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Transfusion and coagulation management in acute type A aortic dissection

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ABSTRACT

Background: In acute type A dissection, the coagulation system is impaired by the dissection and its complications as well as the use of the heart-lung machine with hypothermia. Because of the critical importance of effective haemostasis at the end of the operation, the use of coagulation products and blood transfusions is usually unavoidable.
Aim: This retrospective study aims to analyse the use of blood products and coagulation factors in the context of acute aortic dissections, and the factors influencing their use.
Methods: Between 2017 and 2022, 369 patients were operated on for acute type A dissection. Clinical details, including the status at presentation and perioperatively administered transfusions and coagulation factors were obtained, and patients were stratified according to the Penn classification. A multivariable linear regression analysis for transfusions and coagulation factors was conducted, including typical risk factors.
Results: The use of perioperatively required transfusions and coagulation factor (prothrombin complex concentrate and fibrinogen) substitution increased significantly with a higher ischaemic burden, including both localized and generalized malperfusion (Penn A < B < C < BC; $P \leq 0.017$). Multivariable linear regression analysis revealed that, besides generalized ischaemia, duration of cardiopulmonary bypass, extent of surgery and patient size were other significant factors.
Conclusions: Surgical repair for acute type A dissection remains major surgery, requiring transfusions and coagulation factors in almost all patients. The ischaemic burden was identified as the most important factor that necessitates the use of these products, and was associated with early death. With proper management, acceptable rethoracotomy and chest drain rates with good clinical outcomes can be achieved.

1. Abbreviations

AAD	acute type A aortic dissection
BSA	body surface area
CPB	cardiopulmonary bypass
FFP	fresh frozen plasma
HCA	hypothermic circulatory arrest
ICU	intensive care unit
PCC	prothrombin complex concentrate
pRBC	packed red blood cells

2. Background

In acute type A aortic dissection (AAD), blood in the false lumen interacts with the unendothelialized wall layers of the aorta. This exposition to the extracellular matrix is known to activate coagulation pathways, with increased consumption of coagulation factors and platelets [1,2].

Surgical therapy for AAD, requiring heparin administration, cardiopulmonary bypass (CPB) and hypothermic circulatory arrest (HCA) with subsequent rewarming, further affects coagulation pathways and balance. Haemostasis at the end of the surgery is crucial, as reexploration for bleeding is known to be a significant risk factor for early death [3]. Therefore, substitution of coagulation factors and blood transfusions are routinely required in aortic dissection surgery, both intraoperatively and in the early postoperative period [4]. However, blood transfusions, including packed red

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blood cells (pRBCs) and platelets, have been shown to be associated with kidney injury, prolonged ventilation and in-hospital death [5–9]. Additionally, less restrictive platelet transfusions preventing thrombocytopoenia have been demonstrated to decrease the frequency of early death [10]. The retrospective design of these studies does not allow conclusions to be made regarding a causal relationship, as the aortic dissection itself and the resulting haemodynamic impairment might act as confounding variables.

There is only limited evidence regarding the haemostatic management of patients with AAD. The 2024 European Association for Cardio-Thoracic Surgery/Society of Thoracic Surgeons (EACTS/STS) guidelines recommend avoidance of hypofibrinogenaemia and thrombocytopoenia in patients with clinical signs of bleeding, laboratory and point-of-care thromboelastography for coagulation monitoring and implementation of transfusion strategies in accordance with patient blood management [1].

This retrospective study investigates the impact of the haemodynamic status of patients with AAD, as stratified by the Penn classification, on the quantity of transfusions and coagulation factor substitution [11]. Additionally, a multivariable regression analysis was conducted to quantify the influence of several demographic, preoperative and operative variables on the need for blood transfusions and coagulation factor substitution.

3. Methods

3.1. Patients and variables

All cases of surgically treated AAD between January 2017 and December 2022 were identified from our institutional aortic database, and these consecutive cases were included in this study. Cases in which the diagnosis of AAD was ultimately not confirmed or the patient died before surgery were not included.

Demographics, co-morbidities, preoperative clinical status, surgical details and postoperative course and complications were obtained from clinical records. Localized malperfusions were diagnosed if specific clinical, diagnostic or radiological signs of static or dynamic localized malperfusion were present. Adequate perfusion of an organ system from the false lumen or the mere presence of a dissection membrane in a serving artery were not regarded as malperfusion. The diagnosis of circulatory shock was based on several criteria, including hypotension, tachycardia and clinical signs of generalized malperfusion [12]. The durations of CPB, cross-clamping and HCA, as well as the lowest body temperature during HCA, were obtained from anaesthesia and perfusion protocols. The surgical report was used to gather data on the extent of the surgery, including root and arch replacements.

Administered blood transfusions and substituted coagulation factors during the surgery and within the first 48 hours were obtained from anaesthesia protocols and intensive care unit (ICU) and general ward files. Blood transfusions consisted of 250 mL units of pRBCs, fresh frozen plasma (FFP) and platelets, and the coagulation factors recorded for this analysis were fibrinogen and prothrombin complex concentrate (PCC). Chest drain rates within the first 48 hours were also obtained from the ICU and general ward files.

Intraoperative death was defined as death during the procedure in the operating theatre, and was obtained from surgical documentation. Further outcome variables, including in-hospital death, the duration of postoperative ICU and hospital stay, number of patients undergoing reexploration due to bleeding (rethoracotomy) and neurological status at discharge, were obtained from hospital records. The presence of kidney failure requiring new onset dialysis and expected long-term ventilation necessitating tracheotomy were gathered from ICU records. As our standard of care includes postoperative outpatient follow-up visits, our institutional database contains information about the survival or death of patients after discharge. Mid-term survival was computed using these data.

