	Massive bleeding $n = 344$	No massive bleeding $n = 344$	Standardized difference
Age, years	62.5 ± 10.8	61.1 ± 12.4	0.1225	61.9 ± 11.1	62.9 ± 11.8	0.0816
Female sex	124 (30.8%)	202 (34.0%)	0.0692	105 (30.5%)	117 (34.0%)	0.0747
Body mass index, kg/m^2	26.6 ± 4.6	26.8 ± 4.8	0.0371	26.6 ± 4.6)	26.8 ± 4.8	0.0501
Hypertension	225 (55.8%)	285 (48.0%)	0.0690	185 (53.8%)	163 (47.4%)	0.0470
Diabetes mellitus	11 (2.7%)	8 (1.3%)	0.0980	9 (2.6%)	3 (0.9%)	0.1335
Hyperlipidemia	43 (10.8%)	67 (11.3%)	0.0175	32 (9.3%)	39 (11.3%)	0.0669
Prior stroke	15 (3.7%)	23 (3.9%)	0.0079	12 (3.5%)	16 (4.7%)	0.0589
Chronic kidney disease	11 (2.7%)	6 (1.0%)	0.1272	5 (1.5%)	6 (1.7%)	0.0232
Chronic obstructive pulmonary disease	24 (6.0%)	30 (5.1%)	0.0397	18 (5.2%)	20 (5.8%)	0.0255
EuroSCORE II	9.1 (3.5-12.7)	7.0 (3.1-12.0)	0.2359	8.8 (3.3, 12)	7.4 (3.5, 13)	0.0548
History of smoking	144 (46.2%)	182 (41.5%)	0.0948	125 (46.8%)	95 (40.1%)	0.1361
History of aortic aneurysm	14 (4.8%)	19 (4.5%)	0.0139	14 (5.7%)	11 (4.3%)	0.0632
Bicuspid aortic valve	21 (5.2%)	38 (6.5%)	0.0517	19 (5.5%)	16 (4.7%)	0.0385
Previous cardiac surgery	23 (5.7%)	11 (1.9%)	0.2032	6 (1.7%)	9 (2.6%)	0.0597
Acetylsalicylic acid	125 (31.1%)	147 (25.0%)	0.1360	102 (29.7%)	105 (30.5%)	0.0190
Clopidogrel or ticagrelor	63 (15.7%)	53 (9.0%)	0.2035	45 (13.1%)	46 (13.4%)	0.0086
Warfarin	38 (9.5%)	28 (4.8%)	0.1830	25 (7.3%)	27 (7.8%)	0.0220
DeBakey type I	323 (80.1%)	413 (69.5%)	0. 2466	273 (79.4%)	262 (76.2%)	0.0770
Intramural hematoma	28 (6.9%)	53 (8.9%)	0.0731	22 (6.4%)	27 (7.8%)	0.0565
Penn class			0.3587			0.0786
Aa	184 (45.7%)	373 (62.8%)		169 (49.1%)	158 (45.9%)	
Ab	110 (27.3%)	124 (20.9%)		98 (28.5%)	100 (29.1%)	
Ac	82 (20.3%)	75 (12.6%)		56 (16.3%)	65 (18.9%)	
Abc	27 (6.7%)	22 (3.7%)		21 (6.1%)	21 (6.1%)	
Proximal surgical technique			0.0664			0.0285
Supracoronary graft	295 (73.4%)	453 (76.3%)		258 (75.0%)	262 (76.2%)	
Biological or mechanical composite graft	94 (23.4%)	124 (20.9%)		75 (21.8%)	72 (20.9%)	
Valve-sparing root replacement	13 (3.2%)	17 (2.9%)		11 (3.2%)	10 (2.9%)	
Distal surgical technique			0.0858			0.0263
Ascending aorta	283 (71.6%)	424 (72.0%)		250 (72.7%)	252 (73.3%)	
Hemiarch procedure	85 (21.5%)	136 (23.1%)		75 (21.8%)	75 (21.8%)	
Total arch procedure	27 (6.8%)	29 (4.9%)		19 (5.5%)	17 (4.9%)	
Lowest core temperature			0.0277			0.0425
<20 °C	189 (51.8%)	273 (50.6%)		167 (53.5%)	162 (51.4%)	
20–28 °C	142 (38.9%)	217 (40.3%)		119 (38.1%)	125 (39.7%)	
>28 °C	34 (9.3%)	49 (9.1%)		26 (8.3%)	28 (8.9%)	

Data are mean ± standard deviation, n (%), or median (interquartile range). EuroSCORE = European System for Cardiac Operative Risk Evaluation.

