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RESEARCH

Risk factors for postoperative hepatic dysfunction in overweight patients with acute type A aortic dissection

Yu Xu[1], Lin-Zhuo Liu[2], Hong-Qiao Lu[2], Xin-Qing Yang[2], Shi-Kui Guo[2*], Yong-Jiang Tang[1*] and Kun-Mei Gong[2*]

Abstract

Background Acute hepatic dysfunction (AHD) is a common postoperative complication in patients with acute type A aortic dissection. The aim of this study was to identify risk factors for acute hepatic dysfunction after surgery for acute type A aortic dissection.

Methods We performed a retrospective study from March 1, 2019, to February 28, 2021. The primary endpoints of this study were morbidity due to AHD and risk factors for incidence. Univariate analysis and multivariate logistic regression analysis were used to analyse the related factors, and receiver operating characteristic (ROC) curves were plotted to evaluate their predictive value.

Results Among 147 patients, 29 (19.73%) developed postoperative acute hepatic dysfunction, and 9 (6.12%) died. Univariate analysis revealed that the ALT ($P=0.042$), Cr ($P<0.001$), and BUN ($P=0.008$) levels were significantly different between the two groups. Multivariate logistic regression analysis revealed that Cr (OR = 1.013, 95% CI = 1.003–1.023, $P=0.008$) was an independent risk factor for postoperative hepatic dysfunction in overweight (BMI > 24) patients with ATAAD. The area under the ROC curve (AUC) for Cr was 0.745 > 0.7, indicating good predictive value.

Conclusion A high Cr concentration is an independent risk factor for postoperative AHD in overweight (BMI > 24) patients with ATAAD.

Keywords ATAAD, Acute hepatic dysfunction, MELD score, Risk factors

Acute hepatic dysfunction is a common postoperative complication in patients with acute type A aortic dissection. Once diagnosed with ATAAD, surgical treatment is the only way to save the patient's life [1, 2], however, with the development of endovascular technology, a subset of special acute type A aortic dissections may be resolved by endovascular treatment. Moreover, in recent years, with improvements in surgical techniques, the perioperative mortality rate of ATAAD patients has greatly decreased [3]. However, perioperative complications strongly affect the patient prognosis [4]. Acute hepatic dysfunction (AHD) is a common postoperative complication of ATAAD and is closely related to the patient prognosis [5].

Yu Xu, Lin-Zhuo Liu and Hong-Qiao Lu are co-first authors.

Shi-Kui Guo, Yong-Jiang Tang and Kun-Mei Gong are co-corresponding authors.

*Correspondence:
Shi-Kui Guo
guoshikui2008@126.com
Yong-Jiang Tang
450390456@qq.com
Kun-Mei Gong
kunhuagongkunmei@163.com
[1]Panzhihua Central Hospital, 34 Yikang St, Panzhihua, Sichuan Province 617000, China
[2]The Affiliated Hospital of Kunming University of Science and Technology, No. 157 Jinbi Road, Kunming City, Yunnan Province 650500, China

The incidence of acute liver failure after cardiac-related surgery is approximately 13% [6], and cardiopulmonary bypass increases the rate of acute liver injury, leading to death [7]. Obesity is closely related to postoperative mortality in patients with ATAAD [8]. The body mass index (BMI) is positively associated with the incidence of severe adverse outcomes in patients who undergo ATAAD [9]. The MELD score is a good model for evaluating the occurrence of acute dysfunction after surgery. The MELD score is calculated as MELD = 11.2In (INR) + 3.8ln[bilirubin (mg/mL)] + 9.6 In [serum creatinine (μmol/L)] + 6.4× cause (biliary or alcoholic = 0; Other = 1) [10]. However, studies on the risk factors for acute liver injury in overweight patients with ATAAD are rare. In this study, relevant data on overweight ATAAD patients were retrospectively analysed, and the risk factors for acute hepatic insufficiency after surgery were discussed to provide a theoretical basis for the clinical treatment of these diseases.

Methods

We retrospectively analysed the clinical data of 147 overweight (BMI > 24) patients with ATAAD at the Affiliated Hospital of Kunming University of Science and Technology from March 1, 2019, to February 28, 2021. All the patients were diagnosed with ATAAD by CTA before surgery, and all underwent surgical treatment. There were 109 males and 38 females with an average age of 51.04 ± 10.17 years.