In accordance with the Declaration of Helsinki, this study was approved by the institutional ethics committee of the medical association of the state of Rheinland-Pfalz (2018-13574-Epidemiologie) on 09 August 2018 and informed patient consent was waived because of the retrospective study design.

3.2. Surgical procedure

The surgical procedure varied depending on the underlying pathology, the clinical condition of the patient and the surgical team; nevertheless, the routine approach can be described as follows. Anaesthesiologic monitoring and instrumentation routinely included a central venous catheter, arterial lines in both radial arteries and one femoral artery, near-infrared spectroscopy (NIRS; Medtronic, Minneapolis, MN, USA) to monitor cerebral oxygenation and a temperature probe in the Foley catheter for core body temperature monitoring. Patients were intubated using videolaryngoscopy after induction of anaesthesia with propofol, sufentanil and rocuronium. Anaesthesia was sustained with sevoflurane before switching to intravenous propofol and sufentanil at the onset of CPB. Additionally, intraoperative transoesophageal echocardiography was performed. In haemodynamically stable patients with non-dissected supra-aortic vessels, the right subclavian artery was used in preference for cannulation. In haemodynamically unstable patients or those with dissected supra-aortic vessels, a direct true lumen cannulation of the ascending aorta or proximal aortic arch was performed after sternotomy. Following the initiation of CPB, the patient was cooled towards the desired target temperature. After cardiac arrest, the root was inspected and, if necessary, a replacement was prepared. However, this was interrupted upon reaching the target temperature to perform either an open distal anastomosis or aortic arch replacement utilizing the frozen elephant trunk technique in low moderate hypothermic circulatory arrest. After completing the distal anastomosis, rewarming was started and the proximal part of the aortic repair was concluded. CPB weaning was initiated once sufficient reperfusion and a target temperature of 36.5 °C was achieved. After protamine administration, in accordance with the initial heparin dose, and surgical haemostasis, transfusions and coagulation factor substitution were performed as necessary for sufficient haemostasis. Following closure of the sternum and surgical wound, the patient was transferred to the ICU for further monitoring and treatment. In case of persisting true lumen compression in the descending thoracic aorta resulting in malperfusion of downstream organs, the patient was evaluated for thoracic endovascular aortic repair. If, instead, the malperfusion was caused by a localized vessel pathology (e.g. stenosis), interventional and surgical treatment options were considered.

3.3. Statistical analysis

The patients were stratified according to the ischaemic burden at presentation, as assessed by the Penn classification, and a descriptive comparison of the obtained demographic, preoperative, operative and postoperative variables between these groups was performed. According to the Penn classification, patients without shock and without malperfusion were assigned to Group A, patients with malperfusion were assigned to Group B, patients with shock were assigned to Group C and patients with both shock and malperfusion were assigned to Group BC [11,13–15].

A multivariable linear regression model for the administered transfusions and coagulation factors was computed using Wizard

Pro data analysis, version 1.9.7 (Evan Miller, Chicago, IL, USA). The included variables were selected to characterize the patients and the expected ischaemic burden; these contained age and sex as demographic variables, body surface area (BSA) as a surrogate variable for total blood volume and whether oral anticoagulation had been prescribed before surgery, to factor in its influence on the physiological coagulation systems. To account for the ischaemic burden caused by the aortic dissection, the Penn classification was included, and to account for the ischaemic burden caused by the surgery, the duration of CPB and HCA, the lowest body temperature and the extent of the procedure (root and arch replacement) were included.

The collected data were acquired and stored in a Microsoft Access 2016 database (Microsoft, Redmond, WA, USA), and were exported as a Microsoft Excel 2016 file. Statistical analysis was performed using IBM SPSS Statistics, version 27 (IBM, Armonk, NY, USA) and Wizard Pro data analysis. Survival times were illustrated using Kaplan-Meier curves created with GraphPad Prism, version 10 (GraphPad Software, Boston, MA, USA).

We performed univariate comparisons of the obtained variables between the different Penn groups. The χ^2 test or Fisher's exact test was used to compare discrete variables, as appropriate. After assessing normal distribution using the Shapiro-Wilk test and homogeneity of variance using Levene's test, continuous variables were compared using analysis of variance (ANOVA), or the Kruskal-Wallis test if any condition was not met. For comparisons of continuous variables between two groups, Student's *t* test was used. Mid-term survival was illustrated using Kaplan-Meier curves, and was compared between groups using the log-rank test. Kaplan-Meier curves were truncated when the remaining patients at risk were fewer than 10. All statistical tests were two-sided, with an alpha level of 0.05 for statistical significance and a 95% confidence interval. Continuous data are presented as the mean ± standard deviation, frequency data as absolute number (percentage) and survival as percentage (95% confidence interval).

4. Results

4.1. Patient demographics and preoperative status

In total, 369 consecutive cases of surgically treated AAD were identified and included over the 6-year period. The study cohort included 281 patients (76%) with DeBakey type I dissection and 88 patients (24%) with DeBakey type II dissection. The mean age was 65.5 ± 13.1 years, and 235 patients (64%) were male. The median follow-up was 1.8 (1.5–2.1) years.

Arterial hypertension (70%) was the most prevalent risk factor and co-morbidity. Further typical cardiovascular co-morbidities included smoking history (21%), coronary artery disease (18%), chronic obstructive pulmonary disease (12%) and diabetes mellitus (7%). Preoperative oral anticoagulation had been prescribed in 14% of patients, consisting mainly of apixaban, rivaroxaban or phenprocoumon. Patient demographics and co-morbidities, compared between the different Penn groups, are shown in Table 1.

Patients with localized malperfusion (Penn B and Penn BC) presented significantly more often with DeBakey type I dissection ($P < 0.001$), and were younger ($P = 0.006$). Significantly more female patients were found in the Penn A and Penn C groups, whereas three quarters of the Penn B (74.3%) and Penn BC (74.6%) groups were male ($P < 0.001$).

