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Original Article / Оригинални рад

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In-hospital mortality predictors after surgery for Stanford type A aortic dissection – single-center five-year experience

Предиктори интрахоспиталног морталитета након хируршког лечења аортне дисекције типа Станфорд А – петогодишње искуство једног центра

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SUMMARY

Introduction/Objective Stanford type A aortic dissection is a surgical emergency associated with high mortality.

The aim of this study was to determine which group of patients and which characteristics were associated with postoperative, in-hospital mortality.

Methods The retrospective study included 116 patients with type A aortic dissection surgically treated over a five-year period. The association between postoperative, in-hospital mortality and patient characteristics was examined.

Results Total postoperative, in-hospital mortality was 22.4% (26 out of 116 patients). The variables that, after multivariate analysis, showed a direct correlation with mortality were: admission creatinine value (OR 1.026 [1.006–1.046], p = 0.009), C-reactive protein (CRP) > 10 mg/L (OR 4.764 [1.066–21.283], p = 0.041), and stroke (OR 6.097 [1.399–26.570], p = 0.016). The ROC curve showed that creatinine could be a good predictor of mortality (Area Under the ROC curve = 0.767; p <0.0005). The cut-off point was 124.5 μmol/L. The sensitivity was 65% and the specificity was 80%. The cut-off point for CRP was 14.5 mg/L – sensitivity 71.4%, specificity 75% (Area Under the ROC curve = 0.702, p = 0.021).

Conclusion Surgery for type A aortic dissection is still associated with relatively high mortality. A lower chance of survival may be indicated by elevated admission creatinine and CRP values, as well as stroke.

Keywords: aorta; dissection; mortality; creatinine; CRP; stroke

САЖЕТАК

Увод/Циљ Аортна дисекција типа Станфорд А ургентно је хируршко стање удружено са високим морталитетом.

Циљ ове студије је био са утврди која група оперисаних пацијената и које су карактеристике удружене са постоперативним, интрахоспиталним морталитетом.

Методе Ретроспективна студија је обухватила 116 пацијената са акутном аортном дисекцијом тип А, оперисаних у петогодишњем периоду. Испитивана је повезаност између постоперативног, интрахоспиталног морталитета и карактеристика пацијената.

Резултати Укупан интрахоспитални морталитет је износио 22,4%. Варијабле које су, након мултиваријантне анализе, показале директну корелацију са морталитетом су: креатинин на пријему (ОР 1,026 [1,006–1,046], п = 0,009), *C*-реактивни протеин (*CRP*) > 10 *mg/L* (*OR* 4,764 [1,066–21,283], *p* = 0,041) и мождани удар (*OR* 6,097 [1,399–26,570], *p* = 0,016). *ROC* крива је показала да креатинин може бити добар предиктор за морталитет (*area under the ROC curve* = 0,767; *p* < 0,0005). *Cut-off point* је 124,5 *μmol/L*. Сензитивност је 65%, а специфичност је 80%. *Cut-off point* за *CRP* је 14,5 *mg/L* – сензитивност 71,4%, специфичност 75% (*area under the ROC curve* = 0,702, *n* = 0,021).

Закључак Хируршко лечење акутне аортне дисекције тип А је и даље повезано са релативно високим морталитетом. На мању шансу за преживљавање могу указати повишене вредности креатинина и *CRP*-а на пријему, као и мождани удар.

Кључне речи: аорта; дисекција; морталитет; креатинин; *CRP*; мождани удар

INTRODUCTION

Aortic dissection is the most common aortic emergency disease, which classically presents with excruciating chest pain that, frequently radiating to the back. Type A aortic dissection (TAAD) is a dissection that involves the ascending aorta or the entire aorta down to iliac arteries. It occurs when the intima of the aorta becomes compromised and ruptures

(intimal tear or entry) creating a new lumen that fills with blood between the intima and the media. This false lumen is often larger than the true lumen. The incidence of aortic dissection is 3.5 cases per 100 000 person years [1]. With an unknown number of patients dying before hospitalization, the true prevalence is likely greater. In the first 24–48h, mortality is estimated to increase by 1–2% per hour from the onset of symptoms [2, 3]. It is of paramount importance to diagnose this condition as soon as possible and to transfer the patient into the facility capable of performing emergent surgical treatment [4, 5]. Despite rapid diagnosis, improvements in surgical technique and better perioperative and postoperative treatment, the mortality of surgically treated patients is still high and varies between 17.4 and 33.4% [3, 5, 6, 7]. However, compared to the previous period, the survival trend is certainly better [3].

The aim of this study was to determine in-hospital mortality in patients who underwent surgery at our institution and identify patient characteristics that could indicate a less favorable patient outcome and thus alert clinicians to high-risk patients.

