Predictive Value of Postoperative Indices in Acute Stanford Type A Aortic Dissection

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ABSTRACT

Objective: To identify the risk factors for in-hospital mortality in postoperative patients with acute type-A aortic dissection (ATAAD), and combine a simplified-fit index which is feasible and helpful in a clinical practice.
Study Design: Observational study.
Place and Duration of the Study: The Second Hospital of Shandong University, Jinan, China, from May 2020 to July 2021.
Methodology: Hospitalised patients diagnosed with ATAAD were enrolled. The primary observational end-point of the study was mortality at discharge. Logistic analyses were used for the identification of risk factors. Fit index was calculated according to the results of logistic analysis. Receiver operating characteristic curves were used for the evaluation of diagnostic performance of single factors or fit index.
Results: Two hundred and ninety-five consecutive patients were enrolled, with mortality at discharge of 7.8%. A multivariate analysis revealed that haemoglobin (OR 0.958, p = 0.023), creatinine (OR 1.006, p = 0.045), Troponin I (OR 1.047, p = 0.001), and left ventricular ejection fraction (EF, OR 0.000, p <0.001) were independent factors associated with adverse outcome. Then, the four factors were fitted using the logistic analysis (fit index). The area under the receiver operating characteristic curve (AUROC) of fit index was 0.852.
Conclusion: Lower postoperative haemoglobin and EF, higher postoperative creatinine and Troponin I after ATAAD operation represent a higher patient mortality at discharge. Fit index originated in the above indicator may be feasible and helpful for the identification of patients with adverse prognosis.

Key Words: *Acute type-A aortic dissection, Risk factors, Hospital mortality.*

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INTRODUCTION

Acute type-A aortic dissection (ATAAD) is a highly fatal cardiovascular emergency which requires time-sensitive diagnosis and treatment.[1,2] Surgical reconstruction of aortic aneurysm and dissection is the main treatment option due to the high mortality of medical management.[2,3] In the recent five decades, surgical methods and perioperative care have been greatly improved.[1] However, ATAAD still faces a huge clinical challenge with high in-hospital mortality range from 5% to 24%.[2,4-9]

Some factors, such as malperfusion and shock, have been identified as important predictors associated with poor short-term outcomes.[1,2] Several biomarkers or prognostic models have also been evaluated as prognostic factors by the previous studies.[10-13]

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Although conventional postoperative indexes are characterised with good accessibility and feasible in clinical practice, the sole use of these indexes is inadvisable because of their poor diagnostic performance.[10-13] Meanwhile, the traditional scoring systems for predicting mortality in an intensive care unit (ICU), e.g. Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation–II (APACHE-II), and Acute Physiology and Chronic Health Evaluation–IV model (APACHE-IV) are not initially developed from ATAAD patients; in addition, the calculation of these scoring systems is relatively complex. In view of the above limitations, the logistic fitting of conventional indexes may be a practical solution.

Herein, the present study aimed to identify risk factors for in-hospital mortality in postoperative patients with ATAAD and to combine a simplified fit index which is feasible and helpful in a clinical practice.

METHODOLOGY

It is a retrospective and observational study conducted on hospitalised patients who were diagnosed with ATAAD and admitted in the Second Hospital of Shandong University, Jinan, China, from May 1, 2020 to July 31, 2021. Patients aged <18 years with non type-A aortic dissection operation, failure to perform surgery, voluntary discharge, and incomplete data, were excluded from the study. The study protocol was approved by the Ethical Committee of the hospital. The research process complied with the guidelines of the Declaration of Helsinki.

The primary observational end-point of the study was mortality at discharge. Electronic medical records were reviewed and the following clinical data were collected: patient age, gender, postoperative white blood cell counts (WBC), haemoglobin, platelet counts (PLT), albumin, total bilirubin (TB), blood urea nitrogen (BUN), creatinine, Troponin I (TnI), B-type natriuretic peptide (BNP), left ventricular ejection fraction (EF), outcome at discharge.