Almost half of the patients (47.7%) showed localized malperfusion of at least one organ system, with cerebral malperfusion being the most common, followed by peripheral and coronary malperfusion.

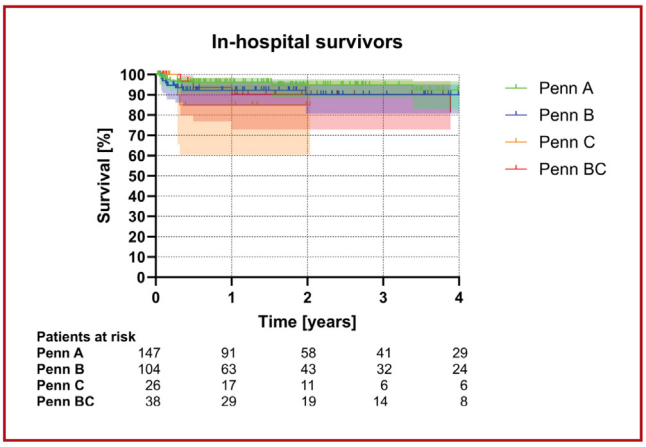


Fig. 1. Mid-term survival of in-hospital survivors after surgically treated acute type A aortic dissection, stratified by ischaemic burden as assessed by the Penn classification.

4.2. Surgery

In line with our centre's surgical strategy, the surgical approach was chosen according to the patient's haemodynamic status, extension of the dissection, need for malperfusion treatment and life expectancy. This resulted in significantly more frequent arch replacement in patients with localized malperfusion due to cerebral malperfusion or true lumen collapse (Penn B), whereas patients with isolated shock (Penn C) were preferably treated with hemiarch replacement ($P = 0.029$; Table 2). The isolated proximal repair without circulatory arrest was only used in few selected cases with localized DeBakey type II dissection (29 cases, 7.9%).

Penn B, Penn C and Penn BC patients had significantly longer CPB ($P < 0.001$) and cross-clamp ($P = 0.005$) times and colder core body temperatures during HCA ($P = 0.002$) compared with Penn A patients. The duration of HCA itself did not show significant differences between the Penn groups.

Whereas Penn A and Penn C groups had similar rates of complete arch replacement (Penn A, 30.8%; Penn C, 29.7%), CPB duration (202 ± 75 vs. 242 ± 80 minutes; $P < 0.001$) and cross-clamp times (115 ± 46 vs. 128 ± 46 minutes; $P = 0.005$) were significantly longer in the Penn C group.

Although concomitant thoracic endovascular aortic repair procedures tended to be required more often in patients with localized malperfusion (Penn B, 4.4%; Penn BC, 6.3%) than in those without (Penn A, 1.9%; Penn C, 2.7%), this difference did not reach statistical significance ($P = 0.35$). Other concomitant procedures, such as aortic valve repair or replacement, root replacement or coronary artery bypass grafting, were mostly equally distributed across all Penn groups.

4.3. Outcome and survival

Postoperative complications, including renal failure requiring dialysis ($P = 0.009$) and the need for long-term ventilation requiring tracheotomy ($P = 0.007$), occurred more frequently in patients with shock and/or malperfusion (Penn B, Penn C and Penn BC).

The in-hospital death rate was significantly higher in Penn BC (40%) and Penn C (30%) patients compared with Penn B (8%) or Penn A (6%) patients ($P < 0.001$).

As an association between Penn class and early death was already observed, the mid-term analysis focused on hospital survivors. The survival of these patients did not reveal significant differences between the Penn classes ($P = 0.43$; Table 3, Fig. 1).

Table 1
Patient demographics and status at presentation.