METHODS

Study population and data collection

This retrospective single-center study included 116 patients with TAAD, who were admitted and operated at the Institute of Cardiovascular Diseases of Vojvodina in Sremska Kamenica, from January 1, 2014 to December 31, 2018. The study was done in accord with standards of the institutional committee on ethics. Upon initial diagnosis established by echocardiography, the final diagnosis was confirmed by computed tomography (CT) – aortography. TAAD was defined, according to the Stanford classification, as involving the ascending aorta and/or aortic arch, progressing distally towards the descending thoracic aorta.

Patients were divided into two groups, depending on the outcome after surgery: the survivors and non-survivors. Postoperative, in-hospital mortality refers to a fatal outcome occurring after the surgery and during hospitalization, regardless of its length. The following patient characteristics and comorbidities were monitored: years of age, gender, body weight, height, body mass index (BMI), hypertension, hyperlipoproteinemia, diabetes, previous cerebrovascular accident, chronic obstructive pulmonary disease (COPD), chronic kidney disease, smoking. Of particular importance was the monitoring of preoperative values of the

following parameters: systolic arterial pressure, diastolic arterial pressure, heart rate, hemoglobin, white blood cells (WBC), neutrophils, lymphocytes, neutrophil to lymphocyte ratio (NLR), eosinophils, platelets, fibrinogen, glycemia, creatinine and C-reactive protein (CRP). All laboratory analyses were performed immediately upon admission. The values of ejection fraction (EF), presence of aortic insufficiency, pericardial and pleural effusion, diameter of the ascending aorta, involvement of the supra-aortic branches, presence of stroke, acute kidney injury (AKI) and mesenteric ischemia were monitored. Intraoperative variables were also monitored: cross clamp time and cardiopulmonary bypass (CPB) time. We also compared the type of surgery, the use of deep hypothermic circulatory arrest (DHCA), the incidence of re-exploration for bleeding, the intensive care unit (ICU) stay, and the total length of hospitalization.

Operative procedures

All patients were operated on in general balanced anesthesia. Perioperative and postoperative monitoring included continuous arterial and central venous pressure measurement, electrocardiography, oxygen saturation (pulse oximetry), body temperature measured in the nasopharynx, diuresis. Arterial blood gas analyses were performed intermittently.

Surgery was performed via median sternotomy, using CPB, in moderate hypothermia or DHCA. CPB was established by arterial cannulation of the femoral or right axillary artery and venous cannulation of the right atrium after systemic heparinization (300 U/kg body weight and maintenance of an activated clotting time of longer than 480 seconds). Antegrade cold crystalloid (St Thomas' Hospital) cardioplegia or cold blood cardioplegia was used for myocardial protection. Depending on the pathological process, we performed tubular graft interposition of the ascending aorta with or without commissural resuspension, tubular graft interposition with aortic valve replacement, interposition of the composite valve graft with implantation of coronary arteries (Bentall procedure) or hemiarch technique.

Statistical analysis

Descriptive statistics measures were used: arithmetic mean, standard deviation, median, quartiles, frequencies and percentages. A t-test for independent samples and a Mann–Whitney test were used to compare the mean values of the variables of the two populations. The correlation of categorical variables was examined using the chi-square test for contingency tables or using the Fisher test. The influence of variables on treatment outcome was determined using univariate and multivariate binary logistic analysis. The predictive quality of the variables on the outcome was evaluated using ROC curves. A $p < 0.05$ value was taken for statistical significance of the test. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 19.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 116 patients who underwent TAAD surgery were included in the study. Total postoperative, in-hospital mortality was 22.4% (26 out of 116). The demographic, anthropometric characteristics and comorbidities of the patients are shown in Table 1. The mean age of the patients was 60.8 ± 11.6 years and 56.9% of patients were male. The youngest patient was 25, while the oldest was 87 years old. Arterial hypertension was presented in 68.1% patients. Other comorbidities were present in a much smaller percentage.

The non-survivors were, on average, older than the survivors (67.5 ± 9.5 vs 58.9 ± 11.5, $p = 0.001$). There were 47 patients older than 65 years (40.5%) and 18 (38.3%) not survived in this group, while in 69 patients younger than 65 years (59.5%), 8 (11.6%) not survived ($p = 0.001$). Out of 66 male patients, 17 died, while out of 50 women patients, 9 died ($p = 0.374$). The two groups did not differ significantly in weight, height, BMI, and comorbidities, except in the presence of COPD which was higher in the non-survivors group ($p = 0.002$).