The variables were expressed as mean ± standard deviation, median (interquartile range [IQR]), or number (percentage) as appropriate. The normality of continuous variables was calculated by Kolmogorov-Smirnov test. The patients were retrospectively divided into two groups (death and survival) according to the outcome at discharge. The Student's *t*-test, the Mann-Whitney U-test, the χ^2 test or the Fisher's exact test were used for the comparison of postoperative characteristics between the two groups. Univariate and multivariate logistic analyses were used for the identification of factors associated with the patient death at discharge. Fit index was calculated by independent factors using the logistic analysis. Receiver operating characteristic (ROC) curves were used for the evaluation of diagnostic performance of single factors and fit index. The value, $p < 0.05$ was considered as statistically significant. The above statistical analyses were performed using software IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA) and MedCalc, version 12.7.0.0 (MedCalc Software bvba, Ostend, Belgium).

RESULTS

A total of 383 patients were preliminarily screened. Forty-two patients, 7 patients, 22 patients, and 17 patients were excluded because of uncertain outcome (discharged voluntarily), non type-A aortic dissection operation, failure to perform surgery, and incomplete data, respectively. Finally, 295 patients were included in the present study.

The mean age was 53.2±11.4 years (median 54.0 years), and most patients were males (216/295, 73.2%). The median length of hospital stay was 24 (IQR 20-30) days. Twenty-three patients (7.8%) suffered clinical death at discharge and were characterised to have greater proportion of males (p = 0.011), higher levels of creatinine (p <0.001) and TnI (p <0.001), and lower levels of haemoglobin (p = 0.011), PLT (p = 0.007), albumin (p = 0.040), and EF (p = 0.001). Table I summarised the postoperative characteristics of the included patients.

A univariate logistic analysis revealed that gender, haemoglobin, albumin, PLT, creatinine, TnI, and EF were the potential predictors of patient death (Table II). Then, the above variables were brought into a multivariate analysis which revealed that haemoglobin (OR 0.958, p = 0.023), creatinine (OR 1.006, p = 0.045), TnI (OR 1.047, p = 0.001), and EF (OR 0.000, p <0.001) were independent factors associated with the adverse outcome (Table II).

The diagnostic performances of the four independent factors associated with patient death at discharge were further assessed. The area under the receiver operating characteristic curve (AUROC) for haemoglobin, creatinine, TnI, and EF were 0.652 (95% CI 0.595 – 0.706), 0.755 (95% CI 0.702 – 0.803), 0.762 (95% CI 0.710 – 0.810), and 0.706 (95% CI 0.651 – 0.757), respectively. Then, the four factors were fitted using the logistic analysis (fit index). The performances of fit index for patient death at discharge were assessed, with an AUROC of 0.852 (95% CI 0.807 – 0.891), a sensitivity of 78.3% (95% CI 56.3%-92.5%), a specificity of 82.4 (95% CI 77.3%-86.7%), a positive likelihood ratio of 4.43, and a negative likelihood of 0.26, respectively. The fit index presented a better diagnostic performance than haemoglobin, creatinine, or EF (fit index *vs.* haemoglobin, p = 0.001; fit index *vs.* creatinine, p = 0.035; fit index *vs.* TnI, p = 0.072; fit index *vs.* EF, p = 0.004) as seen in Figure 1.

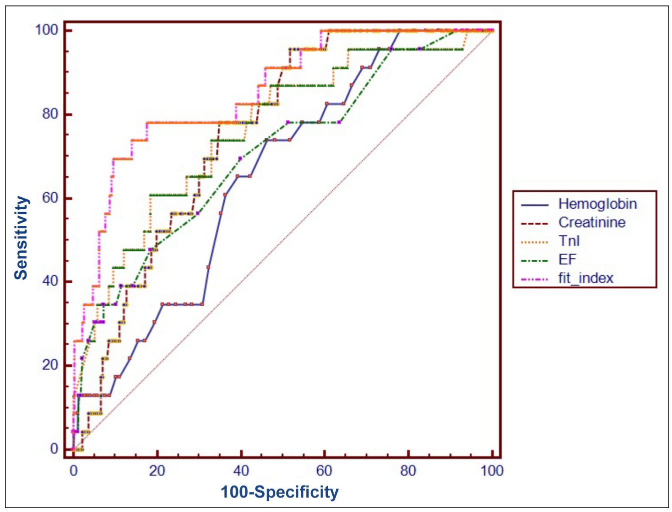

Figure 1: Receiver operating characteristic curves of haemoglobin, creatinine, Troponin I, left ventricular ejection fraction, and fit index.