Variable	Total ($n=369$)	Penn A ($n=156$)	Penn B ($n=113$)	Penn C ($n=37$)	Penn BC ($n=63$)	P
DeBakey						<0.001
Type I	281 (76.2)	102 (65.4)	103 (91.2)	23 (62.2)	53 (84.1)	
Type II	88 (23.8)	54 (34.6)	10 (8.8)	14 (37.8)	10 (15.9)	
Age (years)	65.5 ± 13.1	67.8 ± 13.5	62.8 ± 12.8	67.6 ± 12.1	63.5 ± 12.1	0.006
Male sex	235 (63.7)	86 (55.1)	84 (74.3)	18 (48.6)	47 (74.6)	<0.001
BMI (kg/m^2)	27.3 ± 5.4	27.3 ± 5.6	27.3 ± 6.0	27.7 ± 5.0	27.2 ± 4.2	0.86
BSA (m^2)	2.0 ± 0.3	1.96 ± 0.26	2.01 ± 0.26	1.94 ± 0.22	2.02 ± 0.23	0.056
Co-morbidities						
Hypertension	257 (69.6)	126 (80.8)	75 (66.4)	20 (54.1)	36 (57.1)	<0.001
Diabetes mellitus	27 (7.3)	16 (10.3)	7 (6.2)	2 (5.4)	2 (3.2)	0.33
Smoking history	79 (21.4)	35 (22.4)	22 (19.5)	7 (18.9)	15 (23.8)	0.87
Coronary artery disease	65 (17.6)	29 (18.6)	11 (9.7)	13 (35.1)	12 (19.0)	0.005
COPD	43 (11.7)	20 (12.8)	9 (8.0)	8 (21.6)	6 (9.5)	0.15
Oral anticoagulation	51 (13.8)	23 (14.7)	14 (12.4)	4 (10.8)	10 (15.9)	0.85
Phenprocoumon	13 (3.5)	3 (1.9)	6 (5.3)	2 (5.4)	2 (3.2)	0.37
Apixaban	17 (4.6)	9 (5.8)	3 (2.7)	1 (2.7)	4 (6.3)	0.57
Rivaroxaban	15 (4.1)	8 (5.1)	2 (1.8)	1 (2.7)	4 (6.3)	0.36
Other	6 (1.6)	3 (1.9)	3 (2.7)	1 (2.7)	0 (0.0)	0.63
Previous cardiac surgery	28 (7.6)	11 (7.1)	5 (4.4)	2 (5.4)	10 (15.9)	0.06
Aortic valve regurgitation	218 (59.1)	98 (62.8)	68 (60.2)	19 (51.4)	33 (52.4)	0.39
Bicuspid aortic valve	15 (4.1)	7 (4.5)	6 (5.3)	0 (0.0)	2 (3.2)	0.63
CPR[a]	47 (12.7)	0 (0.0)	0 (0.0)	21 (56.8)	26 (41.3)	<0.001
ROSC before CPB ($n=47$)[a,b]	23 (48.9)	0 (0.0)	0 (0.0)	10 (47.6)	13 (50.0)	0.87
Intubated/ventilated	49 (13.3)	3 (1.9)	11 (9.7)	11 (29.7)	24 (38.1)	<0.001
True lumen collapse	114 (30.9)	19 (12.2)	55 (48.7)	4 (10.8)	36 (57.1)	<0.001
Pericardial effusion/tamponade						<0.001
Pericardial effusion	138 (37.4)	64 (41.0)	41 (36.3)	15 (40.5)	18 (18.6)	
Tamponade	52 (14.1)	5 (3.2)	8 (7.1)	15 (40.5)	24 (38.1)	
Neurological status						<0.001
No neurological deficits	264 (71.5)	152 (97.4)	62 (54.9)	26 (70.3)	24 (38.1)	
Neurological deficits	72 (19.5)	4 (2.6)	47 (41.6)	1 (2.7)	20 (31.7)	
Not obtainable	33 (8.9)	0 (0)	4 (3.5)	10 (27.0)	19 (30.2)	
Malperfusion[c]	176 (47.7)	0 (0)	113 (100)	0 (0)	63 (100)	NA
Coronary[c]	59 (16.0)	0 (0)	33 (29.2)	0 (0)	26 (41.3)	0.073
Cerebral[c]	74 (20.1)	0 (0)	44 (38.9)	0 (0)	30 (47.6)	0.17
Spinal[c]	11 (3.0)	0 (0)	11 (9.7)	0 (0)	0 (0)	0.006
Renal[c]	32 (8.7)	0 (0)	20 (17.7)	0 (0)	12 (19.0)	0.49
Mesenteric[c]	50 (13.6)	0 (0)	28 (24.8)	0 (0)	22 (34.9)	0.11
Peripheral[c]	64 (17.3)	0 (0)	40 (35.4)	0 (0)	24 (38.1)	0.42

Data are expressed as number (percentage) or mean ± standard deviation. BMI: body mass index; BSA: body surface area; COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; CPR: cardiopulmonary resuscitation; NA: not available; ROSC: return of spontaneous circulation.

[a] P-value was calculated between Penn C and Penn BC.

[b] Only patients with CPR were included.

[c] P-value was calculated between Penn B and Penn BC.

Table 2
Procedural details.

Variable	Total ($n=369$)	Penn A ($n=156$)	Penn B ($n=113$)	Penn C ($n=37$)	Penn BC ($n=63$)	P
Extension of aortic repair						0.029
Isolated proximal repair	29 (7.9)	20 (12.8)	5 (4.4)	1 (2.7)	3 (4.8)	
Hemiarch replacement	206 (55.8)	88 (56.4)	56 (49.6)	25 (67.6)	37 (58.7)	
Arch replacement	134 (36.3)	48 (30.8)	52 (46.0)	11 (29.7)	23 (36.5)	
Concomitant procedures						
Aortic valve						0.31
Repair	206 (55.8)	84 (53.8)	72 (63.7)	16 (43.2)	34 (54.0)	
Replacement	59 (16.0)	23 (14.7)	18 (15.9)	8 (21.6)	10 (15.9)	
Aortic root replacement	66 (17.9)	22 (14.1)	24 (21.2)	10 (27.0)	10 (15.9)	0.20
CABG	47 (12.7)	16 (10.3)	13 (11.5)	3 (8.1)	15 (23.8)	0.054
TEVAR	13 (3.5)	3 (1.9)	5 (4.4)	1 (2.7)	4 (6.3)	0.35
CPB time (minutes)	222 ± 76	202 ± 75	229 ± 66	242 ± 80	250 ± 82	<0.001
Cross-clamp time (minutes)	124 ± 48	115 ± 46	132 ± 47	128 ± 46	132 ± 50	0.005
HCA time (minutes)	27.1 ± 13.9	25.4 ± 11.7	28.1 ± 14.0	32.1 ± 23.7	26.5 ± 9.7	0.46
Lowest temperature (°C)	23.4 ± 4.1	24.3 ± 4.0	22.7 ± 4.0	22.8 ± 3.9	22.9 ± 4.1	0.002

Data are expressed as number (percentage) or mean ± standard deviation. CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; HCA: hypothermic circulatory arrest; TEVAR: thoracic endovascular aortic repair.

4.3.1. Transfusions and coagulation factors

Almost all patients (364 patients, 98.6%) received at least some transfusions or coagulation factor substitution perioperatively. On average, patients required 4 units of pRBCs, 2 units of platelets, 2 FFP, 2500 IU of PCC and 4 g of fibrinogen intraoperatively.

Patients with preoperative shock and/or malperfusion received significantly more transfusions and coagulation factor (PCC and fibrinogen) substitution, both intraoperatively ($P \leq 0.002$) and during the first 24 hours postoperatively ($P \leq 0.017$).

Table 3
Outcome and survival.

