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Predictors of in-hospital mortality in emergency surgical treatment involving cardiopulmonary bypass for acute Stanford type A aortic dissection: a retrospective cohort study

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Abstract

INTRODUCTION: Acute Stanford type A aortic dissection is one of the most severe cardiovascular diseases with high in-hospital mortality. **OBJECTIVE:** To establish predictors of in-hospital mortality in the treatment of patients with acute Stanford type A aortic dissection under conditions of artificial circulation and to determine their threshold values. **MATERIALS AND METHODS:** Study design: retrospective, cohort, single-center. Inclusion criteria: surgical intervention with cardiopulmonary bypass, confirmed diagnosis of acute Stanford type A aortic dissection, age > 18 years. The study included 51 patients: 42 men and 9 women aged from 35 to 77 years, median 59 years [47; 65]. All patients (*n* = 51) were treated in 2022 and were divided into 2 groups depending on the outcome: group 1 (*n* = 27) included those who died in the intensive care unit within 30 days, group 2 (*n* = 24) included survived and discharged patients. The endpoint of trial was 30-day in-hospital mortality. **RESULTS:** Postoperative Sequential Organ Failure Assessment (SOFA) score > 7, Acute Physiology And Chronic Health Evaluation (APACHE) II score > 19, and Vasoactive-inotropic score (VIS) > 10, cardiopulmonary bypass time > 177 minutes, and total hypothermic circulatory arrest time > 30 minutes were associated with an increased risk of 30-day in-hospital mortality. **CONCLUSIONS:** Statistically significant predictors of hospital mortality in the treatment of patients with acute Stanford

Предикторы госпитальной летальности при экстренном хирургическом лечении острейшего расслоения аорты типа А по Стенфорду в условиях искусственного кровообращения: ретроспективное когортное исследование

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Реферат

АКТУАЛЬНОСТЬ: Острейшее расслоение аорты типа А по Стенфорду является одним из тяжелейших сердечно-сосудистых заболеваний с высокой госпитальной летальностью. **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Установление предикторов госпитальной летальности при лечении пациентов с острейшим расслоением аорты типа А по Стенфорду в условиях искусственного кровообращения (ИК) и определение их пороговых значений. **МАТЕРИАЛЫ И МЕТОДЫ:** Дизайн исследования — ретроспективное когортное одноцентровое исследование. Критерии включения: проведение хирургического вмешательства в условиях ИК; подтвержденный диагноз острейшего расслоения аорты типа А по Стенфорду; возраст > 18 лет. В исследование вошел 51 пациент: 42 мужчины и 9 женщин в возрасте от 35 до 77 лет, медиана — 59 лет [47; 65]. Все пациенты (*n* = 51) проходили лечение в 2022 г. и были поделены на 2 группы в зависимости от исхода: группа 1 (*n* = 27) включала в себя умерших в отделении реанимации в течение 30 сут, группа 2 (*n* = 24) включала в себя выживших и выписавшихся пациентов. Конечная точка исследования — 30-дневная госпитальная летальность. **РЕЗУЛЬТАТЫ:** Значения индекса Sequential Organ Failure Assessment (SOFA) > 7, индекса Acute Physiology And Chronic Health Evaluation (APACHE) II > 19 и индекса Vasoactive-inotropic score (VIS) > 10 после окончания type A aortic dissection under cardiopulmonary bypass are the SOFA index, the APACHE II index and the VIS index after the end of surgery, as well as the time of cardiopulmonary bypass and the time of total hypothermic circulatory arrest.

операции, время ИК > 177 мин и время полной гипотермической остановки кровообращения (ПГОК) > 30 мин ассоциированы с повышенным риском госпитальной летальности. **ВЫВОДЫ:** Статистически значимыми предикторами госпитальной летальности при лечении пациентов с острейшим расслоением аорты типа А по Стенфорду в условиях ИК являются индексы SOFA, APACHE II и VIS после окончания операции, а также время ИК и время ПГОК.