The patients' basic information, including age, sex, weight, height, history of hypertension, smoking status, diabetes status, hospital white blood cells, neutrophils, lymphocytes and neutrophils/lymphocytes, red blood cells deposited, platelet count, APTT, PT and INR, FIB, FDP, DD2, LVEF, AST, ALT, TBIL, UBIL, albumin, Cr, BUN, K, Na, Cl, Ca, CKMB, aTn1, MYO, intraoperative infusion, platelets, red blood cell count, plasma, transit time, deep low-temperature cycle time stopped, aorta blocking time, intraoperative minimum anus temperature, and minimum nasal temperature, was collected. According to the postoperative bilirubin concentration, INR, and postoperative creatinine level, the patients were divided into an experimental group and a control group according to their MELD score (patients with MELD scores < 15 were defined as the liver dysfunction group, and patients with MELD scores > 15 were defined as the liver dysfunction group). Patient blood samples were used to evaluate the first preoperative blood index after admission and to obtain intraoperative and postoperative data.

All surgeries were standardized for all patients, and patients who underwent endovascular repair were not included. All the operations were performed under deep hypothermic circulatory arrest. The Bentall procedure [11] was used in 20 patients, and 127 patients underwent Sun's operation [12]. A flowchart of the study is shown in Fig. 1.

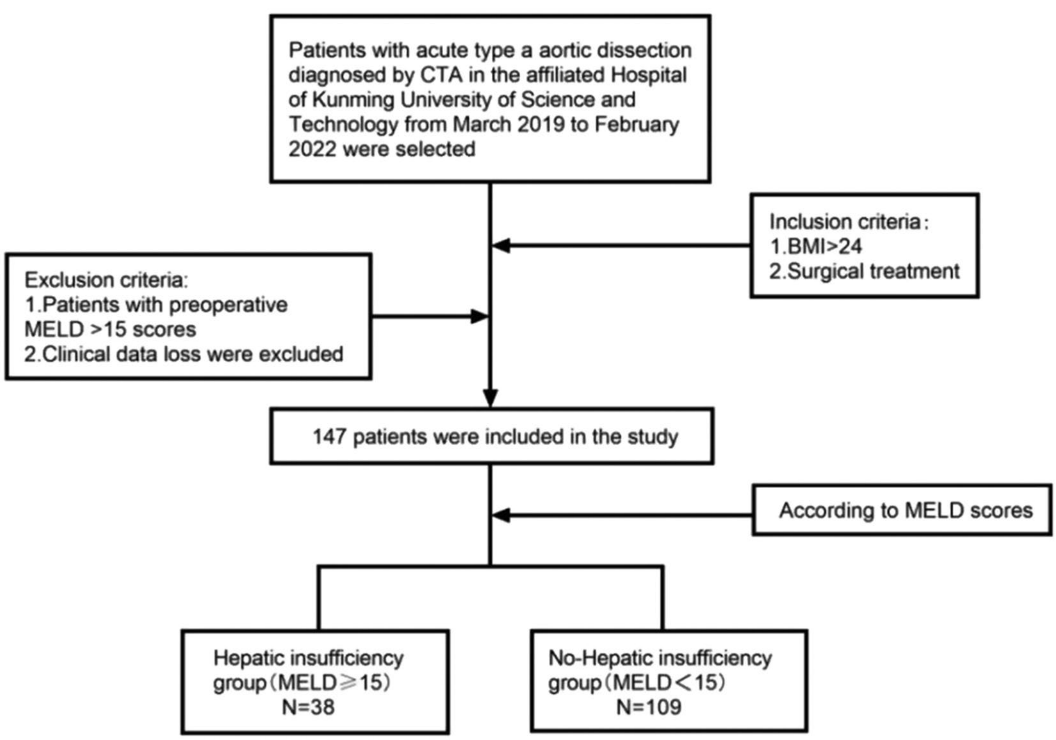

Fig. 1 The flow chart of the study

SPSS 26.0 was used for data analysis. The t test, rank sum test and chi-square test were used for normally distributed data, nonnormally distributed data and count data, respectively. Logistic regression models were used to identify univariate and multivariate risk factors for postoperative HD. ROC curves were drawn to evaluate the predictive value. Flow charts were generated via GraphPad Prism software.