Hemodynamic parameters at admission, blood count parameters, fibrinogen values and glycaemia did not differ significantly (Table 2). However, the admission creatinine values were significantly higher in non-survivors (148 vs 92.5, $p < 0.0005$) as well as CRP values (38.0 vs 4.0, $p = 0.020$); 87 patients had creatinine < 120 μmol/L, 13 of whom died, while 29 patients had creatinine > 120 μmol/L, 13 of whom died ($p = 0.001$). Twenty-four patients had a CRP > 10 mg/L, 10 of whom died ($p = 0.024$). When comparing the remaining parameters

in Table 2, the groups differed significantly in the presence of stroke, which is more present in the non-survivors group (p = 0.004).

Survivors had a significantly higher percentage of tubular graft interposition of ascending aorta (p = 0.012), while non-survivors had a higher percentage of more complicated procedures (Bentall procedure, hemiarch), but did not differ significantly (Table 3). CPB duration was significantly longer in the non-survivors patient group (p = 0.009). Also, surgical work in DHCA was significantly more common in non-survivors (p = 0.044).

Univariate analysis indicated that age > 65 years, admission creatinine and CRP value, CPB time, DHCA, and stroke were associated with in-hospital mortality. These variables were included in the multivariate analysis, which designated the following parameters as independent in-hospital mortality predictors: creatinine (OR 1.026 [1.006–1.046], p = 0.009), CRP > 10 mg/L (OR 4.764 [1.066–21.283], p = 0.041) and stroke (OR 6.097 [1.399–26.570], p = 0.016) – Table 4.

The Receiver Operating Characteristics (ROC) curve analysis was performed to detect the best cut-off point for the admission creatinine and CRP values in the prediction of in-hospital mortality. The cut-off point for creatinine was 124.5 μmol/L (Area Under the ROC curve = 0.767; p <0.0005) (Figure 1). The sensitivity is 65% and the specificity was 80%. The cut-off point for CRP was 14.5 mg/L – sensitivity 71.4%, specificity 75% (Area Under the ROC curve = 0.702, p = 0.021) (Figure 2).

The time distribution and causes of in-hospital mortality are shown in Tables 5 and 6. Mors in tabula (30.8%), septic shock/MODS (23.1%) and stroke (19.2%) were the most common causes of death.

DISCUSSION

It is well known that TAAD is associated with a high mortality rate. The postoperative, in-hospital mortality in our patient group during 5-year observation period was 22.4%. A study conducted in our country, at other institution, a few years ago, showed that postoperative, in-hospital mortality was almost identical – 23.3% [8]. In large surgical registries, postoperative in-hospital mortality ranges from 17.4 to 33.4% [3, 5–7].

Considering the fact that the mortality rate is about 57% after medical treatment [3], we can conclude that surgical emergency is a priority in the treatment of these patients.

Although it can occur in young people, especially in patients with connective tissue disorders such as Marfan syndrome, Loyes–Dietz syndrome, Ehler–Danlos syndrome, this disease is typical of the older population. Our study showed that the average age of patients was 60.8 years. Also, mortality is higher in the elderly population because of the higher prevalence of comorbidities in the elderly. Mortality in adults over 65 years was 38.3% versus 11.6% in those under 65 years. According to the worldwide analysis, death more often occurs in the old and the highest mortality occurs at the age of more than 70 years old [3].

A higher percentage of men than women was affected by TAAD, which can be related to the greater prevalence of risk factors in men, such as hypertension, atherosclerosis, smoking. However, the difference in gender mortality has not been shown to be significant. Some previous studies have shown a worse outcome in female patients [3]. Delays in TAAD diagnosis occurred more often in female patients, is probably the reason for the higher mortality [3].

The inflammatory mechanism plays an important role in the degeneration and reduction of smooth muscle cells leading to weakened blood vessels [9]. Neutrophils are a key factor in an inflammatory response and their percentage may be an indicator of the severity of the inflammatory response and a predictor of fatal outcome [10]. Our study did not confirm the correlation between neutrophil percentage and fatal outcome. Recently, NLR has been used as a predictor of mortality, most commonly in malignancies. It is determined by dividing the absolute neutrophil count by the absolute lymphocyte count. While the neutrophil count rapidly increases in conditions with heightened inflammation, the lymphocyte count is reduced and thus the NLR increases significantly. Karakoyun et al [11] concluded that NLR may be a predictor of fatal outcome in TAAD. Their study was conducted on 37 patients and NLR > 8.51 demonstrated a sensitivity of 77% and specificity of 74% for the prediction of mortality. Our study, which included almost 4 times as many patients, showed no association between NLR and mortality.

