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Original Article

Investigation of factors affecting reintervention after type A aortic dissection

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Abstract

Aim: Our study aims to share the reintervention results of patients who were operated with the diagnosis of Type A aortic dissection and to examine the factors that cause reintervention.
Material and Methods: In our single-center retrospective study, 244 patients who underwent surgery due to Type A aortic dissection between November 2010 and June 2021 were included. Results for patients who underwent reintervention and factors which caused reintervention were compared with demographic data, preoperative, intraoperative and postoperative variables.
Results: A total of 142 patients were included in the study and 15.5% of them underwent reintervention. Reoperation was performed in 8 (36.4%) of 22 patients who underwent reintervention, while thoracic aortic endovascular repair was performed in 14 (63.6%) patients. Post-procedure mortality was observed in 5 (22.7%) of the patients who underwent reintervention. The mean age of the patients who underwent reintervention was 46.6±13.2 and there was a statistically significant ($p<0.05$) difference between the groups (p: 0.026). Results that were significant for reintervention were multivariate analysis with cox regression and it was shown that the persistence of postoperative hypertension with total arch surgery was a risk factor for reintervention (p: 0.03, p: 0.008).
Conclusion: Type A aortic dissection is not considered to be completely cured after the first operation. It is necessary to evaluate the patients in terms of reintervention with close follow-up. We propose that patients who underwent total arch surgery during the first operation and hypertension in the postoperative period are risk factors for reintervention.

Keywords: Aortic dissection, hypertension, risk factors

INTRODUCTION

Type A aortic dissection (TAAD) is a disease with high mortality from the moment it is diagnosed, even with the increase of surgical and perioperative management methods [1]. The strategy is determined by the extent of TAAD, the localization of the intimal tear, and the presence of malperfusion syndromes.

In the TAAD repair 2022 American Heart Association guideline, it was presented that the procedure should be supported with hemiarch replacement with the repair of the ascending aortic surgery even if there is no aneurysm or intimal tear in the aortic arch [2]. In the presence of an intimal tear in the aortic arch or arch aneurysm, more extensive surgery is possible with total arch replacement. However, surgical treatment of the aortic arch without arch aneurysm or intimal tear carries a high perioperative surgical risk of 8% to 34% [3].

In most patients with TAAD, the dissection flap reaches beyond the left subclavian artery, and immediate ascending aorta repair does not abolish the flap in all aortic segments [4]. Aortic interventions are hypothesized to protect the remaining

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fragile aortic tissue from degeneration and lead to pseudo lumen thrombosis. Although the results of surgical intervention have improved, patients are at greater risk of surgical intervention because of the residual dissected distal aorta. Aortic regurgitation due to ineffective resuspension of the native aortic valve, aortic wall necrosis, distal false lumen or dilatation of the proximal aortic sinuses are possible causes of surgical intervention [5].

Due to these reasons, the need for reoperation continues to be quite common. In our study, the aim was to establish the incidence of reintervention and independent risk factors following surgery for acute Type A aortic dissection, as well as to define survival and long-term outcomes.

MATERIAL AND METHODS

Patient Population and Method

In this retrospective case-control study, patients who were operated for TAAD in our clinic between November 2010 and June 2021 were evaluated. During this period, a total of 244 patients were operated on with the diagnosis of TAAD in our clinic. All operated patients were included in the study. Patients who lost their lives due to early mortality (<30 days in-hospital mortality), those with a history of Type B aortic dissection, patients who died from other causes after discharge and patients whose data could not be obtained retrospectively were excluded from the study. 102 patients who met the exclusion criteria were excluded from the study and the study was planned on 142 patients. Patient files were reviewed retrospectively, and preoperative clinical status, preoperative surgical strategy, and postoperative conditions were evaluated.

