

Outcomes and risk factors of postoperative hepatic dysfunction in patients undergoing acute type A aortic dissection surgery

Wei Zhou^{1#}, Guokun Wang^{1#}, Yaoyang Liu^{2#}, Yun Tao¹, Zhen Du¹, Yangfeng Tang¹, Fan Qiao¹, Yang Liu¹, Zhiyun Xu¹

¹Department of Cardiovascular Surgery, Changhai Hospital, The Second Military Medical University, Shanghai 200433, China; ²Department of Rheumatology and Immunology, Changzheng Hospital, The Second Military Medical University, Shanghai 200003, China

Contributions: (I) Conception and design: W Zhou, Y Liu, Z Xu; (II) Administrative support: Z Xu; (III) Provision of study materials or patients: Z Xu; (IV) Collection and assembly of data: W Zhou, Y Tao, Z Du; (V) Data analysis and interpretation: Y Liu, Y Liu, Y Tang, F Qiao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Zhiyun Xu, PhD, MD; Yang Liu, MD. Department of Cardiovascular Surgery, Shanghai Changhai Hospital, The Second Military Medical University, 168 Changhai Road, Shanghai 200433, China. Email: xuzhiyun@smmu.edu.cn; liuyang3722@163.com.

Background: Postoperative hepatic dysfunction (HD) increases the morbidity and mortality risk after cardiac surgery; however, only a few studies have specifically focused on acute type A aortic dissection (AAAD) surgery. We explored the possible risk factors and outcomes of early postoperative HD in patients with AAAD undergoing surgery.

Methods: All patients who underwent AAAD surgery at our institution from April 2015 to April 2017 were retrospectively evaluated. Postoperative model for end-stage liver disease (MELD) score was used to define HD. Independent risk factors for HD were determined by multivariate logistic analysis.

Results: Two hundred fifteen patients with AAAD met the inclusion criteria. The incidence rate of early postoperative HD was 60.9%, and the rate of in-hospital mortality was 16.8%. Patients with a high postoperative MELD score had longer mechanical ventilation time, longer durations of intensive care unit (ICU) stay, and higher in-hospital mortality. During the postoperative period, patients with AAAD complicated by HD needed continuous renal replacement therapy (CRRT), reintubation, tracheostomy, and blood transfusion more frequently. Aortic cross clamp (ACC) time [per 10 min higher; odds ratio (OR): 1.216, 95% confidence interval (CI): 1.017–1.454, P=0.032], postoperative leucocytes (per 2×10°/L higher; OR: 1.161, 95% CI: 1.018–1.324, P=0.026), postoperative respiratory dysfunction (OR: 3.176, 95% CI: 1.293–7.803, P=0.012), and postoperative low cardiac output syndrome (LCOS) (OR: 12.663, 95% CI: 1.432–111.998, P=0.022) were independent risk factors associated with HD in patients undergoing AAAD surgery.

Conclusions: Postoperative HD prolongs mechanical ventilation time and ICU stay, and is associated with increased in-hospital mortality among patients who undergo AAAD surgery. Several factors are associated with a high postoperative MELD score.

Keywords: Hepatic dysfunction (HD); acute type A aortic dissection (AAAD); model for end-stage liver disease score (MELD score); in-hospital mortality; multivariate analysis

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Introduction

2 Acute aortic dissection is the most common medical 3 4 emergency involving the aorta. The mortality of acute type 5 A aortic dissection (AAAD) ranges from 40% to 50% within 48 hours of onset. Surgery for AAAD remains a challenge 6 for cardiovascular surgeons (1-3). Hepatic dysfunction 7 8 (HD) has been suggested as an important postoperative risk factors for mortality and morbidity after cardiovascular 9 surgery (4,5). Moreover, due to the complexity of surgery, 10 long operation time, and substantial trauma, AAAD is easily 11 complicated by renal insufficiency, HD, and bowel ischemia 12 after surgery, which leads to increased mortality (1). 13 Studies focusing on HD after AAAD surgery are rare, and 14 little is known about postoperative HD outcomes and risk 15 factors. 16