CRP is a non-specific inflammatory marker but may be a predictor of fatal outcome [6]. Vrsalovic et al [12] indicated that CRP > 9.8 mg/L is a predictor of poor outcome. In our study, a multivariate analysis showed that admission CRP > 10 mg/L had a direct correlation

with in-hospital mortality. Patients with a CRP > 10 mg/L were 5 times less likely to survive. CRP is produced in the liver, coronary plaques, myocardial infarcts, and aneurysmal tissue [13]. It appears possible that aortic tissue during dissection directly increases the production of CRP, relatively to the severity of the dissection.

In their study on the impact of fibrinogen levels on mortality, Liu et al [14] found that low fibrinogen concentrations could predict poor outcome. TAAD itself activated the coagulation system before surgery. Excessive fibrinogen consumption leads to a procoagulant state and the formation of thrombus. If this procoagulant condition persists, it can lead to microvascular and macrovascular thrombotic complications, the development of disseminated intravascular coagulation, neurological damage and to an unfavorable outcome [15]. Our results showed no significant correlation between fibrinogen values at admission and mortality, although fibrinogen values were lower in the non-survivors.

AKI is a common complication after thoracic aortic surgery that occurs in up to 44% of patients with TAAD, and significantly increases in-hospital mortality [16–18]. The pathogenesis of AKI is multifactorial and the most significant are hemodynamic, inflammatory, metabolic factors [2, 19, 20]. Extension of the dissection may involve the renal artery which may directly impair renal perfusion, thus resulting in AKI [21]. Early detection and prevention of AKI is a key imperative that may help improve patient outcomes [16]. Our study showed that elevated creatinine level at admission may be a good predictor of in-hospital mortality. Wu et al [22] also concluded that elevated creatinine levels at admission were a good predictor of in-hospital mortality. They find that patients with elevated creatinine have a greater proportion of aortic arch or more extensive aortic involvement, requiring more complicated surgery.

Two more recent studies have examined and demonstrated the impact of poorer ejection fraction on postoperative, in-hospital mortality [23, 24]. Our patients did not differ in this parameter. Our study also did not show that aortic insufficiency and the ascending aortic diameter affect mortality, which is correlated with the study by Qiu et al [25]. The presence of pericardial effusion did not prove to be a predictor, as opposed to a study where it proved statistically significant [26].

Regarding CPB time, Nozohoor et al [7] showed that prolonged time directly affects the mortality of patients who underwent TAAD surgery. The duration of CPB is influenced

by the type of surgery. Our results show that there were more complex surgical procedures in the group of non-survivors. It logically affects CPB time and in-hospital mortality. Univariate analysis showed that the length of the CPB affected mortality, however, this was not confirmed by multivariate analysis.

Stroke is one of the most common and severe complications of TAAD surgery, with an incidence of up to 30% in multiple studies [27]. This complication significantly affects the morbidity and mortality of patients. In our study, stroke proved to be an independent predictor of postoperative, in-hospital mortality. In-hospital mortality was observed in 43.3% of patients who had a stroke and in 15.1% of those who did not have this complication. Whether these strokes were due to embolic phenomena, dissection of the arch or distal intracranial vessels, or hypoperfusion at the time of surgery is not known. A study conducted by Ghoreishi et al [27], on 7353 patients from 772 centers, found that stroke is an independent predictor of in-hospital mortality, and the independent risk factors for stroke were: femoral arterial cannulation, total arch replacement, longer CPB time, cerebral perfusion time, and total circulatory arrest time. They indicate that all types of hypothermic strategy, including mild, moderate, and deep, result in similar incidence of stroke postoperatively. Improving neuroprotective techniques during circulatory arrest is a leading topic in recent studies. Ghoreishi et al [27] found that retrograde cerebral perfusion was associated with significantly reduced risk for stroke compared with no cerebral perfusion or antegrade cerebral perfusion. A group of authors from Serbia examined the clinical outcomes of two different surgical techniques: open distal anastomosis in hypothermic circulatory arrest compared to anastomosis with clamped aorta while continuing on extracorporeal circulation [28]. This prospective, randomized study showed that there was no difference in in-hospital mortality between the groups, nor in the de novo resulting neurological deficits.

This study had some limitations. It is a single center, retrospective study and the number of patients studied is limited. The etiology of TAAD in most patients wasn't investigated so the presence of pre-existing aortic pathologies was unknown. Due to insufficient data, we were unable to include in the analysis the time from onset of symptoms to surgery, which affects mortality.

CONCLUSION

Despite easier and more accessible diagnostics, advanced surgical techniques and better postoperative treatment, TAAD surgery carries a high risk of mortality. Variables suggestive of poor outcome following the surgery are: elevated admission creatinine and CRP values, and stroke. These are variables that should alert the clinician to high-risk patients and contribute to lower mortality rates after this serious disease.