Results

A total of 147 patients (109 males and 38 females) were included in this study; the average age was 51.04±10.17 years, and the average BMI was 27.53. The medical history collected included hypertension (74.83%), diabetes (7.48%), and smoking history (53.74%). Sun's procedure was performed in 127 patients, and 20 patients underwent the Bentall procedure. All the patients were divided into two groups according to their MELD score. The mean MELD score of all the patients was 11.68. Patients with a MELD score<15 were defined as the nonhepatic dysfunction group, for which the average MELD score was 10.03. Patients with a MELD score>15 were defined as the hepatic dysfunction group, for which the average MELD score was 18.38. There were 84 males and 34 females in the nonhepatic insufficiency group and 25 males and 4 females in the hepatic dysfunction group. In the nonhepatic insufficiency group, 89 patients had a history of high blood pressure (22 females and 67 males), 60 patients had a smoking history (2 females and 58 males), and 9 patients had a history of diabetes (2 females and 7 males). In the hepatic insufficiency group, 21 patients had hypertension (2 females and 19 males), 19 patients had a smoking history (19 males), 2 patients had a history of diabetes (2 males), the mean white blood cell count was 12.39±3.59 (x10^9/L), the mean neutrophil count was 10.21±3.53 (x10^9/L), and the median and interquartile range of lymphocytes was 1.16 (0.74, 1.67). The median preoperative creatinine level was 113 μmol/L. Among the 147 patients, the celiac artery and superior mesenteric artery were not involved in 4 patients, and dissection in the other patients involved the celiac artery and superior mesenteric artery (although the dissection involved the celiac trunk and superior mesenteric artery, liver function was not significantly impaired before the operation). Moreover, 9 patients died (3 patients with haemorrhagic shock, 2 patients with electrolyte disturbance, 1 patient with renal failure, 1 patient with coagulation collapse, and 2 patients with longitudinal cadmium infection). Postoperative renal insufficiency occurred in 44 patients (7 patients were treated with haemodialysis, 1 of whom died), 59 patients had different degrees of pulmonary infection, and 9 patients had severe thrombocytopenia (possibly caused by heparin-induced thrombocytopenia). The basic data of the patients are shown in Table 1. Nine patients died in the hospital (6.12%), eight in the hepatic insufficiency group and one in the nonhepatic insufficiency group.

As shown in Table 1, univariate analysis revealed no statistically significant differences in sex, age, hypertension status, diabetes status, smoking status, WBC count, neutrophil count, granulocyte count, lymphocyte count, or neutrophil/lymphocyte ratio between the 2 groups. There were statistically significant differences ($P<0.05$) in the preoperative ALT level ($P=0.042$), preoperative Cr level ($P<0.001$), and preoperative BUN level ($P=0.008$) between the 2 groups. The multivariable analyses of risk factors for postoperative AHD included the preoperative ALT level, preoperative Cr level, and preoperative BUN level, and the multivariate logistic regression analysis revealed that preoperative Cr ($P=0.008$, 95% CI=1.003–1.023, OR=1.013) was a risk factor for postoperative AHD in overweight patients with acute aortic dissection (Table 2). ROC curves were generated to explore the predictive ability and cut-off value of preoperative Cr for postoperative AHD. As shown in Fig. 2, the area under the curve (AUC) of the preoperative Cr level used for predicting postoperative AHD in patients with ATAAD was 0.745>0.7 (cut-off: 107 U/L; sensitivity: 0.586; specificity: 0.856), indicating good predictive value (Table 3; Fig. 2).

Discussion

Few studies have reported risk factors for postoperative AHD in overweight patients with ATAAD. In this study, a total of 38 overweight patients with ATAAD developed postoperative AHD, and 9 patients ultimately died; 8 patients in the hepatic dysfunction group (3 patients with haemorrhagic shock due to severe postoperative bleeding, 2 patients with electrolyte disturbance, 1 patient with renal failure, and 2 patients with mediastinal infection) and 1 patient in the nonhepatic dysfunction group died of postoperative coagulation collapse. The overall mortality rate was 6.12%. Multivariate logistic regression analysis revealed that preoperative Cr was an independent risk factor for postoperative AHD in overweight patients with acute AAD.