In the past 30 years, the principal indicator of HD has 17 been the Child-Turcotte-Pugh (CTP) classification (6). 18 However, as an important clinical method for estimating 19 hepatic function, the model for end-stage liver disease 20 (MELD) score has been reported to constitute a more 21 22 useful assessment tool to predict postoperative mortality and morbidity than CTP classification in patients undergoing 23 cardiac surgery (5,7). MELD scores have been verified as 24 a measure of HD and are used as a tool to prioritize liver 25 transplant candidates based on disease severity (8). Hence, 26 we chose MELD scores as our tools to assess postoperative 27 HD, based on the following clinical indices: (I) international 28 normalized ratio (INR); (II) total serum bilirubin; (III) 29 serum creatinine; and (IV) disease (bilious or alcoholic 30 liver disease =0, all others =1). These score indicators are 31 objective and easy to obtain (9). The aim of our study was 32 to evaluate the risk factors of postoperative HD in patients 33 with AAAD and its impact on clinical outcomes. 34

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³⁶ Methods

37 38 *Patients*

39 We retrospectively reviewed the medical records of patients 40 41 who underwent surgery for AAAD at Changhai Hospital from April 2015 to April 2017. In most cases, enhanced 42 43 computed tomography was used to diagnose AAAD and determine which vessels were affected by the dissection. 44 This study was approved by the Committee on Ethics 45 of Biomedicine Research, The Second Military Medical 46 47 University, Shanghai (No. SMMUEC2018-012), with the need for individual patient consent waived. 48

Data collection

50 We collected data on patients' age, sex, body mass index, 51 52 comorbidities (e.g., hypertension, diabetes, chronic obstructive pulmonary disease), history of smoking and 53 alcohol consumption, preoperative MELD score and 54 renal insufficiency, and laboratory test results [creatinine, 55 leukocytes, hemoglobin, alanine transaminase (ALT), 56 aspartate transaminase (AST), albumin, y-glutamyl 57 transferase, total bilirubin, K⁺, Na⁺, lactic acid, PaO₂, PaO₂/ 58 FiO₂ ratio]. 59

We also collected data on time from symptom onset 60 to surgery, preoperative shock, preoperative moderate/ 61 severe pericardial effusion, dissection involvement (celiac 62 trunk, superior mesenteric artery, and renal artery), and 63 intraoperative conditions [cardiopulmonary bypass (CPB) 64 time, aortic cross clamp (ACC) time, deep hypothermic 65 circulatory arrest, and surgical procedure]. Finally, 66 we recorded the 24-h postoperative drainage volume, 67 perioperative blood product transfusion, and postoperative 68 laboratory test results including ALT, AST, albumin, white 69 blood cells, and INR. 70

Postoperative complications, such as low cardiac 71 output syndrome (LCOS); pneumonia; renal insufficiency; 72 respiratory dysfunction; mechanical ventilation time; time 73 in the intensive care unit (ICU); need for reintubation, 74 continuous renal replacement therapy (CRRT), 75 tracheostomy; sepsis; re-exploration for bleeding; and 76 blood transfusion, including red blood cells, plasma, and 77 cryoprecipitate, were also recorded. 78

Definitions and grouping

To calculate patients' MELD scores, we used the following formula:

MELD = 11.2 In (INR) + 0.378 In (total bilirubin) + 0.957 In (creatinine) + 0.643 (*cause*)

where *cause* equaled 0 for bilious or alcoholic liver disease 87 and 1 otherwise. 88

We used the results of laboratory tests within 7 days to 89 calculate MELD score every day after surgery using the 90 above formula, and the highest value of MELD was used to 91 determine whether patients experienced early postoperative 92 HD to avoid the influence of other factors such as infection. 93 Considering that a few patients were taking warfarin during 94 the study, which may have affected the INR and MELD 95 scores, we collected the INR values of these patients before 96