Conflict of interest: None declared.

REFERENCES

1. Clouse WD, Hallett JW Jr, Schaff HV, Spittell PC, Rowland CM, Ilstrup DM et al. Acute aortic dissection: population-based incidence compared with degenerative aortic aneurysm rupture. Mayo Clin Proc. 2004;79(2):176–80. doi: 10.4065/79.2.176
2. Liu H, Luo Z, Liu L, Yang X, Zhuang Y, Tu G. Inflammatory biomarkers to predict adverse outcomes in postoperative patients with acute type A aortic dissection. Scand Cardiovasc J. 2020;54(1):37–46. doi: 10.1080/14017431.2019.1689289.
3. 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):1846–1860. doi: 10.1161/CIRCULATIONAHA.117.031264.
4. Susak S, Redzek A, Torbica V, Rajic J, Todic M. Surgical treatment of intramural hematoma of the ascending aorta. Srp Arh Celok Lek. 2016;144(3–4):196–199. doi: 10.2298/SARH1604196S
5. Wang TKM, Wei D, Evans T, Ramanathan T, Haydock D. Surgery for Type A Aortic Dissection: 14-year Contemporary Cohort Study. Heart Lung Circ. 2020 Feb 17. pii: S1443–9506(20)30036–6. doi: 10.1016/j.hlc.2020.01.008. "in press"
6. Yang G, Zhou Y, He H, Pan X, Li X, Chai X. A nomogram for predicting in-hospital mortality in acute type A aortic dissection patients. J Thorac Dis. 2020;12(3):264–275. doi: 10.21037/jtd.2020.01.41.
7. Nozohoor S, Ahmad K, Bjurbom M, Hansson EC, Heimisdottir A, Jeppsson A et al. ABO blood group does not impact incidence or outcomes of surgery for acute type A aortic dissection. Scand Cardiovasc J. 2020;54(2):124–129. doi: 10.1080/14017431.2019.1679387.
8. Kocica M, Cvetkovic D, Soskic Lj, Vucicevic F, Grujic M, Jovicic V et al. Surgery for the acute dissections of the ascending aorta and the arch. J Cardioth Surg. 2013; 8(Suppl 1):O23. doi: 10.1186/1749-8090-8-S1-O23.
9. Del PF, Proietta M, Tritapepe L, Miraldi F, Koverech A, Cardelli P et al. Inflammation and immune response in acute aortic dissection. Ann Med. 2010; 42:622–629. doi: 10.3109/07853890.2010.518156.
10. Peng W, Zhu QY, Zhou XH, Chai XP. A Simple Emergency Prediction Tool for Acute Aortic Dissection. Iran J Public Health. 2013;42(10):1085–91. PMID: 26060615.
11. Karakoyun S, Gursoy MO, Akgun T, Ocal L, Kalcik M, Yesin M et al. Neutrophil-lymphocyte ratio may predict in-hospital mortality in patients with acute type A aortic dissection. Herz. 2015;40(4):716–21. doi: 10.1007/s00059-014-4121-2.
12. Vrsalovic M , Zeljkovic I, Presecki AV, Pintaric H, Kruslin B. C-reactive protein, not cardiac troponin T, improves risk prediction in hypertensives with type A aortic dissection. Blood Press. 2015;24(4):212–6. doi: 10.3109/08037051.2015.1025607.
13. Vainas T, Lubbers T, Stassen FR, Herngreen SB, van Dieijen-Visser MP, Bruggeman CA et al. Serum C-reactive protein level is associated with abdominal aortic aneurysm size and may be produced by aneurysmal tissue. Circulation. 2003;107:1103–5. doi:10.1161/01.cir.0000059938.95404.92.
14. Liu J, Sun LL, Wang J, Ji G. The relationship between fibrinogen and in-hospital mortality in patients with type A acute aortic dissection. Am J Emerg Med. 2018;36(5):741–744. doi: 10.1016/j.ajem.2017.10.001.
15. Nomura F, Tamura K, Yoshitatsu M, Katayama A, Katayama K, Ihara K. Changes in coagulation condition, cytokine, adhesion molecule after repair of type A aortic dissection. Eur J Cardiothorac Surg. 2004;26:348–50. doi:10.1016/j.ejcts.2004.05.001.
16. Dong N, Piao H, Du Y, Li B, Xu J, Wei S et al. Development of a practical prediction score for acute renal injury after surgery for Stanford type A aortic dissection. Interact Cardiovasc Thorac Surg. 2020; 30(5):746–753. doi:10.1093/icvts/ivaa011.
17. Ko T, Higashitani M, Sato A, Uemura Y, Norimatsu T, Mahara K et al. Impact of acute kidney injury on early to long-term outcomes in patients who underwent surgery for type A acute aortic dissection. Am J Cardiol. 2015;116(3):463–468. doi: 10.1016/j.amjcard.2015.04.043.
18. Nishigawa K, Fukui T, Uemura K, Takanashi S, Shimokawa T. Preoperative renal malperfusion is an independent predictor for acute kidney injury and operative death but not associated with late mortality after surgery for acute type A aortic dissection. Eur J Cardiothorac Surg. 2020 Mar 17. pii: ezaa063. doi: 10.1093/ejcts/ezaa063. "in press"
19. Babovic Stanic K, Dejanovic J, Vulin A, Velicki L, Redzek A. Cardiac surgery in patients with chronic renal failure. Srp Arh Celok Lek. 2017;145(9–10):470–474. doi: 10.2298/SARH161025097B.
20. Jovanovic I, Tesic M, Antonijevic N, Menkovic N, Paunovic I, Ristic A et al. Acute renal failure and hepatocellular damage as presenting symptoms of type II aortic dissection. Srp Arh Celok Lek. 2016;144(5–6):320–324. doi: 10.2298/SARH1606320J.
21. Ren HM, Wang X, Hu CY, Que B, Ai H, Wang CM et al. Relationship between acute kidney injury before thoracic endovascular aneurysm repair and in-hospital outcomes in patients with type B acute aortic dissection. J Geriatr Cardiol. 2015;12:232–238. doi: 10.11909/j.issn.1671-5411.2015.03.002.