Overweight and obesity have recently been identified as risk factors for many diseases [13–15]. Similarly, a high body mass index (BMI) has been found to be associated with a high risk of adverse outcomes in patients undergoing cardiac surgery [16, 17]. A total of 9 patients died in this study, and the mortality rate was 6.12%, which is similar to or even lower than that reported in previous studies. Several large studies have shown that overweight and obese patients are more likely than healthy individuals to have serious complications after surgery, leading to death [18]. Therefore, early detection of postoperative hepatic

Table 1 Basic clinical data and univariate analysis of overweight ATAAD patients

Variable	The overall	No-AHD	AHD	P
Gender (male/female)	109/38	84/34	25/4	0.098
Age	51.04 ± 10.17	51.47 ± 10.45	49.28 ± 8.85	0.299
Weight(Kg)	75(69,83)	73.5(69,81.25)	76(70,85)	0.201
Height(cm)	166.7 ± 8.34	166.91 ± 8.63	165.93 ± 7.10	0.574
Hypertension (yes/no)	110/37	89/29	21/8	0.738
Smoking history (yes/no)	79/68	60/58	19/10	0.156
Diabetes (yes/no)	11/136	9/109	2/27	0.893
WBC	11.92 ± 3.64	11.81 ± 3.66	12.39 ± 3.59	0.442
Neutrophile granulocyte	9.77 ± 3.47	9.66 ± 3.460	10.21 ± 3.53	0.449
Lymphocyte	1.18(0.83,1.62)	1.19(0.83,1.56)	1.16(0.74,1.67)	0.963
Neutrophil/lymphocyte ratio	7.6(5.43,13.65)	7.52(5.36,13.29)	7.6(5.66,15.03)	0.653
HCT	0.41(0.38,0.44)	0.41(0.38,0.44)	0.427(0.39,0.44)	0.174
PLT	175(141,218)	175(143,218)	176(139,210)	0.848
APTT	37.1(33.7,38.9)	37(33.55,38.96)	37.1(34.15,38.7)	0.586
PT	13.75 ± 0.93	13.76 ± 0.91	13.71 ± 1.05	0.811
INR	1.05(1,1.13)	1.05(1,1.13)	1.05(1,1.125)	0.779
FIB	2.95(2.22,3.83)	2.94(2.22,3.83)	2.97(2.14,4)	0.697
FDP	29.9(11.82,54.34)	26.51(9.48,54.71)	34.2(14.71,53.43)	0.607
DD2	9.74(4.57,17.43)	9.5(4.43,17.31)	10.85(6.61,17.95)	0.519
LVEF	0.63(0.59,0.68)	0.63(0.59,0.68)	0.66(0.61,0.69)	0.264
AST	23(17,36)	22(16,35.25)	27(19,57.5)	0.054
ALT	23(17,46)	22.4(16.4,43.75)	39(20.8,46.5)	0.042
TBIL	14.7(11.5,21.3)	14.4(10.8,20.18)	17.2(12.2,24.3)	0.171
UBIL	8.9(6.8,13.2)	8.9(6.7,13.05)	9.3(7.55,15.7)	0.351
Albumin	38.5(35.2,40.6)	38.65(35.18,40.83)	37.7(35.6,39.3)	0.553
Cr	84(64,105)	81(61,95.5)	113(83,138.5)	<0.001
BUN	6.1(4.8,8.3)	5.65(4.5,7.85)	7.1(6,8.35)	0.008
K	3.8(3.6,4.1)	3.8(3.6,4.1)	3.9(3.75,4.25)	0.139
Na	139(137,140)	139(138,140)	138(137,140)	0.169
Cl	107(105,109)	107(105,109.25)	106(104,108.5)	0.061
Ca	2.14 ± 0.12	2.14 ± 0.12	2.13 ± 0.13	0.793
CKMB	1.5(0.6,3.9)	1.4(0.6,4)	1.7(0.85,3.15)	0.472
aTn1	0.015(0.004,0.108)	0.0135(0.004,0.0995)	0.022(0.007,0.245)	0.189
MYO	54.25(33.78,124.3)	53.5(31.2,118.88)	60.65(43.15,167.83)	0.181
Intraoperative infusion of RBCs	800(400,800)	800(400,800)	800(750,800)	0.468
Infusion of plasma	600(600,600)	600(600,600)	600(600,600)	0.575
Platelet transfusions	150(150,300)	150(150,300)	150(150,300)	0.391
Operation (Sun's/Bentall)	127/20	99/19	28/1	0.139
Turnaround time	147(129,170)	146.5(129,169.5)	147(129,170.5)	0.961
Deep hypothermia time	13(12,15)	13(12,15)	13(12,13.5)	0.054
Aortic cross-clamping time	87(75,97)	86.5(74.75,96)	89(79,101.5)	0.415
Lowest rectal temperature	27.8(26.8,28.6)	27.9(26.8,28.7)	27.6(26.95,28.4)	0.512
Minimum nasal temperature	23.92 ± 1.42	23.89 ± 1.35	24.00 ± 1.70	0.712

