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Correction

Correction: Single-Center Retrospective Analysis of Acute Type A Aortic Dissection Outcome and Reoperation Focusing on Extended Versus Limited Initial Repair

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In this article, there are some text corrections that need to be incorporated. The original article has been corrected.

The authors wish to make the following corrections to this paper:

In the Result section in the Abstract, "Type of the initial repair had no statically significant relationship with in-hospital mortality with a *p*-value of 0.12, however in multivariable analysis, cross-clamp time had a statistically significant relation with mortality ($p = 0.4$)." should instead read "Type of the initial repair had no statistically significant relationship with in-hospital mortality with a *p*-value of 0.12, however in multivariable analysis, cross-clamp time had a statistically significant relation with mortality ($p = 0.04$). And "The relationship between the type of the initial repair and the need for reoperation didn't reach a statically significant value ($p = 0.9$)." should instead read "The relationship between the type of the initial repair and the need for reoperation didn't reach a statistically significant value ($p = 0.9$)".

The authors confirm that the mistakes do not affect the results and conclusions of the study and apologize for any inconvenience caused by this mistake.

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Single-Center Retrospective Analysis of Acute Type A Aortic Dissection Outcome and Reoperation Focusing on Extended Versus Limited Initial Repair

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ABSTRACT

Background: The optimal management strategy for acute aortic type A dissection remains controversial. Whether a limited primary (index) repair would increase the need for late aortic reintervention is still an open debate.

Methods: A total of 393 consecutive adult patients with acute type A aortic dissection who underwent cardiac surgery were analyzed. Our research hypothesis was whether limited aortic index repair (i.e., isolated aorta ascending replacement without an open distal anastomosis with and without a concomitant aortic valve replacement, including hemiarch replacement procedure) is associated with a higher incidence of late aortic reoperation compared with extended repair (i.e., any other surgical procedure that goes beyond that limited approach).

Results: Type of the initial repair had no statistically significant relationship with in-hospital mortality with a P-value of 0.12, however in multivariable analysis, cross-clamp time had a statistically significant relation with mortality (P = 0.04). From the patients who survived until discharge (N = 311), 40 patients needed a reoperation on the aorta; the mean interval until reoperation was 4.5 years. The relationship between the type of the initial repair and the need for reoperation didn't reach a statistically significant value (P = 0.9). In-hospitable mortality after the second operation was 10% (N = 4).

Conclusion: We reached two conclusions. 1) An extended prophylactic repair in the initial operation of an acute type A aortic dissection might not lead to a lower incidence of reoperations on the aorta and could increase in-hospital mor-tality by increasing cross-clamp time, and 2) Reoperation on the aorta could be done safely with acceptable mortality outcomes.

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INTRODUCTION

In October 1760, Dr. Frank Nicholls did a necropsy on the king of England, George II, after his sudden mysterious death, which allowed Nicholls to uncover and meticulously document some of the early and precise findings. He wrote: " … the pericardium was found distended with a quantity of coagulated blood, nearly a pint …; the whole heart was so compressed as to prevent any blood contained in the veins from being forced into the auricles; therefore the ventricles were found absolutely void of blood …; and in the trunk of the aorta we found a transverse fissure on its inner side, about an inch and a half long, through which some blood had recently passed under its external coat and formed an elevated ecchymosis" [Nicholls 1761]. More than two centuries later, the following remarkable breakthrough occurred in Houston, Texas, on 7 July 1954, when DeBakey et al. performed the first successful surgical resection of a dissecting thoracic aorta aneurysm [DeBakey 1955].

The fulcrum of the treatment is to determine the extent of the injury to build an appropriate surgical management plan. (Figure 1) However, the optimal surgical approach to managing an acute type A aortic dissection remains controversial; there is no consensus on whether to adopt a limited repair (i.e., ascending aorta replacement without an open anastomosis) or extended repair (i.e., total arch replacement with a conventional or frozen elephant trunk) [Rylski 2014]. Hence, acute aortic dissection is most probably an acute insult to a chronically diseased aorta. A question must arise: Would an extended primary repair reduce the potential of reoperation?