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they took their medicine. We grouped patients based on 97 their postoperative score into high-MELD (MELD ≥ 14) 98 and low-MELD (MELD <14) groups. Some previous 99 studies set a cutoff point of 13 for patients with cirrhosis 100 undergoing cardiac surgery (10,11), and recent research 101 predicted postoperative mortality and morbidity after 102 cardiac surgery based on a cutoff of 12 (5). Moreover, a 103 recent study on outcomes of patients undergoing cardiac 104 surgery after liver transplantation showed that the optimal 105 cutoff point for predicting late mortality is 13.8 (12). In 106 another study, the Youden index identified the optimal 107 MELD score cutoff value of 13.5 for predicting surgical 108 mortality of cardiac surgery in liver transplant recipients (13). 109 Consequently, considering that AAAD surgery is more 110 complicated than other cardiac surgeries, and based on the 111 optimal cutoff values of MELD scores for risk of mortality 112 in previous studies, we used 14 as our cutoff point. 113

Renal insufficiency was defined by an estimated 114 glomerular filtration rate of <60 mL/min/1.73 m², and 115 hyperbilirubinemia was defined by total bilirubin >3 mg/dL. 116 Respiratory dysfunction was defined as inadequate 117 oxygenation (PaO₂ <60 mmHg with a FiO₂ of 0.5 or 118 $PaO_{2}/FiO_{2} \leq 120$) or ventilation (PCO₂ > 50 mmHg) during 119 mechanical ventilatory support (14). LCOS was diagnosed 120 if the patient required two or more inotropic medications 121 to maintain systolic blood pressure above 90 mmHg and a 122 cardiac output greater than 2.2 L/min/m² postoperatively 123 after adjusting the preload and correcting for all electrolyte 124 or blood gas abnormalities (15). Transfusion threshold 125 and policies were as follows: if the patient's hematocrit 126 was lower than 25, we transfused packed red cell to 127 increase the intravascular volume and maintain satisfactory 128 tissue oxygenation; if the patient was bleeding in the 129 early postoperative period, blood component therapy, 130 selected based upon identification of specific coagulation 131 abnormalities by point-of-care testing and treatment 132 algorithms, plasma infusion, or cryoprecipitate were 133 considered: fresh frozen plasma was usually given at 134 2-4 units for average adults, cryoprecipitate was given 1 135 unit at 1 unit/7-10 kg of body weight. Massive transfusion 136 was defined as ≥ 10 units of blood transfused (16). Prolonged 137 ICU stay was defined as >7 days (17). 138

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¹⁴⁰ Statistical analysis

Continuous variables are presented as means ± standard
deviation or medians and interquartile range. Comparisons
of continuous variables between the two groups were

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performed using the Student's t-test for variables with a 145 normal distribution. The Wilcoxon rank-sum test was used 146 for variables with a non-normal distribution. Categorical 147 variables were analyzed using the Pearson's chi-squared or 148 Fisher's exact test. Receiver operating characteristic (ROC) 149 curve and the Youden index were used to determine the 150 optimal cutoff value of MELD score for predicting the 151 surgical risk of mortality. 152

Multivariate logistic regression analyses were performed 153 to identify risk factors for a high MELD score. Significant 154 variables (P<0.05) associated with a high MELD score in 155 the univariate analysis and clinically relevant variables were 156 included in the multivariate analysis. The multivariate 157 regression analysis was performed using a forward stepwise 158 (conditional) procedure to determine the independent 159 significant prognostic factors. The multivariate regression 160 analysis was performed to determine the effect of a 161 postoperative high MELD score on mortality, prolonged 162 ICU stay, and massive transfusion after adjusting for 163 relevant confounding variables in the three models. All 164 P-values were two-sided. Statistical significance was defined 165 as P<0.05. All statistical analyses were performed using 166 SPSS 24.0 (IBM Corp.). 167