DISCUSSION

The present study enrolled 295 ATAAD patients and identified that lower postoperative haemoglobin and EF, higher postoperative creatinine and TnI were independent risk factors for the higher mortality at discharge. A fit index with better diagnostic efficiency was also combined, which may be helpful in a clinical practice.

Acute aortic dissection is a relatively rare, acute, and severe disease. An emergency surgical therapy is indicated for the overwhelming majority of patients, except for those who are moribund or severely comorbid.[1,2] According to the Stanford classification, ATAAD is the most lethal type because of the involvement of ascending aorta. The surgical mortality of ATAAD patients was still as high as 18% in the last two decades.[8,9]

Table I: Postoperative characteristics of included patients.

	Total (n=295)	Death (n=23)	Survival (n=272)	p-values*
Age, years	53.2±11.4	53.8±14.7	53.1±11.1	0.775
Gender, male (n, %)	216 (73.2%)	22 (95.7%)	194 (71.3%)	0.011
WBC(10^9/L)[a]	9.99 (7.85, 12.84)	9.48 (6.89, 11.29)	10.06 (7.87, 12.95)	0.411
Haemoglobin (g/L)	105.6±13.8	98.6±12.8	106.2±13.7	0.011
PLT(10^9/L)[a]	98.0 (76.0, 130.0)	71.0 (54.0, 105.0)	100.0 (78.0, 130.8)	0.007
Albumin (g/L)	37.4 (34.2, 40.0)	36.1 (30.2, 39.3)	37.5 (34.6, 40.0)	0.040
TB (umol/L)[a]	35.5 (20.1, 56.2)	44.8 (20.6, 65.5)	35.2 (20.0, 56.1)	0.335
BUN(mmol/L)[a]	10.50 (8.60, 14.60)	12.39 (10.50, 15.00)	10.00 (8.50,14.58)	0.056
Creatinine[a] (umol/L)[a]	111.0 (85.0, 150.9)	163.0 (128.0, 208.0)	107.0 (83.4, 143.0)	<0.001
TnI (pg/ml)[a]	4.02 (2.08, 9.60)	12.62 (4.64, 40.00)	3.78 (1.93, 8.56)	<0.001
BNP (pg/ml)[a]	674.0 (305.0, 1176.0)	614.0 (229.0, 1571.0)	674.3 (307.0, 1169.5)	0.792
EF[a]	0.56 (0.54, 0.58)	0.54 (0.44, 0.56)	0.56 (0.54, 0.58)	0.001

*WBC, White blood cell counts; PLT, Platelet counts; TB, Total bilirubin; BUN, Blood urea nitrogen; TnI, Troponin I; BNP, B-type natriuretic peptide; EF, left ventricular ejection fraction. a: Median (interquartile range). * Student's t-test, Mann-Whitney U-test or Chi-square test according to the characteristics of distribution.*

Table II: Univariate and multivariate logistic analyses revealing predictors for patient death at discharge.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.006 (0.968, 1.044)	0.774		
Gender#	0.113 (0.015, 0.853)	0.035		
WBC	0.936 (0.825, 1.062)	0.302		
Haemoglobin#	0.961 (0.931, 0.991)	0.012	0.958 (0.923, 0.994)	0.023
PLT#	0.984 (0.972, 0.996)	0.009	0.987 (0.974, 1.000)	0.055
Albumin#	0.896 (0.821, 0.978)	0.014		
TB	1.008 (0.994, 1.022)	0.283		
BUN	1.058 (0.973, 1.151)	0.186		
Creatinine#	1.007 (1.001, 1.012)	0.013	1.006 (1.000, 1.012)	0.045
TnI#	1.063 (1.035, 1.091)	<0.001	1.047 (1.020, 1.075)	0.001
BNP	1.000 (1.000, 1.001)	0.166		
EF#	0.000 (0.000, 0.004)	<0.001	0.000 (0.000, 0.001)	<0.001

WBC, White blood cell counts; PLT, Platelet counts; TB, Total bilirubin; BUN, Blood urea nitrogen; TnI, Troponin I; BNP, B-type natriuretic peptide; EF, Left ventricular ejection fraction. # Variables brought into multivariate analysis.