This study aimed to assess outcomes of the primary (index) repair after acute type A dissection and its correlation with the incidence of reoperation to provide further evidence around decision-making for an index operative strategy.

PATIENTS AND METHODS

Study design and patient population: We undertook a single-center retrospective cohort study, using our cardiothoracic database and electronic patient records. From January 2000 through 2020, 393 consecutive adult patients with acute type A aortic dissection underwent cardiac surgery at a quaternary acute care university hospital in northern Bavaria. Our research question was whether a primary limited surgical approach in managing type A aortic dissection would be

associated with a higher reoperation incidence. All patients included in the analysis had a documented excision of the primary entry in the aorta in their index repair.

Definitions and outcome measures: Limited repair is defined as an isolated aorta ascending replacement without an open distal anastomosis with and without a concomitant aortic valve replacement, including hemiarch replacement procedures; however, the extended repair is any other surgical procedure that goes beyond that limited approach. Reoperation was defined as a necessary re-intervention, either open surgical or endovascular. The primary endpoint of the analysis was set to be late reoperation on the aorta.

Human participant protection: This retrospective study complied with the Helsinki Declaration (2000), and the local Ethics Committee (EC) approved to perform this analysis (EC, No.22_143-Br) based on retrospective data retrieval. For this reason, the EC waived the need for written patients' informed consent.

Data collection: Demographic characteristics, data on diagnosis, cardiac surgery, and hospital stay, as well as data on cross-clamp time and duration of hospital admission pre-and post-surgery, were collected in routine clinical care. Moreover, the diagnosis of aortic dissection was determined before surgery utilizing computed tomography angiography. During the follow-up time, the indication for reoperation and type of the reoperation procedure were moreover retrospectively collected. We deliberately omitted the data concerning cerebral perfusion (CP), as it was not relevant to answer the research question of reoperation; furthermore, given the variety of cerebral protection techniques used in the timeline of 20 years covered by the analysis, this might have led to statistical bias.

Statistical analysis: In the first step, entries with missing values in the selected variables were removed from the data yielding 393 observations of 11 variables. Our research hypothesis was that limited aortic index repair is associated with a higher requirement for reoperation. The probability of rejecting the null hypothesis (H0), a statistical significance

Table 1. Patients and their clinical characteristics

Characteristics	
Male, n (%)	280 (71%)
Age (years), mean [SD]	57 [±13.7]
EuroSCORE module I, mean [SD]	33.5 [±19.8]
Days in the Intensive care unit (days), mean [SD]	6 [±11]
Iatrogenic etiology, n (%)	11 (2.8%)
Hypertension, n (%)	311 (79%)
Chest pain as a presenting symptom, n (%)	269 (68%)
Marfan syndrome, n (%)	3 (0.75%)
Loeys-Dietz syndrome, n (%)	1 (0.25%)

SD, standard deviation; EuroSCORE, European System for Cardiac Operative Risk Evaluation

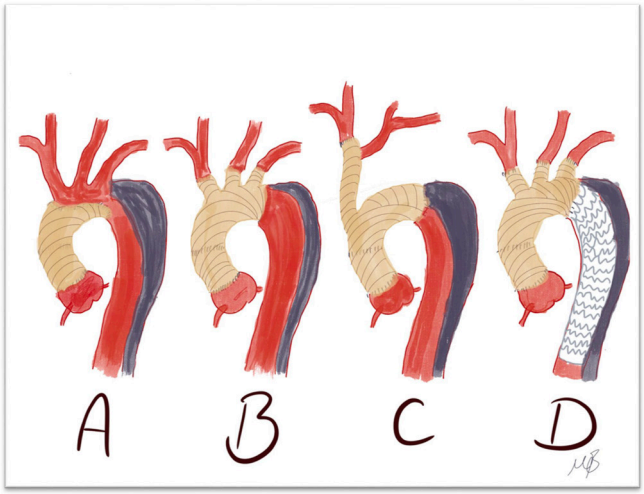

Figure 1. (A) aorta ascends replacement, (B) aorta ascends and arch replacement, (C) aortic ascends and arch replacement with debranching of the supra-aortal vessels, (D) hybrid technique using frozen elephant trunk prostheses.