The medical data of the patients were obtained from the hospital's registry system and patient files. The procedures to be performed on the patients (open operation or TEVAR) were decided upon by a cardiac team composed of non-invasive and interventional cardiologists, cardiovascular surgeons and anesthesiologists. Telephone conversations were made with patients who did not attend their planned follow-up visits in our hospital and with patients living in remote areas. The study protocol was approved by the Ethics Committee of the University of Health Sciences (Date: 18/01/2022-No: 2022.01-02). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Preoperative, Operative and Postoperative Data

Patients with hypertension (HT) were accepted as patients with systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg. Criteria for diagnosis of Diabetes Mellitus (DM) were: Fasting blood glucose ≥126 mg/dL (7.0 mmol/L) or 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) in oral glucose tolerance test or HbA1C ≥6.5% during the classic signs of hyperglycemia or hyperglycemic crisis with a random plasma glucose of ≥200 mg/dL (11.1 mmol/L). Patients with airflow resistance with a forced 1 second expiratory volume to forced vital capacity ratio (FEV1/FVC) of <0.70, despite bronchodilator therapy, symptoms of shortness of breath and cough, and significant exposure to harmful stimuli were considered to have chronic obstructive pulmonary disease (COPD). Patients with a Glomerular Filtration Rate (GFR) below 60 ml/min/1.73m^2 were considered to have chronic renal failure.

Shock was specified as the patient's systolic blood pressure of ≤90 mmHg from the time of diagnosis. Prolonged ventilation time was determined as 24 hours. The need for inotropics has been indicated as the follow-up of patients with one or more inotropic drugs in the postoperative period.

Postoperative hypertension was defined as systolic blood pressure of ≥140 mmHg with or without medical treatment after discharge.

Operational procedures were performed according to the perioperative evaluations of the surgical teams. The main purpose of the operation is complete resection of the primary intimal tear. After the resection, the false and true lumen fusion was achieved and it was aimed to completely close the false lumen with the anastomosis of the distal aortic segment.

Indications for reintervention were rapid aneurysmal degeneration with a maximum aortic diameter of >5.5 cm for aortic arch and >6.5 cm for the descending aorta, growth rate of >1 cm/year, suture line aneurysm, malperfusion syndrome due to compression of the true aortic lumen, and re-entry in the descending aorta between the false lumen and the true lumen.

Statistical Analysis

Statistical results were obtained using the IBM Statistical Package for the Social Sciences version 23 (SPSS Inc., Chicago, IL, USA) program. Mean±standard deviation was given for continuous variables, percentage and number values were given for categorical variables. Normality of distribution was evaluated based on the Kolmogorov Smirnov test. For comparison of clinical and laboratory characteristics, Student's t test was used if the data were normally distributed, otherwise the Mann-Whitney U test was used. Differences between categorical variables were evaluated using the chi-square test and Fisher's exact test. Normally distributed continuous data were presented as mean and SD. Abnormally distributed continuous data were presented as median and interquartile (Q1–Q3). A “cox” regression analysis was indicated to determine the factors affecting “Reintervention”. Multivariate analysis was performed for the values that were significant in the univariate analysis. Event-free survival curves were constructed using the Kaplan-Meier method and compared using the long-rank test. A p value of <0.05 was considered statistically significant.

RESULTS

The mean age of the participants was 52.2±12.8 years (18-82) and 77.5% (110/142) were male. The mean age of the patients who went to reintervention after TAAD was 46.6±13.2 years. There was a statistically significant difference between the groups (p: 0.026). No difference was found in other demographic data (Table 1).

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The findings of the preoperative data of the patients are shown in Table 1. There was no difference in comorbidity data between groups. Among the surgical procedures, a significant difference was found in terms of reintervention in patients who underwent Bentall, Total arch replacement and elephant trunk procedures (p: 0.026, p: 0.007, p: 0.027, respectively). There was no difference in reintervention in cannulation strategy and cardiopulmonary bypass data. The results of the preoperative data are shown in Table 2.

Table 1. Demographic data of patients

Demographic data	Total patients=142	Reinterven (-)=120	Reinterven (+)=22	p
	Mean SD	Mean SD	Mean SD	
Age	52.2±12.8	53.2±12.5	46.6±13.2	**.026***
Gender (male) n%	110 (77.5%)	91 (75.8%)	19 (86.4%)	0.277
Weight/kg	82.5±14.6	83.2±15	78.7±11.8	0.195
Height/cm	171.8±8.6	171.2±8.8	175±6.6	0.069
BSA	1.95±0.19	1.95±0.19	1.95±0.16	0.978
Preoperative data				
Admission n%	T: 79 (55.6%)	66 (55%)	13 (59.1%)	0.723
	H: 63 (44.4%)	54 (45%)	9 (40.9%)	
CVI/TIA n%	11 (7.7%)	8 (6.7%)	3 (13.6%)	0.377
Shock n%	28 (19.7%)	23(19.2%)	5 (22.7%)	0.771
CRF n%	10 (7%)	9 (7.5%)	1 (4.5%)	0.619
HT n%	114 (80.3%)	97 (80.8%)	17(77.3%)	0.7
COPD n%	34 (25.8%)	31 (25.8%)	3 (13.6%)	0.218
DM n%	25(17.6%)	23 (19.2%)	2 (9.1%)	0.366
LV±EF	56.8±4.3	56.7±4.2	57.2±4.5	0.651