Primary outcome measure

Postoperative outcome data are presented in Table 2. Thirty-day mortality was higher in patients with massive bleeding both in the overall (19.6 versus 6.4%, $p < .001$) as well as the propensity score-matched cohort (17.2 versus 7.6%, $p < .001$).

Secondary outcome measure

The secondary outcome measures (mechanical ventilation more than 48 h, perioperative stroke, new-onset dialysis, and longer intensive care unit stay) were more common in the massive bleeding group (propensity score-matched

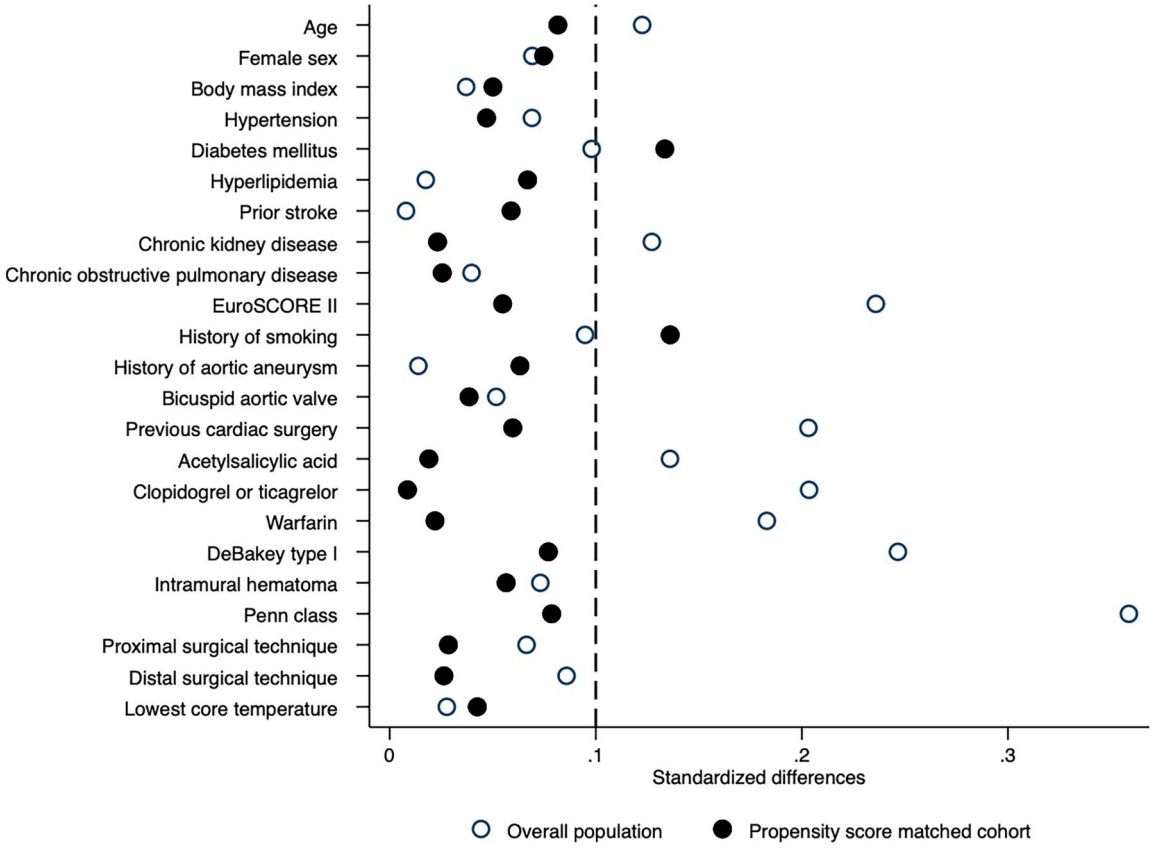

Figure 1. Standardized differences for variables in the overall population and in the propensity score matched cohort.