Table 2. Operative mortality outcome for index and re-operation

In-hospital mortality outcome for index and re-operations		
Index operation	No n, (%)	311, (79%)
	Yes n, (%)	82, (21%)
Re-operation	No n, (%)	36, (90%)
	Yes n, (%)	4, (10%)

Table 3. Independent predictor of late reoperation on the aorta determined by multivariable analysis using logistic regression module

Variable	OR	95% CI	*P*-value
Age	1.0	(0.97, 1.03)	0.87
EuroSCORE	0.9	(0.95, 0.98)	0.03
Type of initial repair	0.5	(0.22, 1.14)	0.10

CI, confidence interval; OR, odds ratio

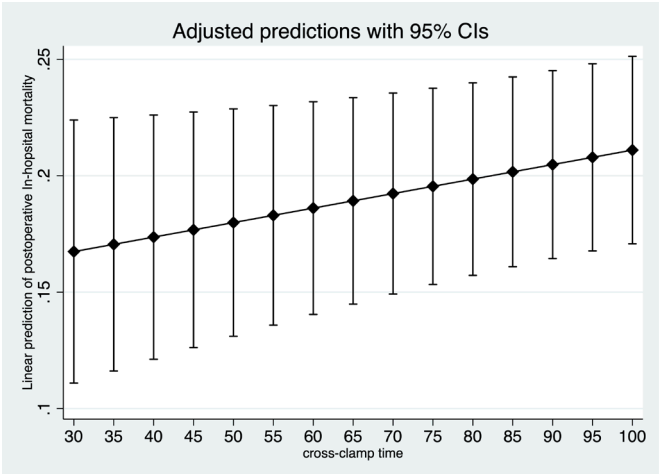

Figure 3. A graphic demonstrates cross-clamp time's marginal effect on the probability of dying in patients with acute type A aortic dissection.

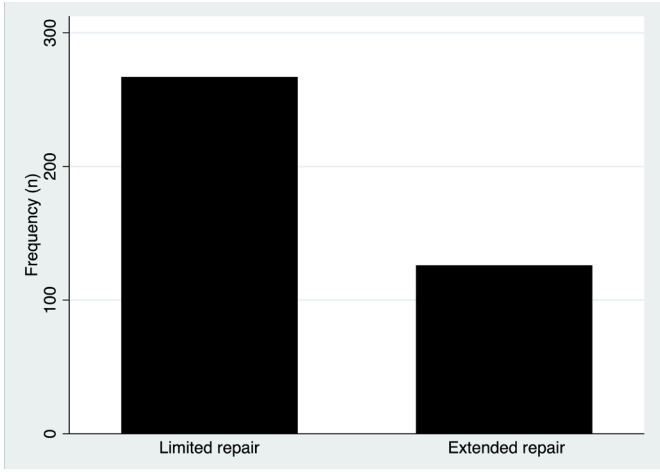

Figure 2. Bar chart demonstrating the frequency of the undertaken surgical approach in the initial operation (limited vs. extended repair).