In this study, twenty-three patients (7.8%) from a total of 295 suffered clinical death at discharge. The relatively low fatality rate may be related to the improvement of surgical techniques and perioperative nursing in the recent years. Meanwhile, the exclusion of patients with uncertain outcomes is also prone to attrition bias.

The early identification of risk factors for postoperative mortality can help clinicians take measures to prevent deterioration of the disease to the greatest extent, thereby reducing the postoperative mortality in patients with ATAAD. This study focused on conventional postoperative indexes, which may have the potential to be widely used in a clinical practice because of better accessibility.

According to the existing studies, the prognosis of patients with ATAAD is associated with organ malperfusion. The Penn classification has been summarised to predict surgical mortality in patients with ATAAD according to the degree of poor perfusion, which has been validated by cohort from other centres.[14-16] Meanwhile, it is well known that aortic dissection requires extracorporeal circulation support techniques. In the case of cardiopulmonary bypass, even if the operation is very successful, the risk of organ ischemia, such as kidney, myocardial, liver and bowel, is unavoidable. Investigators have found that ischemic manifestations such as hypotension, myocardial ischemia, acute renal insufficiency, intestinal ischemia, lower-limb ischemia, and disturbance of consciousness are independent risk factors for postoperative death in patients with ATAAD.[1,2,8,17] The present study also emphasised the role of ischemia in the outcome of patients after aortic dissection repair. For example, elevated creatinine and troponin, as manifestations of renal and myocardial ischemia, were independent risk factors for postoperative mortality in patients with aortic dissection. This conclusion was consistent with the results of previous studies. Ghoreishi *et al*. also identified that patients with liver malperfusion were more likely to present a poor outcome after type A aortic dissection surgery.[12] In the present study, it was found that total bilirubin in the death group was higher than what was found in the survival group, but there was no statistical difference (44.8 umol/L *vs.* 35.2 umol/L, p = 0.335). This phenomenon may be attributed to the better tolerance to ischemia and hypoxia of liver compared with kidney and myocardium (1-2 hours *vs.* 30 minutes). In addition to the direct organ injury caused by ischemia, the ischemia-reperfusion injury caused by free radicals, calcium overload, ferroptosis, activation of white blood cells and so on, seems to be more serious.[18,19]

Other independent predictors identified by the present study included haemoglobin and EF. The decrease of postoperative haemoglobin represents more severe haemorrhage, which usually occurs during prolonged intra-operative cardiopulmonary bypass assistance, and is more likely to lead to ischemia and hypoxia of vital organs. Decreased cardiac EF after surgery could lead to a lower cardiac output, which in turn causes persistent multiple organ injury and increased mortality. Recently, Huo *et al*. also concluded that postoperative low cardiac output was an independent risk factor for postoperative death in ATAAD, which was consistent with the results of the present study.[11]

A retrospective study of 144 patients with ATAAD found that serum lactate levels obtained quickly before surgery may be a potential predictor of hospitalisation and one-year mortality.[20] But soon after, another study found unsatisfactory predictive value of the sole use of lactic acid levels for postoperative mortality.[13] This study failed to adopt this indicator since the lactic acid level could not be obtained from the electronic medical records. Hence, further studies are needed to confirm this potential indicator.

Compared with single indicator and traditional scoring systems predicting mortality in ICU (e.g. SOFA, APACHE-II, APACHE-IV), the combination of fit index in the present study gives consideration to both practicability and accurate prediction for adverse outcomes. An AUROC of 0.852 represents a relatively acceptable diagnostic performance, which was better or similar with the performance of traditional scoring systems.[10] The present study suggests a new and easily acquired marker for assessing in-hospital mortality after ATAAD repair.