Table 2. Postoperative outcomes.

	Overall cohort			Propensity score-matched cohort		
	Massive bleeding $n = 403$	No massive bleeding $n = 594$	*p*-value	Massive bleeding $n = 344$	No massive bleeding $n = 344$	*p*-value
Perioperative stroke	97 (24.2%)	70 (11.8%)	<.001	83 (24.3%)	51 (14.8%)	.002
Postoperative coma	64 (17.5%)	34 (6.4%)	<.001	53 (17.0%)	27 (8.8%)	.002
Perioperative myocardial infarction	35 (8.8%)	26 (4.4%)	.005	33 (9.7%)	20 (5.8%)	.060
Mechanical ventilation > 48 h	218 (55.6%)	124 (21.1%)	<.001	178 (52.8%)	77 (22.6%)	<.001
Postoperative cardiac arrest	35 (8.9%)	15 (2.5%)	<.001	28 (8.3%)	11 (3.2%)	.004
New-onset dialysis	93 (23.2%)	28 (4.7%)	<.001	77 (22.5%)	17 (4.9%)	<.001
Septicemia	72 (18.0%)	35 (5.9%)	<.001	60 (17.6%)	25 (7.3%)	<.001
Deep sternal wound infection	8 (2.0%)	16 (2.7%)	.51	8 (2.4%)	12 (3.5%)	.39
Intensive care unit stay, days	6 (3-13)	3 (2-5)	<.001	6 (3, 13)	3 (2, 5)	<.001
30-day mortality	79 (19.6%)	38 (6.4%)	<.001	59 (17.2%)	26 (7.6%)	<.001
Bleeding-related outcomes						
12-hour chest tube output, ml	1150 (530–2010)	470 (340–700)	<.001	1060 (510–2020)	500 (340–730)	<.001
Resternotomy for bleeding	157 (39.0%)	68 (11.4%)	<.001	138 (40.1%)	46 (13.4%)	<.001
Postoperative cardiac tamponade	113 (28.2%)	41 (6.9%)	<.001	96 (28.1%)	24 (7.0%)	<.001
Transfusions						
Red blood cell units	13 (9–20)	4 (2–6)	<.001	13 (9–19)	4 (2–6)	<.001
Platelet units	4 (2–8)	2 (1–4)	<.001	4 (2–8)	2 (1–4)	<.001
Plasma units	12 (6–21)	3 (2–5)	<.001	12 (6–20)	3 (2–6)	<.001
Hemostatic drugs						
Recombinant factor VIIa	169 (41.9%)	0	<.001	148 (43.0%)	0 (0.0%)	<.001
Fibrinogen concentrate	236 (70.4%)	225 (51.6%)	<.001	200 (69.4%)	130 (52.2%)	<.001
Tranexamic acid	291 (72.8%)	248 (79.5%)	.038	210 (78.9%)	169 (72.5%)	.094
Aprotinin	33 (11.3%)	69 (17.6%)	.021	28 (11.1%)	39 (17.0%)	.059

Data are mean ± standard deviation, n (%), or median (interquartile range).