Variable	Total (n = 369)	Penn A (n = 156)	Penn B (n = 113)	Penn C (n = 37)	Penn BC (n = 63)	P
Hospital stay (days)	14.8 ± 11.1	14.6 ± 7.9	15.5 ± 10.6	15.5 ± 15.6	13.3 ± 15.2	0.07
ICU stay (days)	5.3 ± 6.6	3.9 ± 4.0	6.4 ± 6.1	7.3 ± 10.9	5.8 ± 8.6	0.003
Rethoracotomy	41 (11.1)	12 (7.7)	12 (10.6)	5 (13.5)	12 (19.0)	0.11
Dialysis	66 (17.9)	16 (10.3)	25 (22.1)	8 (21.6)	17 (27.0)	0.009
Tracheotomy	26 (7.0)	4 (2.6)	9 (8.0)	5 (13.5)	8 (12.7)	0.007
Neurological status						< 0.001
No neurological deficits	254 (68.8)	138 (88.5)	66 (58.4)	21 (56.8)	29 (46.0)	
Neurological deficits	76 (20.6)	13 (8.3)	42 (37.2)	6 (16.2)	15 (23.8)	
Not obtainable	39 (10.6)	5 (3.2)	5 (4.4)	10 (27.0)	19 (30.2)	
Intraoperative death	16 (4.3)	1 (0.6)	1 (0.9)	4 (10.8)	10 (15.9)	< 0.001
In-hospital death[a]	54 (14.6)	9 (5.8)	9 (8.0)	11 (29.7)	25 (39.7)	< 0.001
Mid-term survival (n = 315)[b]						0.43
1-year survival	93.7 (90.0 to 96.0)	96.2 (91.0 to 98.4)	92.3 (84.4 to 96.3)	85.0 (60.4 to 94.9)	93.6 (76.9 to 98.4)	
2-year survival	91.9 (87.6 to 94.8)	94.9 (88.8 to 97.7)	90.1 (80.7 to 95.1)	85.0 (60.4 to 94.9)	90.3 (72.8 to 96.8)	
3-year survival	91.9 (87.6 to 94.8)	94.9 (88.8 to 97.7)	90.1 (80.7 to 95.1)	85.0 (60.4 to 94.9)	90.3 (72.8 to 96.8)	
4-year survival	89.5 (83.6 to 93.4)	92.4 (83.0 to 96.7)	90.1 (80.7 to 95.1)	85.0 (60.4 to 94.9)	80.3 (49.1 to 93.4)	

Data are expressed as mean ± standard deviation, number (percentage) or percentage (95% confidence interval). ICU: intensive care unit.
[a] Including intraoperative death.
[b] Only including hospital survivors.

Table 4
Transfusions and coagulation factors.

Variable	Total (n = 369)	Penn A (n = 156)	Penn B (n = 113)	Penn C (n = 37)	Penn BC (n = 63)	P
pRBC (250 mL units)						
Intraoperatively	3.99 ± 4.15	3.08 ± 2.67	3.37 ± 3.26	5.89 ± 4.99	6.25 ± 6.35	< 0.001
First 24 hours postoperatively	1.31 ± 2.56	0.76 ± 1.58	1.16 ± 1.90	1.90 ± 2.68	2.94 ± 4.66	< 0.001
Platelets (250 mL units)						
Intraoperatively	1.95 ± 2.14	1.60 ± 0.95	1.93 ± 1.08	2.38 ± 1.40	2.62 ± 4.55	0.002
First 24 hours postoperatively	0.19 ± 0.71	0.06 ± 0.32	0.14 ± 0.55	0.16 ± 0.58	0.72 ± 1.43	< 0.001
FFP (250 mL units)						
Intraoperatively	2.22 ± 3.60	1.47 ± 2.71	2.29 ± 3.42	2.73 ± 3.91	3.67 ± 5.00	< 0.001
First 24 hours postoperatively	1.82 ± 3.54	1.05 ± 2.10	1.49 ± 2.98	3.26 ± 5.05	3.96 ± 5.47	< 0.001
PCC (IU)						
Intraoperatively	2475 ± 1590	2035 ± 1174	2720 ± 1462	2795 ± 1552	2934 ± 2331	< 0.001
First 24 hours postoperatively	178 ± 699	59 ± 260	130 ± 444	329 ± 953	551 ± 1413	0.006
Fibrinogen (g)						
Intraoperatively	3.94 ± 2.44	3.35 ± 1.79	4.02 ± 2.30	5.03 ± 2.85	4.63 ± 3.30	< 0.001
First 24 hours postoperatively	0.35 ± 1.28	0.17 ± 0.76	0.30 ± 1.04	1.10 ± 2.69	0.53 ± 1.46	0.017
Chest drain (mL)						
First 24 hours postoperatively	786 ± 614	681 ± 507	739 ± 485	841 ± 542	1165 ± 974	0.006

Data are expressed as mean ± standard deviation. FFP: fresh frozen plasma; PCC: prothrombin complex concentrate; pRBC: packed red blood cells.

With increasing malperfusion characterized by localized malperfusion in Penn B, generalized malperfusion in Penn C and both localized and generalized malperfusion in Penn BC, the use of transfusions and coagulation factor substitution as well as chest drain rates increased significantly (Penn A < B < C < BC; Table 4). Increased chest drain rates resulted in higher rethoracotomy rates (Penn A 7.7%; Penn BC 19%; P = 0.11).

Intraoperatively, the increase in transfusions of pRBCs was most evident in patients with shock (Penn C 5.89 ± 4.99 units; Penn BC 6.25 ± 6.35 units) compared with patients without shock (Penn A 3.08 ± 2.67 units; Penn B 3.37 ± 3.26 units; P < 0.001).

4.3.2. Multivariable linear regression analysis

Whereas the previous observations indicate that localized malperfusion and shock both resulted in an increased need for blood transfusions and coagulation factor substitution, the influence of other risk factors was assessed by a multivariable linear regression analysis (Table 5).