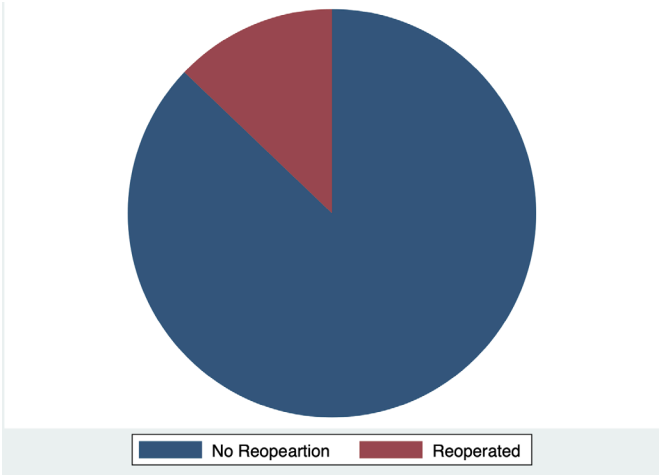

Figure 4. Pie chart of the patients, who survived to discharge after the initial repair, showing the percent of the patients who needed a reinvention on the aorta during the follow-up time (13%).

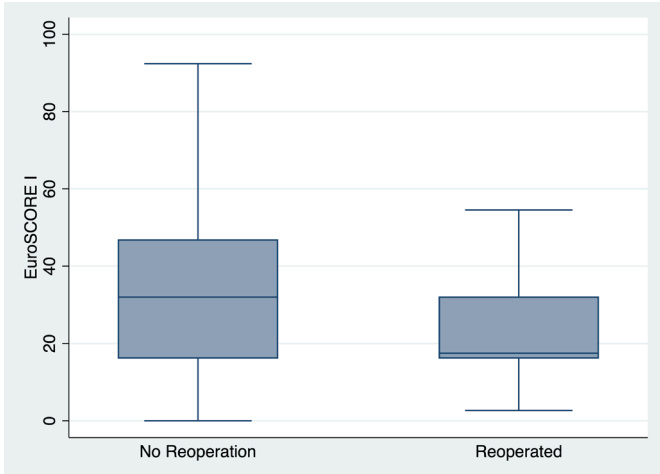

Figure 5. Box plot showing the difference in the EuroSCORE I median in both groups of patients.

was set at $\alpha \leq .05$ with 95% confidence intervals. Univariate analysis was performed using the independent t-test or Fisher's exact test via the R functions. Multivariate analysis was performed by estimating a multivariable logistic regression model via the R function. All of the analysis was conducted on R Version 4.1.

RESULTS

Patient and clinical characteristics: As of September 1, 2020, 393 patients were enrolled. Of these patients, 71% (*N* = 280) were males. The mean age of all patients was 57.6 years (95% CI, with an SD of around 13 years). Type A aortic dissection with iatrogenic etiology was reported in 11 patients (2.8%), and a history of hypertension was present in 311 patients (79%) of patients. The chief complaint was chest pain in 279 patients (70%). A documented genetic mutation was present in four patients (1%) (three patients with Marfan syndrome and a single patient with Loeys-Dietz syndrome). Eighty-one patients (20%) presented with cardiogenic and/or hemorrhagic shock with the required administration of intravenous catecholamine. The mean serum creatinine upon presentation was 1.3 mg/dl. The mean EuroSCORE I upon presentation for the initial repair operation was 33.5 (SD ± 19.8). The chief complaint upon presentation was sharp tearing chest pain in 68% of the patients (*N* = 269). Emergency and life-saving indications were settled in 94% of the primary (index) operations. (Table 1)

Operative management and outcome: Of 393 patients, in the index (primary) repair, 267 patients (68%) received a limited repair, and 126 patients (32%) received an extended repair. (Figure 2)

The mean cross-clamp time was 96 minutes, with a standard deviation of 67 minutes and a median of 84 minutes. The

mean length of stay in the intensive care unit was six days. The peak serum creatinine level during the hospital admission had a mean of 1.8 mg/dl; however, the mean level upon discharge was 0.57 mg/dl. A venoarterial extracorporeal membrane oxygenation (ECMO) system was used in 12 patients (3%). The stroke incidence in this cohort was 7% (N = 27). Overall, in-hospital mortality was 21% (N = 82). (Table 2)

We sought to assess the effect of cross-clamp on mortality using a multivariate analysis model adjusted for patient age and EuroSCORE I. The odds ratio for the cross-clamp time was 1.003 with a confidence interval of (1.009, 1.007) and P-value = 0.04. We developed a statistical graphic that shows the marginal effect of cross-clamp time on the probability of dying in patients with acute aortic dissection. (Figure 3)

A chi-square test of independence was performed to examine the relation between in-hospital mortality and initial repair types (limited versus extended). The association between the variables was not significant (P = 0.012).