22. Wu ZN, Guan XL, Xu SJ, Wang XL, Li HY, Gong M et al. Does preoperative serum creatinine affect the early surgical outcomes of acute Stanford type A aortic dissection? J Chin Med Assoc. 2020;83(3):266–271. doi: 10.1097/JCMA.0000000000000264.
23. Thurau J, Habazettl H, El Al Md AA, Mladenow A, Zaschke L, Adam Md U et al. Left Ventricular Systolic Dysfunction in Patients With Type-A Aortic Dissection Is Associated With 30-Day Mortality. J Cardiothorac Vasc Anesth. 2019;33(1):51–57. doi: 10.1053/j.jvca.2018.07.046.
24. Langer NB, Ando M, Simpson M, van Boxtel BS, Sorabella RA, Patel V et al. Influence of left ventricular ejection fraction on morbidity and mortality after aortic root replacement. J Thorac Cardiovasc Surg. 2019;158(4):984–991. doi: 10.1016/j.jtcvs.2018.10.147.
25. Qiu J, Wu J, Xie E, Luo X, Chen JF, Gao W et al. Surgical Management and Outcomes of the Aortic Root in Acute Type A Aortic Dissection. Ann Thorac Surg. 2019 Nov 26. pii: S0003-4975(19)31746-1. doi: 10.1016/j.athoracsur.2019.10.014. "in press"
26. Lingzhi C, Hao Z, Weijian H, Gaoshu Z, Chengchao S, Changxi C et al. Outcome Predictors in Patients Presenting With Acute Aortic Dissection. J Cardiothorac Vasc Anesth. 2016;30(5):1272–7. doi: 10.1053/j.jvca.2016.03.149.
27. Ghoreishi M, Sundt TM, Cameron DE, Holmes SD, Roselli EE, Pasrija C et al. Factors associated with acute stroke after type A aortic dissection repair: An analysis of the Society of Thoracic Surgeons National Adult Cardiac Surgery Database. J Thorac Cardiovasc Surg. 2019 Jun 18. pii: S0022-5223(19)31213-9. doi: 10.1016/j.jtcvs.2019.06.016. "in press"
28. Cvetkovic D, Kocica M, Soskic Lj, Milicic B, Aleksic N, Ristic M. Open distal anastomosis technique in acute type A aortic dissection. J Cardioth Surg. 2013;8(Suppl 1):O15. doi:10.1186/1749-8090-8-S1-O15.