Results

170 171 Of the 216 patients with AAAD who underwent surgery from April 2015 to April 2017, one patient was excluded due 172 to persistent bleeding and death within 24 h after surgery; 173 the remaining 215 patients were divided into high-MELD 174 (MELD score \geq 14; n=131) and low-MELD (MELD score 175 <14; n=84) groups. Based on MELD scores, the incidence 176 rate of early postoperative HD was 60.9%, with an in-177 hospital mortality rate of 16.8%. 178

Baseline and preoperative characteristics

Patients with high postoperative MELD scores tended to have high preoperative MELD scores and preoperative renal insufficiency. Laboratory examination showed that the high-MELD group had higher preoperative creatinine levels and leucocyte counts (*Table 1*).

Surgery and postoperative characteristics

Patients in the high-MELD group had longer CPB and ACC times than those in the low-MELD group and underwent higher number of total-arch replacements and

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Table 1 Baseline characteristics of the 215 AAAD patients

Table I Daschne characteristics of the 213 AAAD patter	1105		
Patients' characteristics	MELD <14 (N=84)	MELD ≥14 (N=131)	P value
Age (years)	47±12.4	48.8±12.4	0.302
Men	66 (78.6)	108 (82.4)	0.481
BMI	25.0±4.55	25.9±3.8	0.129
Hypertension	49 (58.3)	84 (64.1)	0.394
Diabetes	1 (1.2)	3 (2.3)	0.948
COPD	2 (2.4)	3 (2.3)	1.000
Ischemic heart disease	1 (1.2)	4 (3.1)	0.377
Smoking	39 (46.4)	58 (44.3)	0.757
Drinking	16 (19.0)	18 (13.7)	0.298
Preoperative hepatic dysfunction (MELD ≥ELD	1 (1.2)	13 (9.9)	0.011
Preoperative renal insufficiency	3 (3.6)	46 (35.1)	<0.001
Leucocytes (10 ⁹ ·L ⁻¹)	10.4 [8.1–14.0]	13.0 [10.4–16.4]	<0.001
Hemoglobin (g·L ⁻¹)	124±19	127±16	0.300
ALT (U/L)	24 [15.3–36.5]	29 [19.0–45.5]	0.053
AST (U/L)	27 [19–36]	29.5 [21–47]	0.134
Albumin (g/L)	38 [35–41]	39 [36–41]	0.364
γ-glutamyl transferase (U/L)	33 [21–83]	36 [22–72]	0.905
Preoperative hyperbilirubinemia	2 (2.4)	3 (2.3)	0.966
Na⁺ (mmol/L)	138 [136–140]	138 [136–140]	0.733
K ⁺ (mmol/L)	3.6 [3.5–3.8]	3.7 [3.4–4.0]	0.234
Lactic acid (mmol/L)	1.3 [0.9–1.8]	1.4 [0.9–2.3]	0.254
PaO ₂ (mmHg)	95 [76.5–140.0]	89 [73–133]	0.480
PaO_2/FiO_2 ratio	246 [205–311]	231 [192–305]	0.287
Onset to surgery time (h)	35 [20–165]	31 [21–60]	0.179
Moderate/severe pericardial effusion	22 (26.2)	44 (33.6)	0.251
Shock (systolic blood pressure <80 mmHg)	2 (2.4)	5 (3.8)	0.563
Involving the celiac trunk	15 (17.9)	32 (24.4)	0.255
Involving the superior mesenteric artery	8 (9.5)	18 (13.7)	0.355
Involving the renal artery	8 (9.5)	18 (13.7)	0.355

Data are presented as mean \pm standard deviation, median [interquartile range], or number (%).AAAD, acute type A aortic dissection; MELD, end-stage liver disease; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ALT, alanine transaminase; AST, aspartate transaminase; PaO₂, partial pressure of oxygen; FiO₂, fraction of inspired oxygen.