Reoperation: Of the patients who survived to discharge (N = 311), reoperation on the aorta was necessary for 40 patients (13%). (Figure 4) Main indications for reoperation included newly developed aortic aneurysm and/or dissection. The in-hospital mortality after redo surgery was in four patients (10%). The mean duration until the reoperation was five years with an SD of 4.8. To identify whether the initial operation (limited vs. extended) has an association with the incidence of the reoperation, a chi-squared statistical test was performed. It showed no statistical significance (P = 0.09). A two-sample t-test showed a lower mean EuroSCORE I in the group of patients who had reoperations (mean EuroSCORE I was 24 in reoperated patients vs. 33 in not reoperated patients), with a statistically significant P-value of 0.003. (Figure 5)

In a multivariable logistic regression adjusted for age, EuroSCORE I, and type of initial repair (either limited or extended) module, the type of initial repair wasn't a statistically relevant risk factor for the primary outcome (reoperation) with an odds ratio of 0.5 and 95 % confidence interval between (0.2-1.1) (P = 0.10). (Table 3)

DISCUSSION

Acute aortic dissection, especially type A, is a lethal condition that requires emergency surgery. It has diverse presentations, and the diagnosis can be missed or delayed. Once diagnosed, decisions about initial management, transfer, surgery appropriateness, operation timing, and intervention for malperfusion complications are necessary. Surgery aims to save the patient's life by preventing pericardial tamponade or intra-pericardial aortic rupture, resecting the primary entry tear, and correcting or preventing a malperfusion syndrome and/or aortic valve regurgitation. And, if possible, avert late dissection-related complications in the proximal and distal aorta [Bonser 2011]. No randomized trials of treatment or techniques have been performed in the management of acute type A aortic dissection, as it might be an ethical issue to conduct such randomized trials concerning a life-saving operation. In our practice, retrospective data analysis is the main source of knowledge to manage the disease, which justifies the construction of multiple international registries for aortic dissection.

The mortality was almost 21%, which reflects the seriousness of the disease. It also correlates with the mortality rate of the international registry of acute aortic dissection (IRAD) reports [Hagan 2000]. The small percentage of patients with connective tissue disorders who presented with acute aortic dissection in this recent dataset compared with older reports [Hagan 2000] reflects the raised awareness of the medical community towards the disease. Close follow up and undertaking of prophylactic treatment in this group of patients as early as possible might have contributed to a lower incidence of dissection in acute settings [Pathare].

A review of the patients, who underwent surgery for type A aortic dissection from the IRAD database between 1996 and 2006 [Parikh 2017], showed there had been significant changes in the operative strategy of managing the disease.

Preserving the native valve offers various benefits, including avoiding anticoagulation treatment [Stassano 2009] and a decreased risk of valve-related problems, such as prosthetic endocarditis [Giebels 2013]. However, extended operative time is required to perform valve-sparing procedures, particularly in patients who require a concomitant complete or partial arch repair; it carries the risk of longer cardiopulmonary bypass time. The overall use favored the David procedure compared with the Yacoub procedure as the Yacoub procedure is more time-consuming [Moorjani 2014].

The optimal surgical management for acute aortic type A dissection remains controversial. There is no unanimity over whether to undertake a limited repair (i.e., isolated aorta ascends replacement without an open distal anastomosis) followed by reoperation, if necessary, or to perform an extended repair (i.e., complete arch replacement with a conventional or frozen elephant trunk prostheses) for index repair.