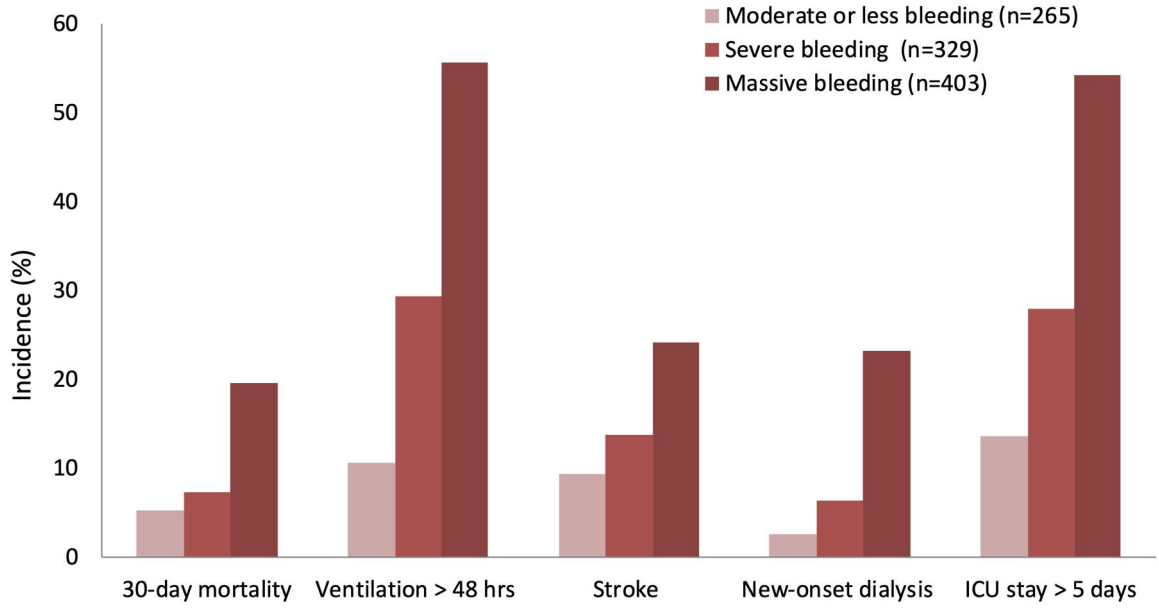

Figure 2. Incidence of 30-day mortality, mechanical ventilation more than 48 h, perioperative stroke, new-onset dialysis, and ICU stay more than 5 days in the overall cohort according to UDPB bleeding class. ICU: intensive care unit, UDPB: Universal Definition of Perioperative Bleeding.

cohort: mechanical ventilation more than 48 h (52.8 versus 22.6%, $p < .001$), perioperative stroke (24.3 versus 14.8%, $p = .002$), new-onset dialysis (22.5 versus 4.9%, $p < .001$), and longer intensive care unit stay (6 versus 3 days, $p < .001$)). Outcomes per UDPB bleeding class are presented in Figure 2.

Long-term mortality

Long-term all-cause cumulative mortality was higher in patients with massive bleeding compared with patients without massive bleeding (Figure 3). There was no difference in long-term mortality between the two groups when analyzed conditional on 60-day survival (defined as surviving the first 60 days after the date of surgery; Figure 4).

Risk factors for massive bleeding

Multivariable logistic regression identified previous cardiac surgery, preoperative clopidogrel or ticagrelor therapy, DeBakey type I, and localized or generalized malperfusion (Penn class) as independent risk factors for massive bleeding (Table 3 and Figure 5).

Discussion

This study demonstrates the detrimental consequences of perioperative bleeding and the necessity to avoid this in order to improve patient outcomes in ATAAD surgery. The effect size of bleeding on the primary (early mortality) as well as the secondary outcome measures (perioperative stroke, mechanical ventilation more than 48 h, new-onset dialysis, and intensive care unit stay) was very high. Bleeding has previously been identified as the cause of death in up to one fifth of deaths following ATAAD surgery [19]. Although repair of ATAAD is a quite extensive surgical procedure, it has been shown that severe bleeding can be avoided in the majority of cases [14, 20]. Indeed, in the current report, the incidence of massive bleeding was higher in the early surgical era versus the later era, indicating that bleeding is a modifiable outcome. In coronary and heart valve surgery, the surgeon has been identified as an important risk factor for re-exploration for bleeding and technical factors is responsible for bleeding in the majority of cases [21]. As for other complex cardiac surgical procedures, ATAAD repair performed by higher-vs. lower-volume surgeons has been shown to have superior outcomes [20, 22, 23]. To concentrate ATAAD surgery to a limited number of high-volume surgeons may be strongly recommended but may be difficult to achieve in low-volume centers.