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Table 2 Surgery and postoperative characteristics of the two groups

Patients' characteristics	MELD <14 (N=84)	MELD ≥14 (N=131)	P value
CPB time (min)	144.5 [122.8–170.0]	152 [138–172]	0.013
ACC time (min)	83.5±24.8	92.3±19.6	0.004
Deep hypothermic circulatory arrest (min)	24 [21–30]	25 [21–32]	0.366
Type of operation			
CABG	5 (6.0)	18 (13.7)	0.071
Ascending aorta replacement	79 (94.0)	127 (96.9)	0.300
Hemi-arch replacement	11 (13.1)	2 (1.5)	0.001
Total-arch replacement	67 (79.8)	125 (95.4)	0.000
Elephant trunk	65 (77.4)	121 (92.4)	0.002
24-h postoperative drainage volume (mL)	445 [302–660]	560 [370–870]	0.009
Leucocyte (×10 ⁹ /L)	17.7 [14.2–21.7]	22.5 [18.1–26.5]	<0.001
LCOS	1 (1.2)	18 (13.7)	0.016
Pneumonia	6 (7.1)	35 (26.7)	<0.001
Postoperative renal insufficiency	17 (20.2)	95 (72.5)	<0.001
Respiratory dysfunction	10 (11.9)	58 (44.3)	<0.001

Data are presented as mean ± standard deviation, median [interquartile range], or number (%). MELD, end-stage liver disease; CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; CABG, coronary artery bypass graft; LCOS, low cardiac output syndrome.

elephant trunk surgical procedures. Postoperative renal
insufficiency occurred more frequently in the high-MELD
group (72.5% vs. 20.2%). LCOS, respiratory dysfunction,
and pneumonia were associated with high MELD scores.
Patients with high MELD scores had a higher leucocyte
count postoperatively and higher 24-h postoperative
drainage volume (*Table 2*).

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In-hospital outcomes of patients with high MELD scores

Patients with a high MELD score after surgery had a
longer mechanical ventilation time, longer ICU stay, and
higher in-hospital mortality rate. Patients with AAAD and
a high MELD score needed more CRRT, reintubation, and
tracheostomy after surgery. In addition, this group had a
greater need for blood transfusion (*Table 3*).

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Logistic regression for high postoperative MELD score

ACC time, postoperative leucocyte counts, postoperative
LCOS, and postoperative respiratory dysfunction were
independent predictive factors of a high postoperative
MELD score (*Table 4*). After adjusting for relevant

confounding variables, a high postoperative MELD score 216 was associated with mortality and prolonged ICU stay, but 217 not with massive transfusion (*Tables 5,S1-S3*). 218

Discussion

The most important finding of our study was that a longer 222 ACC time, higher postoperative leucocyte level, and 223 postoperative LCOS and respiratory dysfunction were 224 independent risk factors of postoperative HD in patients 225 with AAAD. 226

Postoperative HD is a common serious complication 227 in patients with AAAD. The MELD score has been used 228 frequently in recent studies to evaluate hepatic function after 229 cardiac surgery, but its use in AAAD surgery is relatively 230 rare. Liu et al. reported that early postoperative HD 231 incidence was 8.7% after AAAD surgery (18), while another 232 study showed an HD incidence of 1.6% postoperatively 233 among patients with AAAD, with a mortality rate of 234 38% (19). However, these studies relied on biochemical 235 markers to evaluate hepatic function. In our study, we 236 used the MELD score and found that the incidence of 237 postoperative HD was as high as 60.9%, with an in-238