The tested variables included age, sex, BSA, preoperative oral anticoagulation, Penn classification, CPB and HCA durations, lowest body temperature and extent of surgery (root and arch replacement) for the intraoperative use of blood transfusions and coagulation factor substitution.

Penn C (coefficient 1.84 units; P = 0.008), Penn BC (coefficient 1.89 units; P = 0.001) and a longer CPB duration (coefficient 0.03 units/min; P < 0.001) were associated with more pRBC transfusions, whereas an increased BSA was associated with reduced pRBC transfusions (coefficient–2.40 units/m^2; P = 0.016).

Platelets were also more frequently transfused in Penn C patients (coefficient 0.68 units; P = 0.006) and Penn BC patients (coefficient 0.52 units; P = 0.009), as well as in patients undergoing root replacement (coefficient 0.42 units; P = 0.025).

The intraoperative use of FFP was only significantly increased in Penn BC patients (coefficient 1.57 units; P = 0.005).

PCC and fibrinogen administration were both increased in Penn BC patients (coefficient 684 IU [P = 0.007] and coefficient 0.96 g [P = 0.010]), patients with a longer CPB (coefficient 3.46 IU/min [P = 0.023] and coefficient 0.01 g/min [P = 0.024]) and patients with a higher BSA (coefficient 1178 IU/m^2 [P = 0.011] and coefficient 1.69 g/m^2 [P = 0.013]). Furthermore, PCC use was also increased in patients with preoperative oral anticoagulation (coefficient 569 IU; P = 0.037) and Penn B patients (coefficient 501 IU; P = 0.020), whereas fibrinogen use was increased in Penn C patients (coefficient 1.51 g; P = 0.001).

All other tested variables (age, sex, HCA duration and lowest body temperature) did not influence transfusions and coagulation factor substitution significantly.

In conclusion, shock and CPB duration were the most important factors resulting in more transfusions and coagulation factor substitution.

Table 5
Multivariable linear regression analysis (significant findings).

Dependent variable	Independent variable	Coefficient	95% CI	*P*-value
pRBC (250 mL units) intraoperatively	BSA (m^2)	−2.40	−4.35 to −0.45	0.016
	Penn C	1.84	0.49 to 3.19	0.008
	Penn BC	1.89	0.81 to 2.97	0.001
	CPB time (minutes)	0.03	0.02 to 0.03	< 0.001
Platelets (250 mL units) intraoperatively	Penn C	0.68	0.20 to 1.16	0.006
	Penn BC	0.52	0.13 to 0.90	0.009
	Root replacement	0.42	0.05 to 0.79	0.025
FFP (250 mL units) intraoperatively	Penn BC	1.57	0.48 to 2.66	0.005
PCC (IU) intraoperatively	BSA (m^2)	1178	276 to 2081	0.011
	Preoperative oral anticoagulation	569	33 to 1104	0.037
	Penn B	501	78 to 924	0.020
	Penn BC	684	185 to 1183	0.007
	CPB time (minutes)	3.46	0.48 to 6.45	0.023
Fibrinogen (g) intraoperatively	BSA (m^2)	1.69	0.36 to 3.01	0.013
	Penn C	1.51	0.60 to 2.43	0.001
	Penn BC	0.96	0.23 to 1.70	0.010
	CPB time (minutes)	0.01	0.00 to 0.01	0.024

BSA: body surface area; CI: confidence interval; CPB: cardiopulmonary bypass; FFP: fresh frozen plasma; PCC: prothrombin complex concentrate; pRBC: packed red blood cells.

5. Discussion

Compared with larger national and international register studies, our study collective represents a typical group of patients with AAD with regards to age, sex distribution, co-morbidities and haemodynamic status at presentation [16–20]. Therefore, the results of this study should be applicable to the general population of patients with AAD.

The incidence of localized malperfusion varies in published studies [21–23]. The distribution of the Penn classes in this work tends to align with those studies reporting higher incidence of localized malperfusion, which could be attributed to our systematic approach of prospectively searching for malperfusion during operative planning in order to address it optimally [13]. Rates of early death in the different Penn classes are similar to previously published studies, with Penn C patients in the present study showing a slightly higher in-hospital death rate [11,14]. This could be caused by the high incidence of preoperative cardiopulmonary resuscitation (Penn C 57%; Penn BC 41%), which is known to result in hospital death rates of 50–60% [24–27]. Furthermore, fewer than half of these patients achieved return of spontaneous circulation before CPB.

The postoperative outcomes, as well as the short- and mid-term survival rates of the presented cohort are consistent with the anticipated outcomes for AAD cases [20].

The preference for hemiarch replacement in the surgical management of AAD is evident across numerous studies [28,29]. However, its application and the corresponding surgical strategies differ among various institutions [30,31]. Total arch replacement utilizing the frozen elephant trunk technique has seen increased adoption following its introduction to the market, with some experts recommending its routine application in DeBakey type I dissection [32]. Our centre's approach is tailored based on the haemodynamic status as delineated by the Penn classification, adopting a more selective criterion for the use of the frozen elephant trunk technique [33].

Almost all patients required perioperative blood transfusions or coagulation factor substitution. However, the amount varied depending on the haemodynamic status and duration of CPB. This suggests that both the dissection and the resulting ischaemic burden itself as well as the required surgical treatment influence blood transfusions and coagulation factor substitution.