KEYWORDS: cardiopulmonary bypass, aortic dissection, circulatory arrest, deep hypothermia induced, hypothermia, hospital mortality

КЛЮЧЕВЫЕ СЛОВА: искусственное кровообращение, расслоение аорты, полная гипотермическая остановка кровообращения, глубокая гипотермия

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Introduction

Surgical intervention for aortic dissection is one of the most complex procedures in cardiac surgery. Type A acute aortic dissection (AAD) is defined in the Stanford classification as a dissection of the ascending aorta, regardless of the distal extent. [1]. The mortality rate for patients with type A AAD left untreated surgically for 48 hours reaches 50 % and makes 1–2 % per hour in this critical period. The hospital mortality rate after emergency surgical interventions ranges from 17 % to 25 %, and in complicated cases, it can reach 80–90 %. [2]. The anesthetic management and surgical treatment of type A AAD is challenging, especially in older patients [3], and there are no uniform standardized protocols for such interventions [4]. The comprehensive multidisciplinary approach used in the N.V. Sklifosovsky Research Institute for Emergency Medicine in recent years has made it possible to achieve a decrease in hospital mortality rate to 28.1 % in the treatment of acute aortic dissection and it continues improving [2]. Cardiopulmonary bypass (CPB) is an indispensable technique in the treatment of Stanford type A acute aortic dissection [5]. Surgical intervention for this pathology requires maintaining CPB for long time. Despite advances in technology, materials, and treatment strategies, the use of CPB is associated with increased hospital mortality and complications [6, 7, 8]. According to data from Jun Zheng et al., the time on CPB is a significant factor influencing 90-day postoperative mortality in patients after thoracic aorta surgical repair for thoracic aortic dissection [9]. The results from the study by Zhang K. et al. indicate that the duration of CPB is an independent predictor of adverse events such as stroke and fatal outcome within the first 30 days after surgery [5]. Factors negatively affecting the outcome of patients with type A acute aortic dissection include the sudden onset of severe disease and the complexity of treatment [10]. A perioperative risk assessment for this patient category is a complex task due to a large number of factors, including the involvement of different organs in the pathological process with regard to the location and extent of aortic dissection [11].

Objective

The aim of our study was to identify predictors of hospital mortality in patients treated for Stanford type A acute aortic dissection with cardiopulmonary bypass surgery, and to determine the predictor threshold values.

Materials and methods

In a single-center retrospective cohort study, we examined the treatment protocols for the patients with Stanford type A acute aortic dissection who underwent emergency surgery within 48 hours of the disease onset.

Inclusion criteria for the study were: a surgical intervention with cardiopulmonary bypass (CPB), confirmed diagnosis of acute aortic dissection, type A, according to the Stanford classification, age > 18 years, and both favorable and unfavorable treatment outcomes (approximately in equal proportions). Exclusion criteria were as follows: a Sequential Organ Failure Assessment (SOFA) score > 12 at the time of hospital admission, body mass index > 40, and age > 80 years.

The primary endpoint of the study was 30-day hospital mortality.

In conformity with the inclusion and exclusion criteria, 51 patients were enrolled in the study: 42 men and 9 women, aged from 35 to 77 years, a median age being 59 years [47; 65]. In all cases, CPB was performed with total hypothermic circulatory arrest (THCA), and myocardial protection was achieved through the perfusion of Custodiol solution via the coronary sinus. Cerebral protection during THCA was ensured by selective bilateral antegrade perfusion.

Malperfusion syndrome was diagnosed in 37.3 % of patients, being the complication of an aortic dissection described in the literature as a disruption of blood flow to one or more organs due to the obstruction or occlusion of aortic branches by the intima, leading to ischemia and dysfunction [12] and considered an independent predictor of mortality in this patient category [13]. In the majority of deceased patients, type A AAD was accompanied by complications in the form of malperfusion syndrome, including the coronary circulation malperfusion (*n* = 15). Upon admission, during preoperative preparation, patient's condition was assessed using the SOFA and Acute Physiology and Chronic Health Evaluation II (APACHE II) tools. Preoperative data are presented in table 1.

All 51 (100 %) study patients with Stanford type A acute aortic dissection underwent cardiopulmonary bypass (CPB) surgery. CPB was ensured using either Jostra HL 20 system (Maquet, Germany), or Stockert C3, S3, S5 heart lung machine (Sorin, USA). For the CPB procedure, separate cannulation of the superior and inferior vena cava was performed (using cannulas sized 32, 34, 36 Fr) to divert venous blood from the body into the CPB circuit. Depending on the aortic dissection extent, the cannulation of the femoral arteries, aorta, right subclavian artery, right axillary artery, or brachiocephalic trunk was performed for blood return (for this purpose cannulas sized 17, 19, 20, 21, 22, 23, or 24 Fr were used). To assess the volume of vasoactive inotropic support after surgery, the Vasoactive-Inotropic Score (VIS) was used, calculated by the formula: dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/min) + 100 × epinephrine dose (mcg/kg/min) + 100 × norepinephrine dose (mcg/kg/min) [13]. Data on the surgical intervention types, cardiopulmonary bypass parameters, and the volume of vasoactive inotropic support after CPB are presented in table 2.