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Table 3 Outcomes

Variable	MELD <14 (N=84)	MELD ≥14 (N=131)	P value
In-hospital mortality	1 (1.2)	22 (16.8)	<0.001
Mechanical ventilation time (h)	37 [20–58.5]	67 [40–109.5]	<0.001
ICU stay (h)	99 [66.3–139]	158 [92–290.3]	<0.001
Reintubation	2 (2.4)	20 (15.3)	0.002
CRRT	2 (2.4)	18 (13.7)	0.005
Tracheostomy	2 (2.4)	14 (10.7)	0.024
Sepsis	0 (0)	6 (4.6)	0.118
Re-exploration for bleeding	1 (1.2)	6 (4.6)	0.331
Blood transfusion			
Erythrocytes (U)	6 [4–11.3]	10 [6–15]	<0.001
Plasma (U)	6.5 [3–10]	9 [5.5–15]	<0.001
Cryoprecipitate (U)	10 [10–10]	10 [10–20]	<0.001

Data are presented as median [interquartile range], or number (%). MELD, end-stage liver disease; ICU, intensive care unit; CRRT, continuous renal replacement therapy.

Table 4 Univariable and multivariate as	alysis of the risk factors for	postoperative high MELD score
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Variable		Univariable analysis Multivariable analysis				sis
		95% CI	P value	OR	95% CI	P value
Preoperative hepatic dysfunction (MELD ≥14)	9.144	1.173–71.261	0.035	-	-	-
Preoperative renal insufficiency	14.612	4.371–48.849	0.000	3.846	0.977–15.14	0.054
Preoperative leucocytes (10 ⁹ ·L ⁻¹)	1.232	1.074–1.413	0.003	-	-	-
Preoperative hyperbilirubinemia	0.961	0.157–5.875	0.966	-	-	-
Preoperative pericardial effusion	1.425	0.777–2.614	0.252	-	-	-
Preoperative shock (systolic blood pressure <80 mmHg)	1.627	0.308-8.585	0.566	-	-	-
CPB time (min) (per 10 min higher)	1.013	1.003-1.022	0.009	-	-	-
ACC time (min) (per 10 min higher)	1.198	1.052-1.363	0.006	1.216	1.017–1.454	0.032
Hemi-arch replacement	0.103	0.022-0.477	0.004	-	-	-
Total-arch replacement	5.286	1.99–14.041	0.001	3.040	0.885–10.44	0.077
Elephant trunk	3.537	1.553-8.054	0.003	-	-	-
24-h postoperative drainage volume (mL) (per 200 mL higher)	1.116	1.029-1.209	0.008	-	-	-
Postoperative leucocyte (×10 ⁹ /L) (per 2×10 ⁹ /L higher)	1.276	1.141–1.428	0.000	1.161	1.018–1.324	0.026
Postoperative LCOS	13.221	1.73–101.021	0.013	12.663	1.432–111.998	0.022
Postoperative pneumonia	4.740	1.896–11.847	0.001	-	-	-
Postoperative respiratory dysfunction	5.879	2.791–12.384	0.000	3.176	1.293–7.803	0.012

The final model for high MELD score had an area under receiver operating characteristic curve of 0.787, and the Hosmer-Lemeshow test with P>0.05. MELD, end-stage liver disease; CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; LCOS, low cardiac output syndrome; OR, odds ratio; CI, confidence interval.

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 Table 5 Multivariate analysis for risk factors of mortality, prolonged

 ICU stay and massive transfusion

Variable	OR	95% CI	P value
Mortality			
Postoperative MELD ≥14	8.911	1.029–77.179	0.047
Prolonged ICU stay (>7 days)			
Postoperative MELD ≥14	2.465	1.121–5.420	0.025
Massive transfusion (≥10 units)			
Postoperative MELD ≥14	0.774	0.344–1.744	0.537

The multivariate regression analysis was performed after adjusting for relevant confounding variables in the three models. MELD, end-stage liver disease; ICU, intensive care unit; OR, odds ratio; CI, confidence interval.

hospital mortality rate of 16.8%. We also found that highly
suspected risk factors (e.g., peritoneal artery involvement,
onset to surgery time) were not independent risk factors for
postoperative HD.