Several limitations should be mentioned of the present study. The most important limitation was the adoption of mortality at discharge as the primary outcome, which could not reflect the medium-term and long-term prognosis of these patients. Furthermore, as mentioned above, the existence of attrition bias may underestimate the in-hospital mortality of patients. The above limitations stem from the natural defects of a retrospective study. However, the single-centre nature of the present study and the relatively short enrollment periods ensured the homogeneity of the enrolled patients, which may represent the advances in diagnosis and treatment of ATAAD in East Asia in the recent years.

CONCLUSION

Lower postoperative haemoglobin and EF, higher postoperative creatinine and TnI after ATAAD operation represent a higher patient mortality at discharge. Identification of patients with adverse prognosis using a single indicator may be inaccurate, while the fit index may be feasible and helpful in a clinical practice.

ETHICAL APPROVAL:
The study protocol was approved by the Ethical Committee of The Second Hospital of Shandong University, Jinan, China

PATIENTS' CONSENT:
Written informed consent was waived due to the retrospective and observational design of the study. However, patients agreed that their electronic medical records may be used for possible observational study without identification and leakage of personal information.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
YC: Patients' follow-up, data collection, statistical analysis, and manuscript writing.
WYY: Patients' follow-up, data collection, and manuscript revision.
TF: Conception of the manuscript, study design, patients' follow-up, data collection, and manuscript revision.
GY: Conception of the manuscript, study design, patients' follow-up, data collection, statistical analysis, manuscript writing and revision.
All authors have approved the final version of the manuscript to be published.

REFERENCES

1. Zhu Y, Lingala B, Baiocchi M, Tao JJ, Toro Arana V, Khoo JW, *et al*. Type A aortic dissection-experience over 5 decades: JACC historical breakthroughs in perspective. *J Am Coll Cardiol* 2020; **76(14)**:1703-13. doi: 10.1016/j.jacc.2020.07.061.
2. Gudbjartsson T, Ahlsson A, Geirsson A, Gunn J, Hjortdal V, Jeppsson A, *et al*. Acute type A aortic dissection - A review. *Scand Cardiovasc J* 2020; **54(1)**:1-13. doi: 10.1080/14017431.2019.1660401.
3. Olsson C, Thelin S, Ståhle E, Ekbom A, Granath F. Thoracic aortic aneurysm and dissection: Increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. *Circulation* 2006; **114(24)**: 2611-8. doi: 10.1161/CIRCULATIONAHA.106.630 400.
4. Arsalan M, Squiers JJ, Herbert MA, MacHannaford JC, Chamogeorgakis T, Prince SL, *et al*. Comparison of outcomes of operative therapy for acute type a aortic dissections provided at high-volume *versus* low-volume medical centres in North Texas. *Am J Cardiol* 2017; **119(2)**:323-7. doi: 10.1016/j.amjcard.2016.09.034.
5. Hawkins RB, Mehaffey JH, Downs EA, Johnston LE, Yarboro LT, Fonner CE, *et al*. Regional practice patterns and outcomes of surgery for acute type a aortic dissection. *Ann Thorac Surg* 2017; **104(4)**:1275-81. doi: 10.1016/ j.athoracsur.2017.02.086.
6. Nishida H, Tabata M, Fukui T, Sato Y, Kin H, Takanashi S. A systematic approach to improve the outcomes of type A aortic dissection. *J Thorac Cardiovasc Surg* 2017; **154(1)**: 89-96.e1. doi: 10.1016/j.jtcvs.2017.03.050.