In the postoperative period, acute kidney injury (AKI) with indications for renal replacement therapy was diagnosed in 56.9% of patients. Severe cardiovascular failure developed in 13.7 % of patients, and extracorporeal membrane oxygenation (ECMO) was used for its correction. The SOFA and APACHE II scores were calculated after the patient has been delivered to the Intensive Care Unit. Postoperative data are presented in table 3.

Statistical analysis of the data obtained during the study was conducted using a personal computer operating system Windows 10 with Microsoft Excel 2007. Data statistical processing was performed utilizing the R 3.6.3

Table 1. Demographic indicators and preoperative data

Parameter	Patients (*n* = 51)
Stanford type A acute dissection, *n* (%)	51 (100 %)
Proportion of male patients, *n* (%)	42 (82.3 %)
Obesity, *n* (%)	32 (62.7 %)
Hypertension disease, *n* (%)	39 (76.5 %)
CAD, *n* (%)	3 (5.9 %)
Cerebrovascular accident, *n* (%)	6 (11.8 %)
Malperfusion syndrome, *n* (%)	19 (37.3 %)
Age, years, median [q 1; q3]	59 [47; 65]
LVEF, %, median [q1; q3]	60 [58; 61.5]
SOFA, median [q1; q3]	3 [2; 5]
APACHE II, median [q1; q3]	14 [12; 16]

CAD — coronary artery disease; CVA — cerebrovascular accident; LVEF — left ventricular ejection fraction; SOFA — Sequential Organ Failure Assessment; APACHE II — Acute Physiology and Chronic Health Evaluation II; q — quartile; *n* — number of cases.

Table 2. Intraoperative data

Parameter	Patients (n = 51)
Bentall-De Bono operation, n (%)	2 (3.9 %)
Bentall-De Bono operation + hemiarch replacement, n (%)	3 (5.9 %)
Bentall-De Bono operation + total arch replacement, n (%)	3 (5.9 %)
Supracoronary ascending aortic replacement, n (%)	15 (29.4 %)
Supracoronary ascending aortic + hemiarch replacement, n (%)	17 (33.3 %)
Supracoronary ascending aortic + total arch replacement, n (%)	9 (17.7 %)
Supracoronary ascending aortic replacement + AVR, n (%)	2 (3.9 %)
CPB duration, minutes, median [q1; q3]	177 [156; 261]
Cross-clamp time, minutes, median [q1; q3]	110 [82; 139]
THCA time, minutes, median [q1; q3]	32 [25; 43]
Nasopharyngeal temperature, °C, median [q1; q3]	26.2 [24.1; 28]
VIS, median [q1; q3]	10 [5; 16]

VIS — Vasoactive-Inotropic Score; CPB — cardiopulmonary bypass; THCA — total hypothermic circulatory arrest; AVR — aortic valve replacement; q — quartile; n — number of observations.

Table 3. Postoperative data

Parameter	Patients (n = 51)
CVA, n (%)	6 (11.8 %)
AKI, n (%)	29 (56.9 %)
Transfusion of RBC suspension, n (%)	49 (96 %)
ECMO, n (%)	7 (13.7 %)
LVEF, %, median [q1; q3]	56 [52; 60]
SOFA score, median [q1; q3]	7 [4; 10]
APACHE II score, median [q1; q3]	22 [16; 29]
Time on mechanical ventilation, days, median [q1; q3]	3 [1; 7]
ICU length of stay, days, median [q 1; q 3]	5 [3; 10]
Hospital length of stay, days, median [q 1; q 3]	9 [5; 15]

CVA — cerebrovascular accident; AKI — acute kidney injury; RBC-suspension — red blood cell suspension; ECMO — extracorporeal membrane oxygenation; LVEF — left ventricular ejection fraction; SOFA — Sequential Organ Failure Assessment; APACHE II — Acute Physiology and Chronic Health Evaluation II; ICU — Intensive Care Unit; q — quartile; n — number of cases.

free software environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria) and the STATISTICA 12 software package (Starsoft, USA). The normality of distribution for quantitative variables was checked using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For the analysis of quantitative variables, the Mann-Whitney nonparametric test was used. Quantitative data are presented as medians (M) and quartiles (25 %; 75 %), percentages, or frequencies with regard to the variable characteristics. Logistic regression analysis was conducted to identify significant risk factors for hospital mortality. ROC analysis with calculating the area under the ROC curve was performed to assess the potential of using the studied parameters as hospital mortality predictors. If statistical significance was found, the Youden's J-statistic was utilized to select an optimal threshold values. Testing of statistical hypotheses and the presence of statistical significance were established at a value of $p < 0.05$.