Almost all open thoracic AAAD surgeries are performed 243 with extracorporeal circulation i.e. CPB. Since CPB is 244 a non-physiological state, and liver perfusion would be 245 significantly reduced, leading to liver function damage. 246 Although there is distal perfusion during the ACC time, 247 liver perfusion is significantly reduced (20). It has previously 248 been reported that the blood volume in liver arteries 249 decreases by 20% to 25% during CPB (21). Hence, a long 250 251 ACC time can induce a critical reduction in perfusion, and significant hypoxemia in the abdominal organs is inevitable, 252 thus overwhelming the protective mechanisms and causing 253 hypoxic liver damage (22). Furthermore, a long ACC time is 254 associated with serious clinical conditions and complicated 255 procedures can also lead to an inflammatory response. 256 The subsequent activation of a variety of inflammatory 257 mediators, such as adhesion molecules, thrombin, cytokines, 258 endothelin and macrophages weakens the immune response, 259 and a combination of these factors causes multi-organ 260 dysfunction (23-25). 261

Increased postoperative HD was associated with a higher 262 postoperative leucocyte count in our study. The leucocyte 263 count is an important index for inflammatory response, and 264 an early postoperative increase is highly associated with an 265 inflammatory response rather than infection. When AAAD 266 occurs, it activates multiple responses in the circulatory 267 system, which can cause severe systemic inflammatory 268 response syndrome and coagulation disorders. The 269 inflammatory response is closely linked to the development 270

of AAAD (26); however, due to its critical nature, rapid 271 progression, requirement of a complex surgery, high 272 requirements for extracorporeal circulation, and longer 273 turnaround time, AAAD is more likely to cause a systemic 274 inflammatory response. This is consistent with our previous 275 discussion about ACC. In addition, CPB induces a certain 276 degree of hemolysis, which promotes the release of free 277 hemoglobin, production of endogenous substances play 278 an important role in aggravating body's inflammatory 279 response (27), the risk of multi-organ failure increases, 280 especially in the liver, kidney, lung, and other important 281 organs. 282

As a common and serious complication in cardiac 283 surgeries, postoperative respiratory dysfunction may 284 prolong the ICU stay and increase in-hospital mortality 285 (28,29). The incidence of postoperative hypoxemia is up to 286 51% after surgery for AAAD (30). In addition, prolonged 287 respiratory dysfunction requires extended mechanical 288 ventilation time, and the resulting hypoxia can damage vital 289 organs, especially those that are more sensitive to hypoxia, 290 such as the lung and liver. This damage causes other serious 291 complications, such as sepsis and HD. 292

Pérez Vela et al. showed that patients who 293 experienced LCOS after cardiac surgery had a poorer 294 postoperative course, with a greater incidence of 295 multi-organ failure and higher mortality (31). When 296 LCOS develops, it directly causes insufficient hepatic 297 perfusion pressure, leading to hepatic ischemia and 298 hypoxia. In addition, inotropic agents used to improve 299 patients' cardiac output were found to increase 300 myocardial consumption and in-hospital mortality (32), 301 leading to ischemia of other organs. The treatment goal of 302 LCOS is to promote tissue DO₂ by providing appropriate 303 hemodynamic support to avoid dysfunction and failure of 304 critical organs (33), leading to a good clinical outcome. 305

This study has some limitations related to its 306 retrospective design and the fact that all data was generated 307 by a single center. The conclusions may be influenced by 308 this center's practice standards; thus, multi-center studies 309 should be carried out to obtain further insights. Moreover, 310 the MELD score includes INR in the formula, and thus, 311 warfarin administration may have an impact on the score; 312 perhaps the MELD-XI score that excludes INR may be 313 more appropriate for such analysis (34), and we hope 314 that research on this aspect will be carried out in future. 315 Finally, a strength of this study was the use of the MELD 316 score to estimate liver function. We set a score of 14 as the 317 cutoff point, which was higher than that used in previous 318

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cardiac surgery studies. However, AAAD surgery is more
complicated than other types of cardiac surgery, and we
consider that a higher cutoff point is more reasonable in
this setting. We look forward to further studies on the
appropriate cutoff point for the MELD score to classify
hepatic function in patients with AAAD.