Values are expressed as N (%) or mean±SD. BSA: body surface area, COPD: chronic obstructive pulmonary disease, CRF: chronic renal failure, CVI: cerebrocascular incident, DM: diabetus mellitus, EF: ejection fraction, H: hospital, HT: hypertension, T: transfer, TIA: transient ischemic attack

Table 2. Analysis of patients with peroperative data

Perioperative data	Total patient=142	Reinterven (-)=120	Reinterven (+)=22	p
	Mean SD	Mean SD	Mean SD	
SCG n%	85 (59.9%)	68 (56.7%)	17 (77.3%)	0.07
Bentall n%	56(39.6%)	52 (43.3%)	4 (18.2%)	**.026***
Hemiarch n%	35 (24.6%)	31 (25.8%)	4 (18.2%)	0.444
Total arch n%	22(15.5%)	14 (11.7%)	8 (36.4%)	**.007***
ET n%	5 (3.5%)	2 (1.7%)	3 (13.6%)	**.027***
ADD CABG n%	7 (4.9%)	5 (4.2%)	2 (9.1%)	0.296
ADD AVP n%	11 (7.7%)	9 (7.5%)	2 (9.1%)	0.797
Cannulation types				
Axillary n%	87 (61.3%)	73 (60.8%)	14 (63.6%)	0.804
Femoral n%	54 (38%)	47 (39.2%)	7 (31.8%)	0.514
CPB data				
ACP n%	55 (38.7%)	47 (39.2%)	8 (36.4%)	0.804
TCA n%	53 (37.3%)	45 (37.5%)	8 (36.4%)	0.919
ACP+TCA n%	13 (9.2%)	11 (9.1%)	2 (9.2%)	>.99
Temperature/'C	22.9±3.7	22.9±3.7	22.8±3.8	0.593
CPB/min	170.9±52.2	168,6±52.2	183.6±51.4	0.215
Cross X/min	89.6±37.3	90.4±36.4	85.7±42.8	0.591
ACP/min	33.1±16.6	32.6±16.5	35.7±18.1	0.801

Values are expressed as N (%) or mean±SD, ACP: antegrade cerebral perfusion, ADD: additional, AVP: aortic valvuloplasty, Cross X: cross clamp time, CPB: cardiopulmonary bypass, ET: elephant trunk, TCA: total circulatory arrest, SCG: supracoronary graft implantation

In the analysis of postoperative data shown in Table 3, a significant difference was found in terms of reintervention of Vitamin-K antagonist and postoperative HT (p: 0.022, p: 0.006, respectively). There was no significant difference between inotropic use, duration of intensive care unit stay and hospital stay on reintervention.

Table 3. Analysis of postoperative data of patients

Postoperative data	Total patient=142	Reinterven (-)=120	Reinterven (+)=22	p
	Mean SD	Mean SD	Mean SD	
Inotrope n%	94 (66.2%)	79 (65.8%)	15 (68.2%)	0.83
ICU stay/day	5.6±8.6	5.7±9.1	5.1±4.6	0.561
Hospital stay/day	13.6±11.4	13.7±12	13.1±7.2	0.601
VENT time/h	63.8±88.2	66.2±93.5	50.9±50.2	0.709
VIT-K ANT n%	57 (40.1%)	53 (44.2%)	4 (18.2%)	**.022***
POST HT n%	93 (65.5%)	73 (60.8%)	20 (90.9%)	**.006***

Values are expressed as N (%) or mean±SD. ICU: intensive care unit, POST HT: postoperativehypertension, VENT: ventiation, VIT-K ANT: Vitamin-K antagonist use

Reintervention

The mean age of the patients who underwent reintervention was 46.6±13.2, and it was performed in 15.5% (22/142) of the total patients. While 36.4% (8/22) of the patients were reoperated, the mean time for reintervention was 40.6±27.3 months. Among 142 patients, 22 (15.5%) patients underwent a reintervention procedure. The first reintervention was applied 6 months after the initial operation. The initial procedure performed was TEVAR. The first reoperation occurred at 8 months after the initial operation.