Results

In the present study, a comparative assessment was made between the groups of survived (Group 2, n = 24) and deceased (Group 1, n = 27) patients. The presented parameters of the patients in the two groups (table 4) showed no statistically significant differences in such preoperative parameter assessments as SOFA and APACHE II scores. This indicated that the severities of patient conditions before their being brought to the operating room were comparable between the two study groups.

On surgery completion the SOFA score, APACHE II score, and VIS were statistically significantly lower in the group of survivors (p = 0.0064, p = 0.0060, and p = 0.0008, respectively) compared to those in the group of the deceased, which may be a consequence of varying intraoperative tactics. The cardiopulmonary bypass (CPB) duration and total hypothermic circulatory arrest time were statistically significantly higher in the group of deceased patients (p = 0.0012, and p = 0.0076, respectively), indicating potentially adverse effects of both the prolonged CPB duration, and the differences in the volume of surgical intervention. Statistically significant differences in the minimal temperature (p = 0.0106) recorded intraoperatively by the nasopharyngeal sensor suggested the absence of an expected protective effect from an increased hypothermia depth.

Logistic regression analysis (table 5) suggested the following independent predictors of hospital mortality: the SOFA score after surgery (p = 0.0079), APACHE II score after surgery (p = 0.0062), VIS (p = 0.0084), CPB duration (p = 0.0124), total hypothermic circulatory arrest time (p = 0.0043), and minimal nasopharyngeal temperature (p = 0.0335).

The obtained values of the area under the ROC curve (Table 7) for the studied parameters allowed us to assess the efficacy of the models.

The application of Youden's J statistic enabled the calculation of threshold values for the postoperative SOFA score, the postoperative APACHE II score, VIS, CPB duration, and total hypothermic circulatory arrest time (table 6). Since the confidence interval for the odds ratio, when analyzing nasopharyngeal temperature data, included 1, a cutoff point was not calculated for this parameter.

Discussion

The data obtained from the study revealed a statistically significant difference between the study groups in the CPB duration, THCA time, and the scores of assessment by SOFA, APACHE II, and VIS after surgery. This corresponds with literature findings [14, 15] and suggests a negative im-

Table 4. Comparison of the patient condition severity assessment scores and cardiopulmonary bypass parameters between the groups

Parameter	Group 1, *n* = 27 median [q1; q3]	Group 2, *n* = 24 median [q1; q3]	*p*
SOFA score before surgery	3 [2; 5]	3 [2; 5]	0.8150
SOFA score after surgery	9.5 [6.5; 12.5]	5 [4; 7]	0.0064
APACHE II score before surgery	14 [12; 20]	14 [12; 15]	0.9607
APACHE II score after surgery	26.5 [21.5; 35]	18 [13; 22]	0.0060
VIS	17 [13; 36]	6 [4; 10]	0.0008
CPB duration, minutes	242 [174.5; 288]	159 [120; 177]	0.0012
Cross-clamp time, minutes	123 [112; 176.5]	85.5 [68; 123]	0.0513
THCA time, minutes	37 [26; 53]	26 [20; 30]	0.0076
Nasopharyngeal temperature, °C	25.9 [24; 27]	27.6 [26; 28]	0.0106

VIS — Vasoactive-Inotropic Score; CPB — cardiopulmonary bypass; SOFA — Sequential Organ Failure Assessment; APACHE II — Acute Physiology and Chronic Health Evaluation II; THCA — total hypothermic circulatory arrest; q — quartile; *p* — significance level; *n* — number of observations

Table 5. Logistic regression analysis and ROC analysis of potential predictors of hospital mortality

Predictor	OR [95% CI]	*p*	AUC [95% CI]
SOFA score after surgery	7.7 [1.66; 35.69]	0.0079	0.79 [0.64; 0.94]
APACHE II score after surgery	4.5 [1.02; 19.9]	0.0062	0.82 [0.68; 0.96]
VIS	17.5 [3.31; 92.47]	0.0084	0.86 [0.75; 0.98]
CPB duration time	2.4 [1.69; 7.06]	0.0124	0.80 [0.66; 0.94]
THCA time, minutes	5.42 [1.2; 24.52]	0.0043	0.75 [0.58; 0.91]
Nasopharyngeal temperature, ℃	3.67 [0.95; 14.09]	0.0335	0.74 [0.58; 0.93]

VIS — Vasoactive-Inotropic Score; CPB — cardiopulmonary bypass; SOFA — Sequential Organ Failure Assessment; APACHE II — Acute Physiology and Chronic Health Evaluation II; THCA — total hypothermic circulatory arrest; OR — odds ratio; CD — confidence interval; AUC — area under the ROC curve; *p* — significance level.