In patients with generalized malperfusion (Penn C and Penn BC) and, to a lesser extent, in those with localized malperfusion (Penn B and Penn BC), the initiation of CPB with antegrade flow in the true lumen leads to reperfusion injury that corresponds in magnitude to the initial ischaemia. This, combined with the injury expected in all patients (including Penn A) as a result of CPB, hypothermia and HCA followed by reperfusion, results in an impairment of the endothelial function [34–36]. The arising capillary leak causes an increased extracellular fluid volume with decreased circulating blood volume, therefore necessitating perioperative fluid administrations, resulting in blood dilution. Whereas hyperfibrinolysis has received limited attention in the setting of AAD, blood dilution and reperfusion injury have been shown to be associated with hyperfibrinolysis in other settings [37–40]. It is reasonable to assume the same underlying pathophysiology to be present in AAD.

Whereas all patients are subject to CPB and HCA with similar durations (CPB mean ± 11%; HCA mean ± 18%), increasing ischaemia with consecutive larger reperfusion injury (Penn A < B < C < BC) seems to increase the need for blood transfusions and the substitution of coagulation factors. CPB duration might be a confounding variable, as Penn C and Penn BC patients have the longest CPB.

As the largest ischaemic burden has to be anticipated for resuscitated patients, a descriptive comparison with non-resuscitated patients in the Penn C and Penn BC subgroup was conducted (Table 6). Patients with cardiopulmonary resuscitation had a significantly higher early death rate, with an in-hospital death rate of almost 50% (48.9% vs. 24.5%; $P = 0.011$), but favourable mid-term results, without significant differences between resuscitated and non-resuscitated patients ($P = 0.08$). As expected, resuscitated patients required more transfusions, with pRBCs reaching statistical significance: intraoperatively 8.23 ± 6.61 vs. 4.25 ± 4.37 units ($P < 0.001$); first 24 hours postoperatively 9.76 ± 8.81 vs. 6.08 ± 6.43 units; $P = 0.037$.

The similar mid-term outcome of hospital survivors in the different Penn groups suggests that if the ischaemia, reperfusion and related complications can be overcome, the surviving patients share a similar prognosis. This observation further supports our centre's approach of providing surgical treatment to all patients with AAD, regardless of haemodynamic status at presentation.

Point-of-care thromboelastography was only used in a minority of cases (49 cases, 13.3%) at the discretion of the surgeon, anaesthesiologist or ICU physician. Although its usage increased during the study period, point-of-care thromboelastography is not used routinely in every AAD case, and it can be assumed that it was primarily used in patients with bleeding complications; its effect on the need for blood transfusions and coagulation factor substitution cannot be assessed in the present study [30–33].

Table 6
Cardiopulmonary resuscitation subgroup analysis.

Variable	Penn C and BC (n = 100)	CPR (n = 47)	No CPR (n = 53)	P
Rethoracotomy	17 (17.0)	11 (23.4)	6 (11.3)	0.11
Intraoperative death	14 (14.0)	12 (25.2)	2 (3.8)	0.002
In-hospital death[a]	36 (36.0)	23 (48.9)	13 (24.5)	0.011
Mid-term survival (n = 64)[b]				0.08
1-year survival	90.3 (78.2 to 95.8)	85.0 (60.4 to 94.9)	93.6 (76.9 to 98.4)	
2-year survival	88.2 (75.6 to 94.5)	79.7 (54.5 to 91.9)	93.6 (76.9 to 98.4)	
3-year survival	88.2 (75.6 to 94.5)	79.7 (54.5 to 91.9)	93.6 (76.9 to 98.4)	
4-year survival	81.9 (61.6 to 92.1)	69.7 (39.2 to 87.0)	93.6 (76.9 to 98.4)	
pRBC (250 mL units)				
Intraoperatively	6.12 ± 5.86	8.23 ± 6.61	4.25 ± 4.37	< 0.001
First 24 hours postoperatively	7.45 ± 7.56	9.76 ± 8.81	6.08 ± 6.43	0.037
Platelets (250 mL units)				
Intraoperatively	2.53 ± 3.70	3.02 ± 5.19	2.09 ± 1.35	0.24
First 24 hours postoperatively	2.73 ± 2.23	3.28 ± 2.80	2.41 ± 1.78	0.14
FFP (250 mL units)				
Intraoperatively	3.32 ± 4.63	4.17 ± 5.93	2.57 ± 2.90	0.10
First 24 hours postoperatively	6.92 ± 8.00	9.45 ± 10.25	5.43 ± 5.92	0.06
PCC (IU)				
Intraoperatively	2883 ± 2070	2874 ± 2507	2891 ± 1611	0.97
First 24 hours postoperatively	3468 ± 2779	3990 ± 3606	3159 ± 2131	0.27
Fibrinogen (g)				
Intraoperatively	4.78 ± 3.14	4.79 ± 3.51	4.77 ± 2.80	0.98
First 24 hours postoperatively	5.74 ± 4.12	7.00 ± 5.16	5.00 ± 3.20	0.07

Data are expressed as number (percentage), percentage (95% confidence interval) or mean ± standard deviation. CPR: cardiopulmonary resuscitation; FFP: fresh frozen plasma; PCC: prothrombin complex concentrate; pRBC: packed red blood cells.
[a] Including intraoperative death.
[b] Only including hospital survivors.

A higher BSA was associated with lower pRBC transfusions, but greater amounts of administered PCC and fibrinogen. A possible explanation might be the higher total blood volume of patients with a higher BSA, which enables them to better compensate for blood loss. The increased use of PCC and fibrinogen in patients with higher BSA might in part be explained by the weight-dependent substitution of PCC and fibrinogen.

Studies with comparable designs have generally reported similar findings regarding the need for transfusions and coagulation factor substitution during the perioperative period [4,5,8,41]. However, the reviewed literature has not definitively established a correlation between the ischaemic burden and the necessity for transfusions and coagulation factor substitution in AAD. Future research should continue to investigate the impact of ischaemic burden and subsequent reperfusion on the coagulation system, as these factors are crucial to enhancing patient outcomes and optimizing therapeutic strategies.