Table 1. Demographic, anthropometric characteristics and comorbidities

Parameter	Total	Survivors	Non-survivors	p
Patients n (%)	116 (100)	90 (77.6)	26 (22.4)	
Male n (%) Female n (%)	66 (56.9) 50 (43.1)	49 (74.2) 41 (82.0)	17 (25.8) 9 (18.0)	0.374
Age (years) Mean ± SD Range > 65 years n (%) < 65 years n (%)	 60.8 ± 11.6 25–87 47 (40.5) 69 (59.5)	 58.9 ± 11.5 29 (61.7) 61 (88.4)	 67.5 ± 9.5 18 (38.3) 8 (11.6)	 **0.001** **0.001**
Weight (kg) mean ± SD	80.3 ± 14.4	80.0 ± 14.4	81.3 ± 14.9	0.700
Height (cm) mean ± SD	173.5 ± 9.4	173.8 ± 9.6	172.6 ± 9.1	0.595
BMI (kg/m^2) mean ± SD	26.6 ± 3.6	26.4 ± 3.6	27.1 ± 3.7	0.383
Hypertension n (%)	79 (68.1)	62 (68.9)	17 (65.4)	0.812
Hyperlipoproteinemia n (%)	9 (7.8)	8 (8.9)	1 (3.8)	0.681
Diabetes mellitus n (%)	6 (5.2)	4 (4.4)	2 (7.7)	0.615
History of cerebrovascular accident n (%)	8 (6.9)	8 (8.9)	0 (0)	0.196
Chronic obstructive pulmonary disease n (%)	4 (3.4)	0 (0)	4 (15.4)	**0.002**
Chronic kidney disease n (%)	5 (4.3)	4 (4.4)	1 (3.8)	1.000
Smokers n (%)	32 (27.6)	26 (28.9)	6 (23.1)	0.627

BMI – body mass index;
values in bold are statistically significant

Table 2. Clinical characteristics

Characteristics	Survivors	Non-survivors	p value
Hemodynamic parameters at admission			
Systolic arterial pressure (mmHg)	131.6 ± 35.9	127.9 ± 34.2	0.630
Diastolic arterial pressure (mmHg)	73.8 ± 17.8	72.5 ± 17.3	0.739
Heart rate (beats per minute)	77.3 ± 16.8	79.7 ± 23.2	0.560
Laboratory data at admission			
Hemoglobin (g/L)	123.7 ± 22.1	116.9 ± 23.5	0.213
White blood cells (× 10^9/L)	12.2 ± 5.4	11.1 ± 3.7	0.384
Neutrophils (%) median (interquartile range)	76.6 (66.9, 83.9)	81.6 (72.4, 85.2)	0.465
Lymphocytes (%)	14.8 ± 8.7	14.4 ± 11.9	0.840
Neutrophils/Lymphocytes	7.5 ± 4.9	8.5 ± 4.8	0.398
Eosinophils (%) median (interquartile range)	1.1 (0.4, 1.6)	0.95 (0.3, 1.0)	0.369
Platelets (× 10^9/L)	190.5 ± 73.2	189.1 ± 77.9	0.941
Fibrinogen (g/L) median (interquartile range)	2.6 (2.0, 3.6)	2.4 (1.7, 3.5)	0.490
Glycaemia (mmol/L) median (interquartile range)	6.7 (5.8, 8)	7.3 (6.7, 9.2)	0.128
Creatinine (μmol/L) median (interquartile range)	92.5 (81.5, 110.0)	148.0 (114.0, 164.0)	< **0.0005**
Creatinine > 120 μmol/L n (%)	16 (17.8)	13 (50)	**0.001**
Creatinine < 120 μmol/L n (%)	74 (82.2)	13 (50)	
C-reactive protein (mg/L) median (interquartile range)	4.0 (3.5, 7.5)	38.0 (21.0, 106.0)	**0.020**
C-reactive protein > 10 mg/L n (%)	14 (15.6)	10 (38.5)	**0.024**
C-reactive protein < 10mg/L n (%)	76 (84.4)	16 (61.5)	
Other clinical characteristics			
Ejection fraction (%) mean ± SD	58.5 ± 5.9	57.1 ± 7.4	0.376
Aortic insufficiency n (%)	48 (53.3)	13 (50)	1.000
Ascending aortic diameter (mm) mean ± SD	54.0 ± 12.1	56.6 ± 8.7	0.339
Involvement of the supra-aortic branches n (%)	35 (38.9)	11 (42.3)	0.285
Pericardial effusion n (%)	35 (38.9)	15 (57.7)	0.151
Pleural effusion n (%)	38 (42.2)	14 (53.8)	0.341
Acute kidney injury n (%)	25 (27.8)	9 (34.6)	0.625
Mesenteric ischemia n (%)	1 (1.1)	2 (7.7)	0.128
Stroke n (%)	17 (18.9)	13 (50)	**0.004**
Re-exploration for bleeding n (%)	21 (23.3)	9 (34.6)	0.309
Intensive care unit stay (days) median (interquartile range)	5.0 (3.0, 8.0)	4.5 (0, 8)	0.234
Hospital stay (days) median (interquartile range)	20 (13, 28)	10 (1, 44)	0.116