Our group has previously shown that preoperative treatment with antiplatelet drugs before ATAAD repair increase the risk for severe bleeding [15]. In that study, patients with major bleeding had an increased risk for postoperative complications. In the current study, using the same NORCAAD data cohort, we strive to further analyze the association between massive bleeding and major complications. By using propensity score matching and the UDPB classification, the current study adds to the evidence on the association between massive bleeding and severely impaired outcomes after ATAAD repair.

ATAAD repair is complicated by the disturbance of the coagulation system inherent to the disease. The contact between blood and tissue factor and collagen in the false lumen causes a depletion of platelets and coagulation factors [4, 7]. However, surgical strategy employed may potentiate or mitigate the coagulopathy. The use of extracorporeal circulation causes hemodilution, platelet activation, and fibrinolysis [8, 9]. Therefore, short procedural times are desired and a limited proximal and distal repair strategy might enable this. Induced hypothermia and acidosis during

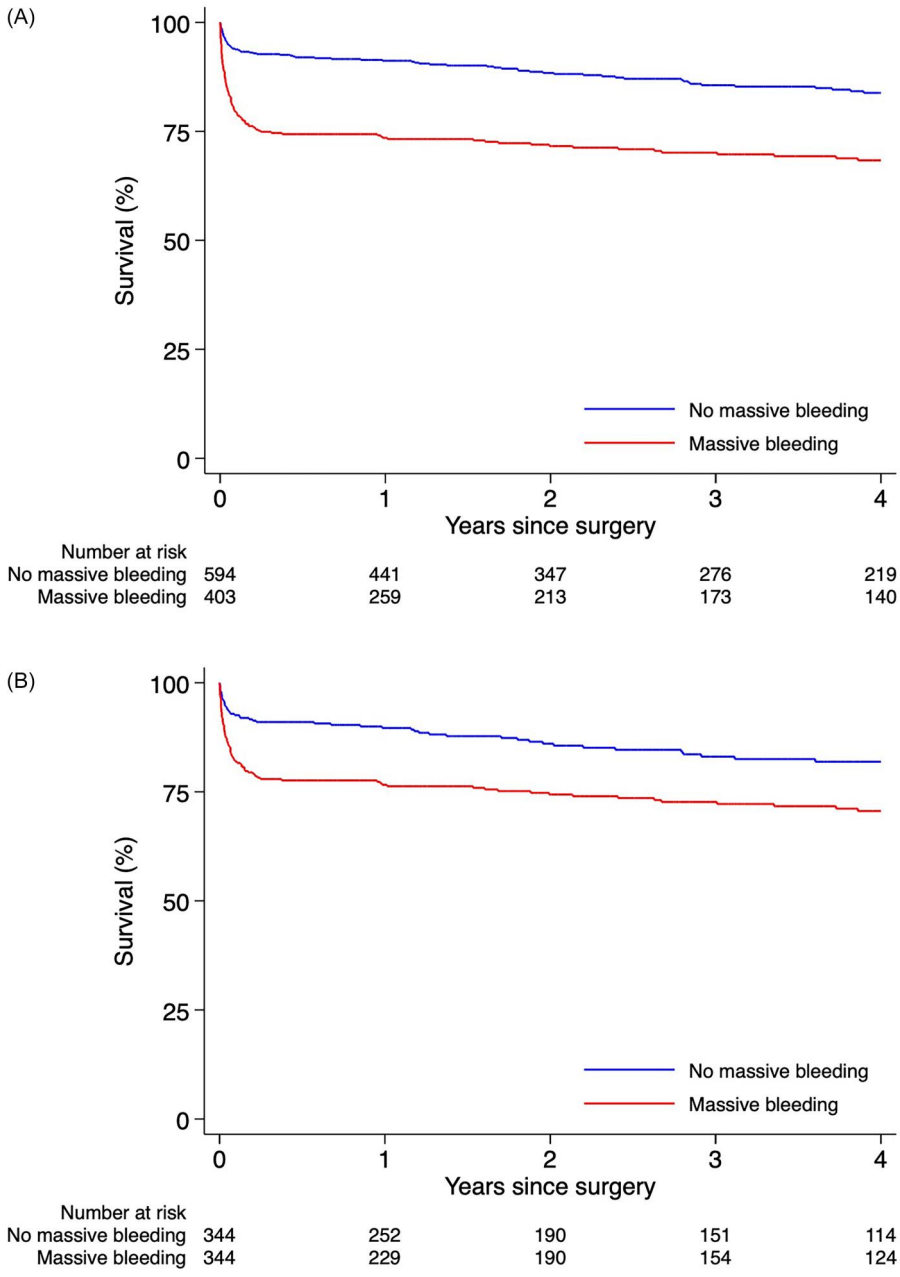

Figure 3. Survival in patients after surgery for acute type a aortic dissection with massive bleeding compared with patients without massive bleeding. The upper panel shows the overall population ($p < .001$) and the lower panel shows the propensity score matched cohort ($p < .001$).

ATAAD repair impair the coagulation system further [10, 11]. The choice of target temperature is dependent of the strategy of cerebral protection. Use of selective antegrade cerebral perfusion will permit moderate hypothermia and it could be hypothesized that this may thereby be preferred [14, 20].