Table 6. Threshold values for the predictors of hospital mortality

Predictor	Threshold	Specificity	Sensitivity
SOFA score after surgery	7	69 %	78 %
APACHE II score after surgery	19	81 %	67 %
VIS	10	83 %	78 %
CPB duration, minutes	177	75 %	78 %
THCA time, minutes	30	68 %	79 %

VIS — Vasoactive-Inotropic Score; CPB — cardiopulmonary bypass; SOFA — Sequential Organ Failure Assessment; APACHE II — Acute Physiology and Chronic Health Evaluation II; THCA — total hypothermic circulatory arrest.

pact of prolonged CPB on the patient condition after completing the surgery for Stanford type A acute aortic dissection. An extension of CPB time is an unfavorable factor that increases the risk of complications regardless of the surgical intervention type [16]. It is not only the choice of the surgical technique that influences the duration of CPB surgery for acute aortic dissection, but also the coordinated and timely efforts of the entire multidisciplinary team involved in surgery performance, preoperative and pre-hospital care. During the surgical procedure, complex problems requiring solutions in no time arise, namely, the choice of regional perfusion tactics, appropriate extracorporeal circuit configuration, strategies for hemofiltration and hemosorption, intraoperative monitoring levels, temperature management, and adequate vasoactive inotropic support considering the myocardial contractility, total peripheral vascular resistance, and other hemodynamic parameters, an acid-base balance compensation, the choice of optimal anticoagulation therapy, and timely hemostatic system monitoring, control of volemic load and hematological compensation, frequently under conditions of a massive blood loss [17, 18, 19, 20].

In emergency surgery for such a complex pathology as Stanford type A acute aortic dissection, the surgical team has very little time, which complicates comprehensive preparations. The optimization of transition times between the stages of surgery is crucial, particularly regarding the speed of preparation, connection and switching of hardware modes and lines. It is essential to proceed as quickly as possible to the main stage of surgery since the outcome of the clinical case largely depends on this. However, striving to speed-up in making manipulations for the sake of patient safety, we cannot go beyond the standard time frames for the use of cardioplegic solution. Cardioplegia takes standard time without the possibility of acceleration, although the route of its delivery and its composition have been the subject of discussion for many years. The nature of the pathology imposes specific conditions, and the intraoperative situation can evolve rapidly and requires maximum concentration from all participants in the surgical process from the moment the patient is delivered to the Operating Room until his/her transfer to the Intensive Care Unit.

When assessing opportunities to reduce the CPB duration, total circulatory arrest time, and patient severity to diminish the risk of hospital mortality, we require reference benchmarks. To identify these benchmarks, we made comparisons between the study groups. Statistically significant differences between the groups of patients allocated by their outcome suggested the presence of several predictors of hospital mortality. Further logistic regression analysis and ROC analysis allowed for the calculation of predictor optimal threshold values. It was established that SOFA > 7, APACHE II > 19, and VIS > 10 after surgery, along with CPB time > 177 minutes and total hypothermic circulatory arrest time > 30 minutes were associated with an increased risk of hospital mortality.

The obtained data have a significant clinical value since they serve as direct or indirect reference benchmarks for all team members and highlight the need for continued research and additional data analysis, taking into account all aspects of preoperative preparation, intraoperative treatment, and a differentiated approach with regard to the extent of aortic involvement. The results of intensive teamwork at the Center in the previous year made it possible to achieve a survival rate of over 73% in the surgical treatment for acute aortic dissection.

The limitation of the study was related to its single-center, retrospective design. The studied patient sample was heterogeneous regarding the extent and level of aortic dissection, the spectrum of complications, and the volume of surgical intervention. The volume of preoperative and intraoperative transfusion therapy was not taken into account in the data analysis.

Conclusions

The conducted study has demonstrated that statistically significant predictors of hospital mortality in patients with Stanford type A acute aortic dissection undergoing cardiopulmonary bypass surgery include the postoperative SOFA score, postoperative APACHE II score, and VIS after surgery, as well as the duration of cardiopulmonary bypass, and total hypothermic circulatory arrest time. The obtained threshold values indicate the appropriateness of modifying the intraoperative treatment strategies to reduce cardiopulmonary bypass duration and total circulatory arrest time, as well as to explore additional methods of organ protection and hemodynamic stabilization to lessen the severity of postoperative patient condition and decrease the risk of hospital mortality.

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