Values in bold are statistically significant

Table 3. Type of surgery and intraoperative data

Type of surgery	Survivors	Non-survivors	p
Tubular graft interposition of ascending aorta n (%)	58 (64.5)	9 (34.6)	**0.012**
Tubular graft interposition of ascending aorta and aortic valve replacement n (%)	9 (10)	1 (3.9)	0.453
Tubular graft interposition of ascending aorta with commissural resuspension n (%)	9 (10)	2 (7.7)	1.000
Bentall procedure n (%)	8 (8.9)	5 (19.2)	0.163
Hemiarch n (%)	4 (4.4)	4 (15.4)	0.074
Tubular graft interposition of ascending aorta + CABG n (%)	2 (2.2)	2 (7.7)	0.217
Inability to reconstruct the aorta n (%)	0 (0)	3 (11.5)	**0.010**
Intraoperative data			
Cross clamp time (min) median (interquartile range)	107 (75, 123)	108 (83, 150)	0.160
CPB time (min) mean ± SD	122.5 ± 42.7	152 ± 57.2	**0.009**
DHCA n (%)	5 (5.6)	5 (19.2)	**0.044**

CABG – coronary artery bypass grafting; CPB – cardiopulmonary bypass; DHCA – deep hypothermic circulatory arrest;

values in bold are statistically significant

Table 4. Results of univariate and multivariate analysis of predictors of in-hospital mortality

Variable	Univariate		Multivariate	
	Odds ratio (95% CI)	**p**	**Odds ratio (95% CI)**	**p**
> 65 years	4.733 (1.843–12.151)	0.001	/	ns
Creatinine	1.021 (1.007–1.034)	0.002	1.026 (1.006–1.046)	0.009
Creatinine > 120 μmol/L	4.625 (1.807–11.836)	0.001	/	ns
CRP > 10 mg/L	3.393 (1.281–8.988)	0.014	4.764(1.066–21.283)	0.041
CPB time	1.012 (1.002–1.022)	0.014	/	ns
DHCA	4.048 (1.072–15.280)	0.039	/	ns
Stroke	4.235 (1.666–10.766)	0.002	6.097(1.399–26.570)	0.016

ns – non significant; CRP – C-reactive protein; CPB – cardiopulmonary bypass; DHCA – deep hypothermic circulatory arrest

Table 5. Time distribution of in-hospital mortality

Time	n (%)
Mors in tabula	8 (30.8)
< 7 days	3 (11.5)
7–30 days	6 (23.1)
> 30 days	9 (34.6)

Table 6. Cause of in-hospital mortality

Cause of death	n (%)
Mors in tabula	8 (30.8)
Septic shock / MODS	6 (23.1)
Stroke	5 (19.2)
Hypovolemic shock	3 (11.6)
Cardiogenic shock	2 (7.7)
Hepatorenal syndrome	1 (3.8)
Respiratory failure	1 (3.8)

MODS – multi-organ dysfunction syndrome

Figure 1. The receiver operating characteristics curve of admission creatinine level

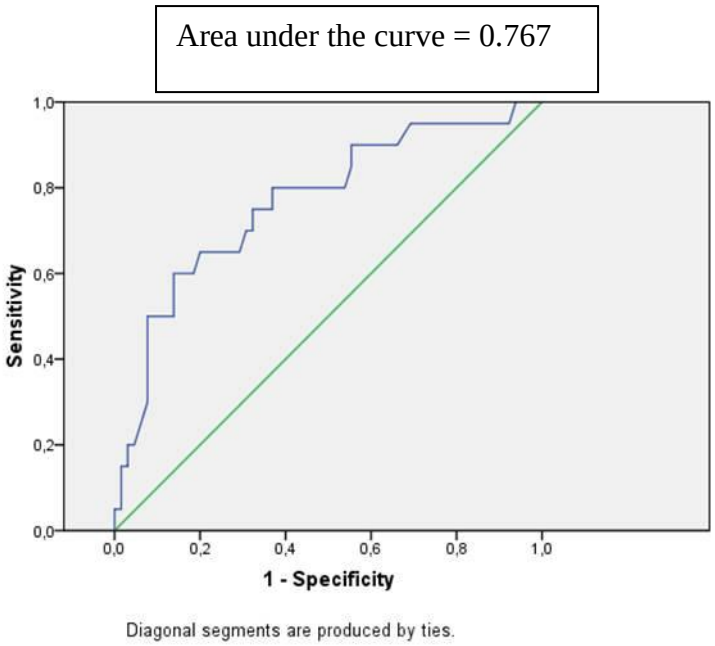

Figure 2. The receiver operating characteristics curve of admission C-reactive protein level