Few studies have investigated the impact of bleeding in ATAAD repair [12–14]. Previous studies in general cardiac surgery have demonstrated major bleeding to be associated with thromboembolic complications and infections [24]. Major bleeding is associated with hemodynamic instability and malperfusion which might be enhanced by the use of vasoconstrictive drugs. The use of hemostatic drugs and transfusion of allogenic blood may lead to thromboembolic events and end-organ ischemia [24]. In the current study, the use of hemostatic drugs and amount of allogenic blood products transfused were very high in patients with massive bleeding. Since there are intercorrelations between bleeding, administration of hemostatic drugs, and transfusion of allogenic blood products, it is hard to tell how each of these parameters are related to adverse outcomes [21,24,25].

Risk factors for massive bleeding included previous cardiac surgery and preoperative clopidogrel or ticagrelor therapy, which are established risk factors for perioperative bleeding [15,26,27]. A recent study found that recent intake of direct oral anticoagulants was associated with an increased risk of bleeding in patients undergoing ATAAD repair [13]. Since the number of patients on direct oral anticoagulants was very low in the current cohort, this was not possible to study. Also preoperative malperfusion and extent

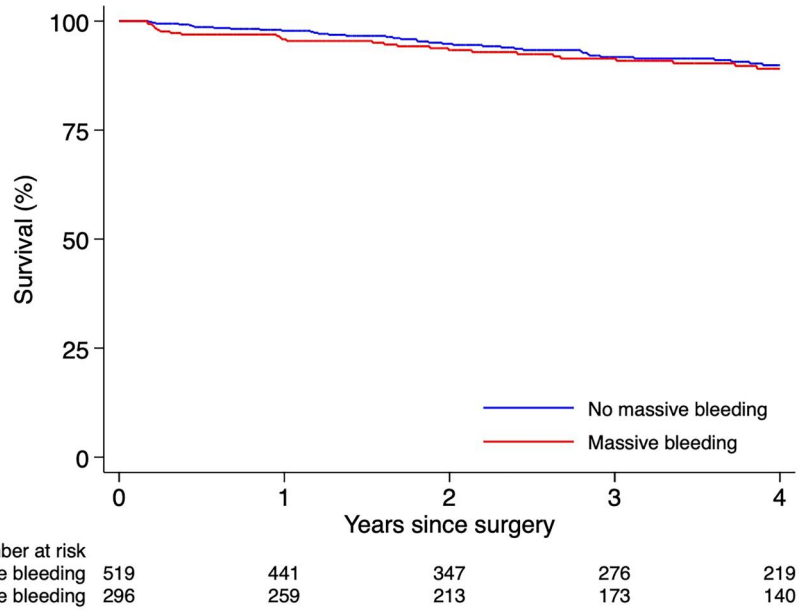

Figure 4. Survival in patients after surgery for acute type a aortic dissection with massive bleeding compared with patients without massive bleeding, conditional on 60-day survival in the overall population ($p = .46$).