Table 2 Multifactor Logistics regression analysis of risk factors for postoperative AHD in overweight ATAAD patients

Variable	P	O	95%CI
Cr	0.008	1.013	1.003～1.023

dysfunction in overweight patients with ATAAD could reduce the incidence of complications and mortality.

In one study, the incidence of postoperative hepatic dysfunction in patients with ATAAD was approximately 25.4% [19], which is slightly different from the incidence reported in our study, possibly because of the use of different inclusion criteria. Most patients with acute type

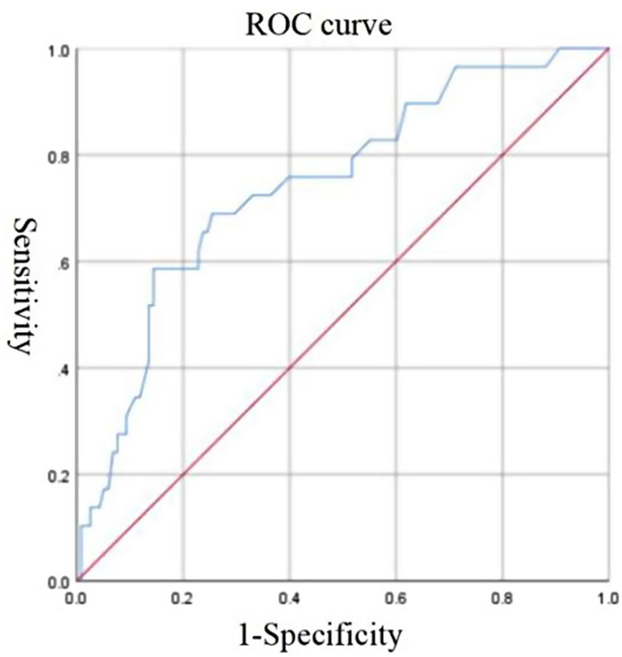

Fig. 2 ROC curve of Cr predicts hepatic dysfunction in overweightpatients with overweight ATAAD

A aortic dissection have involvement of the abdominal branch artery, which can lead to dysfunction. Moreover, dissection involves the aortic valve proximally, and even complications such as pericardial tamponade can lead to ischaemic damage to liver function. Additionally, after a long operation, the release of systemic inflammatory factors increases the burden on liver function to some degree, leading to liver insufficiency.