5.1. Study limitations

The retrospective design and single-centre data source of this study limit the significance of its results. Mid-term observations are restricted by the median follow-up duration of 1.8 years, reflecting the relatively recent study period. Although standard operation procedures regarding coagulation management in the early postoperative period are established at our hospital, the cut-off values can be modified depending on the clinical situation (e.g. acute bleeding), and the ultimate decision remains at the discretion of the treating physicians.

Although fibrinogen and PCC are the most commonly used coagulation factors in our centre, the substitution of other coagulation factors (e. g. Factor XIII or calcium) or other substances influencing the coagulation cascade (e.g. desmopressin) were not evaluated, and might be the subject of further research. Furthermore, laboratory values were not evaluated in this study.

As the extension of the dissection varies between different cases, a different amount of extravascular tissue is exposed to the blood: this probably has an effect on the consumption of coagulation factors and platelets, but was not separately accounted for in the present study.

6. Conclusions

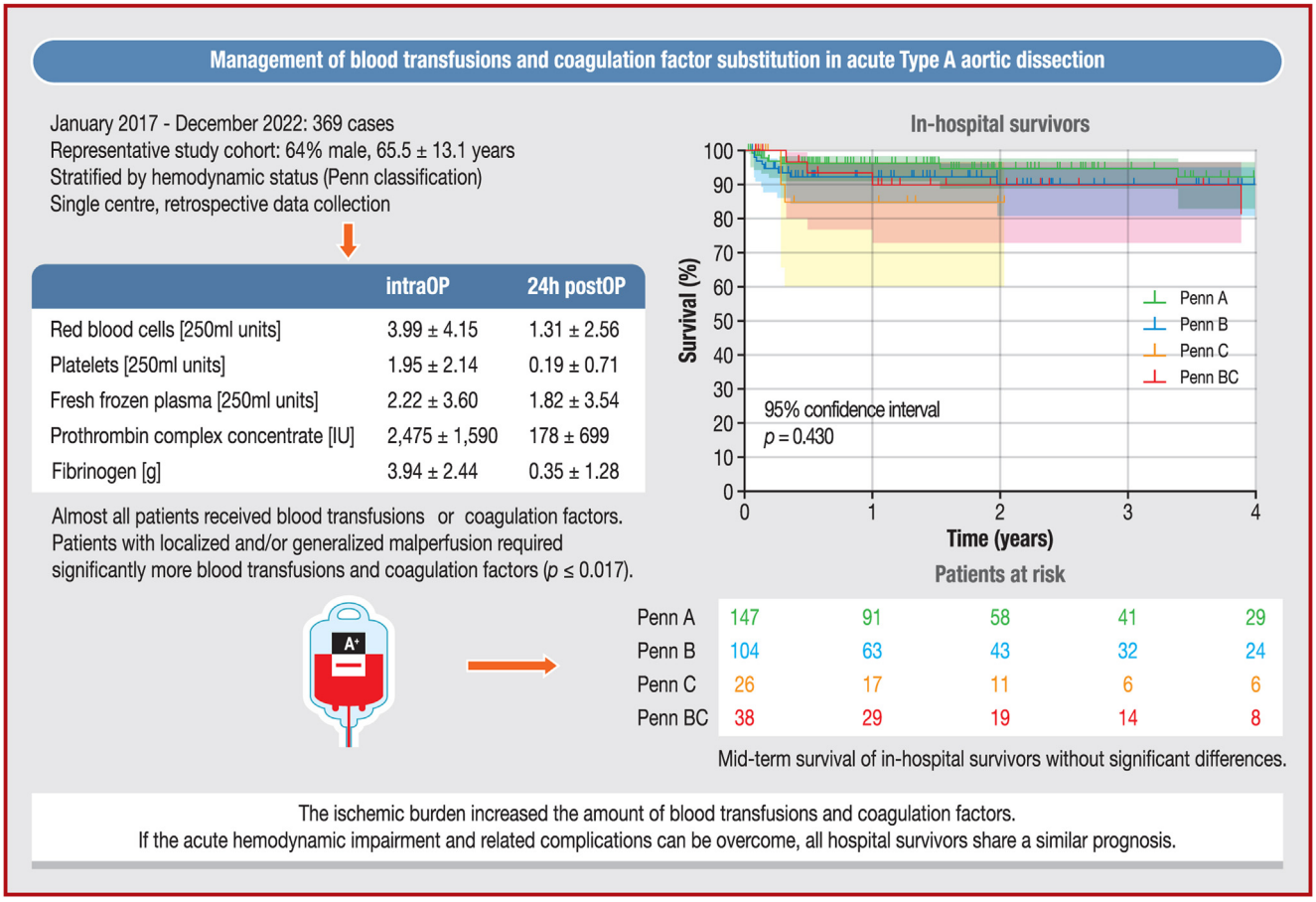
Surgical repair for AAD remains major surgery, requiring blood transfusions and coagulation factor substitution in almost all cases. The generalized and localized ischaemic burden, as assessed by the Penn classification, is the most important factor influencing the use of these products.

The extent of malperfusion, as demonstrated in the progression from Penn A to Penn BC, was directly associated with more transfusions and coagulation factor substitution, along with elevated chest drain rates. This trend underscores the critical impact of malperfusion and ischaemic burden on transfusion and coagulation management.

Further associations with duration of the CPB, extent of the surgery and patient size were found. Although shock and localized malperfusion lead to a higher early death rate, they do not appear to adversely affect the mid-term outcome in hospital survivors.

With proper management, acceptable rethoracotomy and chest drain rates can be achieved with good clinical outcomes.

Further research to establish evidence-based blood transfusion and coagulation factor substitution protocols is necessary (Central Illustration).



Central Illustration. In-hospital survivors share a similar prognosis, regardless of initial haemodynamic status. 24 h postOP: 24 hours postoperatively; intraOP: intraoperatively.

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