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326 Conclusions

Postoperative HD prolongs mechanical ventilation time and ICU stay, and it is associated with in-hospital mortality in patients with AAAD. A longer ACC time, higher postoperative leucocyte count, postoperative respiratory dysfunction, and postoperative LCOS are independent risk factors of HD in patients with AAAD undergoing surgery.

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346 **Footnote** 347

Conflicts of Interest: The authors have no conflicts of interestto declare.

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Ethical Statement: This study was approved by the 351 Committee on Ethics of Biomedicine Research, The 352 Second Military Medical University, Shanghai (No. 353 SMMUEC2018-012), with the need for individual 354 patient consent waived. The authors are accountable for 355 all aspects of the work in ensuring that questions related 356 to the accuracy or integrity of any part of the work are 357 appropriately investigated and resolved. 358

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Supplementary

Table S1 Multivariate analysis for evaluating predictors of mortality

Variable	OR	95% CI	P value
Postoperative MELD ≥14	8.911	1.029–77.179	0.047
Massive transfusion	6.622	1.606–27.307	0.009
Sepsis	5.350	0.698-40.986	0.106
Reintubation	3.911	1.193–12.819	0.024
Age	1.019	0.974-1.066	0.404
Re-exploration for bleeding	1.687	0.239–11.927	0.600
Postoperative leucocyte (×10 ⁹ /L) (per 2×10 ⁹ /L higher)	0.986	0.846-1.149	0.855
Preoperative renal insufficiency	0.817	0.257-2.599	0.733

MELD, end-stage liver disease; OR, odds ratio; CI, confidence interval.

Table S2 Multivariate analysis for evaluating predictors of prolonged ICU stay

Variable	OR	95% CI	P value
Postoperative MELD ≥14	2.465	1.121–5.42	0.025
Massive transfusion	9.938	4.564–21.639	0.000
24-h postoperative drainage volume (per 200 mL higher)	0.928	0.77-1.119	0.433
Re-exploration for bleeding	1.441	0.184–11.261	0.728
ACC time (min) (per 10 min higher)	1.024	0.867-1.209	0.780
LCOS	0.640	0.171-2.401	0.508
CRRT	10.110	1.969–51.907	0.006

MELD, end-stage liver disease; ICU, intensive care unit; ACC, aortic cross-clamp; LCOS, low cardiac output syndrome; CRRT, continuous renal replacement therapy; OR, odds ratio; CI, confidence interval.

Table S3 Multivariate analysis for evaluating predictors of massive transfusion

Variable	OR	95% CI	P value
Postoperative MELD ≥14	0.774	0.344–1.744	0.537
Sepsis	0.712	0.055–9.282	0.795
postoperative pneumonia	3.282	1.111–9.697	0.032
24-h postoperative drainage volume (per 200 mL higher)	1.547	1.239–1.931	0.000
CPB time (per 10 min higher)	1.202	0.912-1.584	0.191
Prolonged ICU stay	5.579	2.197–14.166	0.000
CRRT	2.772	0.604-12.722	0.190
Total-arch replacement	4.517	0.596–34.215	0.144
Preoperative MELD ≥14	1.245	0.243-6.372	0.793
Mechanical ventilation time (h)	1.001	0.994–1.009	0.703

MELD, end-stage liver disease; ICU, intensive care unit; CPB, cardiopulmonary bypass; CRRT, continuous renal replacement therapy; OR, odds ratio; CI, confidence interval.