The philosophy of "Live to Fight another day" is a central argument in favor of limited repair, as it reduces the surgical risk by shortening the cross-clamp time in comparison with extended repair. In addition, several studies have revealed that limited repair has a similar late outcome to extensive repair, such as the development of late aortic dilatation as well as the need for subsequent repair [Li 2015; Eusanio 2015]. The promising good results of endovascular therapy also can play a central role in making the later reintervention less aggressive in selected patients. Arguments favor extensive index repair, focusing on the potentially decreased need for late aortic reoperation. However, these operations frequently are viewed as complex and carry a much higher risk. They need an experienced cardiac surgeon with a well-trained team in a high-volume referral center, which is not easy to access as fast as possible dealing with the disease's aggressive nature.

The European System for Cardiac Operative Risk Evaluation (EuroSCORE) is a cardiac risk model for predicting mortality after cardiac surgery. It was published in 1999 and derived from an international European database of patients, who had undergone cardiac surgery by the end of 1995. The system has been highly successful and used worldwide for

measuring risk and as a benchmark for assessing the quality of cardiac surgical services [Roques 1999]. To the best of our knowledge, this is the first dataset to show a correlation between reoperation on the aorta and EuroSCORE module I. It is interesting to note that the reoperation incidence is higher in patients with lower EuroSCORE module I. The interpretation of this might be those younger patients who underwent acute aortic dissection might need another intervention on the aorta more than older patients with higher EuroSCORE module I, as they tend to live longer, which justifies performing a closer follow up in this group of patients to do the reoperation in more elective settings and avoid the salvage indication.

On multiple occasions in the literature, it was reported that prolonged cross-clamp time (XCL) significantly correlates with major postoperative mortality [Al-Sarraf 2011; Doenst 2008; Salsano 2018]. Despite modern techniques of cardioprotection, XCL time remains an independent predictor of mortality. This dataset supports this conclusion, as we found that longer cross-clamp time was an independent predictor of mortality. However, these results must be interpreted carefully and wisely as more complex dissections need a longer time to repair because of intraoperative technical difficulties. And logically, more complicated aortic dissection has higher mortality.

The results presented within this dataset show no statistical difference between the two techniques (i.e., limited and extended) regarding reoperation, provided that the primary entry is excised. This dataset shows that reoperation can be performed with low mortality rates. Furthermore, the vast majority of the reoperation could be performed in elective settings, giving time for careful case planning and likely accounting for excellent outcomes. Our patients who had limited repair with excision of primary entry didn't particularly have more reoperation incidence compared with the patients who had to have extended repair. So, adapting an extended repair when it is not necessary can increase mortality by increasing cross-clamp and won't offer the patient a lower incidence of reoperation in the future.

Considering the new definition of quaternary prevention, which is "an action taken to prevent individuals from a medical intervention that is likely to cause more harm than good," it is evident that adopting an extended repair when it is unnecessary can be classified as harmful overmedicalization.

Aortic arch replacement is challenging and time-consuming and carries more risk for the neurological deficit, but it is usually unavoidable. However, prior knowledge of the effect of cross-clamp time on the outcome can help prevent some of these complications [Zheng 2019]. Surgeons should be aware of this relationship during the operative procedures in patients with acute aortic dissection and attempt to avoid longer cross-clamp time as far as possible.

Strengths and limitations: Our study had several strengths, including the large number of patients included in the analysis and the 20-year interval, which provided us with enough follow-up time to include the incidence of reoperations. However, the study was limited by the potential bias of a single-center, retrospective analysis.

CONCLUSIONS

An extended prophylactic repair in the initial operation of an acute type A aortic dissection might not lead to a lower incidence of reoperations on the aorta and could increase in-hospital mortality by increasing cross-clamp time.

Reoperation on the aorta after type A aortic dissection could be done safely with acceptable mortality outcomes.

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