In this study, multivariate logistic regression analysis revealed that preoperative Cr was an independent risk factor for postoperative AHD in overweight patients with acute AAD, indicating that preoperative renal dysfunction may lead to postoperative hepatic dysfunction and even failure. First, a high preoperative creatinine level indicates a certain degree of renal injury, and the concentration of erythropoietin (EPO) is correspondingly reduced. EPO is a protective factor for multiple organs, including the kidney [20]. Second, owing to the rapid development of ATAAD, dissection involves the blood supply to multiple organs [21]. The body cannot redistribute blood in a short time, and impaired renal function further leads to a sharp reduction in liver tolerance, toxic clearance and metabolism, greatly increasing the likelihood of postoperative acute liver injury. Third, overweight patients often have a degree of liver and kidney steatosis [22]. In metabolic disorders, liver function and kidney function form a vicious cycle, leading to irreversible liver and kidney failure. A meta-analysis revealed that the incidence of acute kidney injury after ATAAD surgery was as high as 50.7% [23]. A large amount of oestrogen is produced in the adipose tissue of overweight and obese patients [24–26]. Fourth, oestrogen can inhibit the formation and secretion of very low-density lipoprotein in the liver [27], inhibit the export of fat from the liver, and aggravate liver function damage to a certain extent. Finally, the occurrence of preoperative renal dysfunction and postoperative hepatic dysfunction may be related to the hepatorenal reflex, but this has not been clearly confirmed in ATAAD-related diseases [28].

Several studies have investigated the occurrence of AHD after ATAAD surgery, but few have examined the occurrence of AHD after ATAAD surgery in overweight patients. Overweight and obesity have been hot topics in recent years and are the basis of a variety of cardiovascular diseases. Preoperative Cr is an independent risk factor for postoperative AHD in overweight patients with acute AAD. This fact will not only enable clinicians to identify and prevent serious complications early but also provide ideas for research on serious cardiovascular diseases caused by overweight and obesity. Moreover, this study revealed that more than one quarter of patients with severe ATAAD developed AHD after surgery, which suggests that we should pay attention to the occurrence of such complications, actively monitor changes in liver function before and after surgery and intervene as soon as possible for possible serious complications. In addition, we should carry out individualized diagnosis and treatment for patients with severe disease, which is conducive to a good prognosis.

Because acute type A aortic dissection often involves the coronary arteries and sinuses of Valsalva, endovascular treatment alone is of limited utility. Although some large hospitals have attempted to repair acute type A aortic dissection via endovascular techniques, the repair technology is not yet mature. However, endovascular treatment of acute type A aortic dissection can reduce many complications caused by thoracotomy to a certain extent and is conducive to patient recovery, suggesting a direction for future research.

This study has several limitations. (1) The sample size was small, and large-sample studies in large centres are needed to confirm the results. (2) Overweight was defined according to the calculation of weight for height, not for body surface area or fat distribution, to perform more detailed research. (3) All the operations were performed by two surgeons, and there was bias. (4) The type

Table 3 ROC curve of Cr predicts postoperative AHD in overweight ATAAD patients

Variable	Area under curve	95%CI	*P*	Optimal critical value	sensitivity	specificity
Cr	0.745	0.644～0.845	<0.001	107	0.586	0.856

and dose of anaesthetic drugs used during surgery may have contributed to hepatic insufficiency.

Conclusions

This study underscores the morbidity and mortality of postoperative AHD following ATAAD repair surgery, elevated creatinine is an independent risk factor for postoperative acute hepatic insufficiency in overweight patients with ATAAD.

Abbreviations

ATAAD	Acute type a aortic dissection
BMI	Body Mass Index
AHD	Acute hepatic dysfunction
MELD	Model of end-stage liver disease
OR	Odds ratio
CI	Confdence interval
BUN	Blood Urea Nitrogen
Cr	Creatinine
CKMB	Creatine Kinase-MB
MYO	Myoglobin

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Author contributions

Yu Xu, Lin-Zhuo Liu and Hong-Qiao Lu wrote and revised the manuscript and share first author, Xin-Qing Yang and Yu Xu analyzed the data and drew pictures. Hong-Qiao Lu designed the experimental procedure and scheme, Shi-Kui Guo, Yong-Jiang Tang and Kun-Mei Gong reviewed and revised the manuscript. All authors contributed to the article and approved the final manuscript.

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Data availability

All data generated or analysed during this study are included in this published article. The corresponding author can provide all the original data included about this manuscript.

Declarations

Ethics approval and consent to participate

This study has been approved by the Ethics Committee of Kunming University of Science and Technology, The approval number is KMUST-MEC-091. All included patients were informed and consented to this study. Informed consent to participate was obtained from all of the participants in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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