Table 3. Univariable and multivariable predictors of massive bleeding in surgery for type a aortic dissection.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*-value	OR (95%CI)	*p*-value
Age (per 10-year increase)	1.11 (0.99–1.24)	.062	1.10 (0.98–1.24)	.123
Female sex	0.86 (0.66–1.13)	.285	–	
Body mass index (per unit increase)	0.99 (0.96–1.02)	.593	–	
Hypertension	1.15 (0.89–1.49)	.290	–	
Diabetes mellitus	2.06 (0.82–5.16)	.125	1.93 (0.72–5.13)	.190
Hyperlipidemia	0.95 (0.63–1.42)	.787	–	
Prior stroke	0.96 (0.49–1.86)	.903	–	
Chronic kidney disease	2.75 (1.01–7.50)	.048	2.13 (0.74–6.13)	.160
Chronic obstructive pulmonary disease	1.19 (0.69–2.07)	.536	–	
History of smoking	1.21 (0.90–1.62)	.201	–	
History of aortic aneurysm	1.07 0.53–2.17	.854	–	
Bicuspid aortic valve	0.80 (0.46–2.17)	.854	–	
Previous cardiac surgery	3.21 (1.55–6.66)	.002	**3.54 (1.53–8.21)**	**.003**
Acetylsalicylic acid	1.35 (1.02–1.79)	.035	1.19 (0.84–1.68)	.327
Clopidogrel or ticagrelor	1.88 (1.27–2.77)	.002	**1.90 (1.19–3.03)**	**.008**
Warfarin	2.08 (1.26–3.46)	.004	1.54 (0.88–2.70)	.128
DeBakey type I	1.77 (1.31–2.39)	<.001	**1.86 (1.34–2.58)**	**<.001**
Intramural hematoma	0.76 (0.47–1.23)	.264	–	
Penn class				
Aa (Reference)	1.00		1.00	
Ab	1.80 (1.32–2.46)	<.001	**1.68 (1.21–2.33)**	**.002**
Ac	2.22 (1.55–3.18)	<.001	**2.48 (1.71–3.62)**	**<.001**
Abc	2.49 (1.38–4.49)	.002	**2.40 (1.31–4.42)**	**.005**
Proximal surgical technique				
Supracoronary graft (Reference)	1.00		–	
Biological or mechanical composite graft	1.16 (0.86–1.58)	.330	–	
Valve-sparing root replacement	1.17 (0.56–2.45)	.669	–	
Distal surgical technique				
Ascending aorta (Reference)	1.00		–	
Hemiarch procedure	0.94 (0.69–1.28)	.678	–	
Total arch procedure	1.39 (0.81–2.41)	.232	–	
Lowest core temperature				
<20 °C (Reference)	1.00		–	
20–28 °C	0.95 (0.71–1.25)	.695	–	
>28 °C	1.00 (0.62–1.61)	.993	–	

CI: confidence interval; OR: Odds ratio.

of aortic dissection were risk factors for massive bleeding in the current study. The contact between blood and subendothelial tissue in the aortic wall causes consumption of coagulation factors and increased fibrinolysis, which resembles disseminated intravascular coagulation [4]. It has been hypothesized that increased false lumen extent, and thereby more exposed subendothelial tissue, might lead to increased coagulopathy [12]. This could explain why