7. Uchida K, Karube N, Kasama K, Minami T, Yasuda S, Goda M, *et al*. Early reperfusion strategy improves the outcomes of surgery for type A acute aortic dissection with malperfusion. *J Thorac Cardiovasc Surg* 2018; **156(2)**: 483-9. doi: 10.1016/j.jtcvs.2018.02.007.
8. Evangelista A, Isselbacher EM, Bossone E, Gleason TG, Eusanio MD, Sechtem U, *et al*. Insights from the international registry of acute aortic dissection: A 20-year experience of collaborative clinical research. *Circulation* 2018; **137(17)**:1846-60. doi: 10.1161/ CIRCULATIONAHA.117. 031264.
9. Pape LA, Awais M, Woznicki EM, Suzuki T, Trimarchi S, Evangelista A, *et al*. Presentation, diagnosis, and outcomes of acute aortic dissection: 17-Year trends from the international registry of acute aortic dissection. *J Am Coll Cardiol* 2015; **66(4)**:350-8. doi: 10.1016/j.jacc.2015.05. 029.
10. Schoe A, Bakhshi-Raiez F, de Keizer N, van Dissel JT, de Jonge E. Mortality prediction by SOFA score in ICU-patients after cardiac surgery: Comparison with traditional prognostic-models. *BMC Anesthesiol* 2020; **20(1)**:65. doi: 10.1186/ s12871-020-00975-2.
11. Huo Y, Zhang H, Li B, Zhang K, Li B, Guo SH, *et al*. Risk factors for post-operative mortality in patients with acute stanford type A aortic dissection. *Int J Gen Med* 2021; **14**:7007-15. doi: 10.2147/IJGM.S330325.
12. Ghoreishi M, Wise ES, Croal-Abrahams L, Tran D, Pasrija C, Drucker CB, *et al*. A novel risk score predicts operative mortality after acute type A aortic dissection repair. *Ann Thorac Surg* 2018; **106(6)**:1759-66. doi: 10.1016/j. athoracsur.2018.05.072.
13. Zindovic I, Luts C, Bjursten H, Herou E, Larsson M, Sjögren J, *et al*. Perioperative hyperlactemia is a poor predictor of outcome in patients undergoing surgery for acute type-A aortic dissection. *J Cardiothorac Vasc Anesth* 2018; **32(6)**: 2479-84. doi: 10.1053/j.jvca.2018.03.030.
14. Augoustides JG, Geirsson A, Szeto WY, Walsh EK, Cornelius B, Pochettino A, *et al*. Observational study of mortality risk stratification by ischemic presentation in patients with acute type A aortic dissection: The Penn classification. *Nat Clin Pract Cardiovasc Med* 2009; **6(2)**:140-6. doi: 10.1038/ ncpcardio1417.
15. Tien M, Ku A, Martinez-Acero N, Zvara J, Sun EC, Cheung AT. The Penn classification predicts hospital mortality in acute stanford type A and type B aortic dissections. *J Cardiothorac Vasc Anesth* 2020; **34(4)**:867-73. doi: 10.1053/j.jvca.2019. 08.036.
16. Kimura N, Ohnuma T, Itoh S, Sasabuchi Y, Asaka K, Shiotsuka J, *et al*. Utility of the penn classification in predicting outcomes of surgery for acute type a aortic dissection. *Am J Cardiol* 2014; **113(4)**:724-30. doi: 10.1016/j.amjcard.2013. 11.017.
17. Zindovic I, Sjögren J, Ahlsson A, Bjursten H, Fuglsang S, Geirsson A, *et al*. Recombinant factor VIIa use in acute type A aortic dissection repair: A multicenter propensity-score--matched report from the nordic consortium for acute type A aortic dissection. *J Thorac Cardiovasc Surg* 2017; **154(6)**: 1852-9.e2. doi: 10.1016/j.jtcvs.2017.08.020.
18. Wu MY, Yiang GT, Liao WT, Tsai AP, Cheng YL, Cheng PW, *et al*. Current mechanistic concepts in ischemia and reperfusion injury. *Cell Physiol Biochem* 2018; **46(4)**: 1650-67. doi: 10.1159/000489241.
19. Luo L, Mo G, Huang D. Ferroptosis in hepatic ischemia-reperfusion injury: Regulatory mechanisms and new methods for therapy [Review]. *Mol Med Rep* 2021; **23(3)**:225. doi: 10.3892/mmr.2021.11864.
20. Bennett JM, Wise ES, Hocking KM, Brophy CM, Eagle SS. Hyperlactemia predicts surgical mortality in patients presenting with acute stanford type-A aortic dissection. *J Cardiothorac Vasc Anesth* 2017; **31(1)**:54-60. doi: 10. 1053/j.jvca.2016.03.133.

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