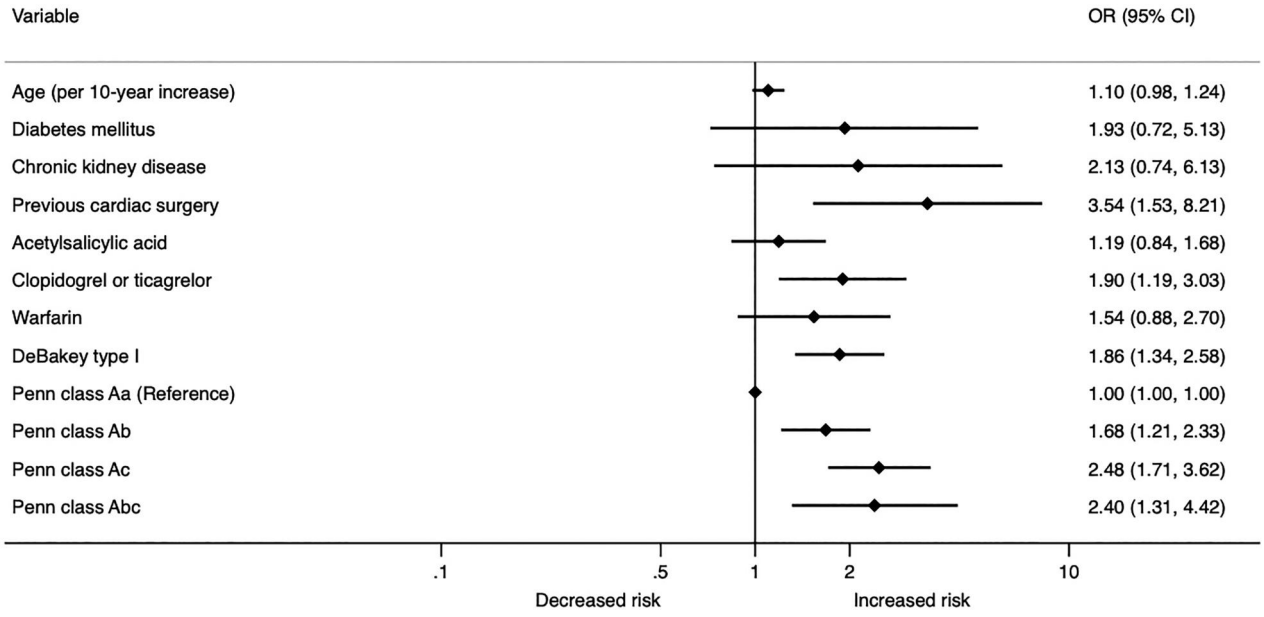

Figure 5. Multivariate adjusted odds ratios and 95% confidence intervals for massive bleeding in patients who underwent surgery for type a aortic dissection. CI: confidence interval; ECC: extracorporeal circulation; OR: odds ratio.

DeBakey type I dissection was associated with increased risk for bleeding in the present study, which has also been shown in a previous study [12]. Another previous study found that patients with massive bleeding after ATAAD repair had preoperative increased D-dimer levels and fibrin degradation products [14], indicative of a more widespread dissection, since level of D-dimer increase is associated with the severity of the extent of the dissection.

Acidosis is known to induce coagulopathy which could explain why malperfusion was a risk factor for massive bleeding. Meticulous surgical technique is especially important in ATAAD patients presenting with risk factors for bleeding such as previous cardiac surgery, preoperative dual antiplatelet therapy, preoperative malperfusion, and extent and severity of the aortic dissection. Coagulation point-of-care testing and possible optimization with hemostatic medication should always be used.

Limitations

Residual confounding might be present even after propensity score matching. Transfusion protocols were implemented at all centers but no general protocols for transfusion policy, administration of hemostatic drugs, closing of the chest, or indication for reoperation for bleeding were used. In order to be able to compare bleeding-related outcomes between centers that used different bleeding management protocols, we used a composite primary outcome (UDPB massive bleeding) that includes multiple parameters to classify perioperative bleeding. Furthermore, we did not have information about pre- or postoperative coagulopathy laboratory or point-of-care testing.

Conclusions

Massive bleeding in ATAAD repair was associated with a markedly increased risk for severe complications. Further improvement of surgical technique is paramount to prevent excessive bleeding and thereby possibly improve outcomes in ATAAD repair.

Disclosure statement

There are no conflicts of interest to be reported.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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