To show possible risk factors for reintervention, univariate and multivariate cox regression analysis were applied and the results are shown in Table 4 and Table 5. In univariate analyses, Bentall procedure (HR: 0.307, CI: 0.104-0.907, p: 0.033), total arch replacement (HR: 1.073, CI: 0.355-3.244, p: <0.001) and elephant trunk procedure (HR: 5.448, CI: 1.607-18.473, p: 0.007) were found to be related to reintervention in terms of surgical procedure. In the univariate analysis of postoperative data, the use of vitamin-k antagonists (HR: 0.543, CI: 0.223-1.346, p: 0.031) and the presence of postoperative HT (HR: 8.373, CI: 1.947-36.016, p: 0.004) were found to be significant in favor of reintervention. As a result of the evaluation of the data with multivariate regression analysis; total arch replacement (HR: 3.574, CI: 1.134, CI: 1.134-11.267, p: 0.03) and presence of postoperative HT (HR: 7.325, CI: 1.688-37.193, p: 0.008) were found to be significant risk factors for reintervention. Kaplan-Meier curves for reintervention are shown in Figure 1 and 2. Presence of postoperative HT (log-rank p: 0.001) and patients who underwent total arch replacement (log rank p: 0.0001) had a high incidence of reintervention.

Table 4. Univariate analysis of demographic and operative data with cox regression

	UNIVARIATE ANALYSIS		
	HR	CI (95%)	P
Age	0.972	0.940-1.005	0.101
Gender	0.628	0.186-2.125	0.455
Height	1.044	0.993-1.098	0.091
Weight	0.982	952-1.012	0.229
BSA	0.776	0.081-7.457	0.826
CVI/TIA	3.879	1.117-13.471	**0.033***
CRF	0.739	0.098-5.566	0.769
HT	0.679	0.249-1.855	0.451
COPD	0.46	0.136-1.559	0.213
DM	0.48	0.112-2.055	0.323
SCG	2.619	0.965-7.107	0.059
Bentall	0.307	0.104-0.907	**0.033***
Hemiarch	1.073	0.355-3.244	0.9
Total arch	5.086	2.111-12.255	**<0.001***
Elephant trunk	5.448	1.607-18-473	**0.007***
Additional CABG	1.829	0.427-7.838	0.416
Additional AVP	1.385	0.323-5.941	0.661
Axillary cannulation	1.088	0.459-2.575	0.849
Femoral cannulation	0.558	0.130-2.392	0.432
ACP	2.05	0.843-4.987	0.113
TCA	0.732	0.310-1.728	0.476
Temperature	1.075	0.968-1.195	0.176
CPB	1.002	0.995-1.009	0.602
CROSS X	0.994	0.984-1.005	0.288
ACP time	1.019	0.985-1.053	0.277
VENT time	0.997	0.991-1.004	0.424
Inotrope usage	1.231	0.501-3.022	0.65
ICU stay	0.997	0.943-1.053	0.904
Hospital stay	1.004	0.965-1.045	0.847
POSTOP HT	8.373	1.947-36.016	**0.004***
VIT-K ANT	0.548	0.223-1.346	**0.031***

ACP: antegrade cerebral perfusion, AVP: aortic valvuloplasty, BSA: body surface area, COPD: chronic obstructive pulmonary disease, CRF: chronic renal failure, CROSS X: cross clamp time, CPB: cardiopulmonary bypass, CVI: cerebrocascular incident, DM: diabetus mellitus, ICU: intensive care unit, SCG: supracoronary graft implantation, HT: hypertension, POST HT: postoperativehypertension, TCA: total circulatory arrest, TIA: transient ischemic attack, VENT: ventilation, VIT-K ANT: Vitamin-K antagonist use

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Table 5. Multivariate analysis of factors affecting reintervention

	HR	CI (95%)	P
CVI/TIA	3.997	0.900-17.671	0.069
Bentall	1.09	0-3.89	0.961
Total arch	3.574	1.134-11.267	**0.03***
ET	1.134	0.236-5.452	0.876
POST HT	7.325	1.688-37.193	**0.008***
VIT-K ANT	0.004	0-1.494	0.955

CVI: cerebrovascular incident, ET: elephant trunk, POST HT: postoperative hypertension, VIT-K ANT: vitamin-K antagonist use

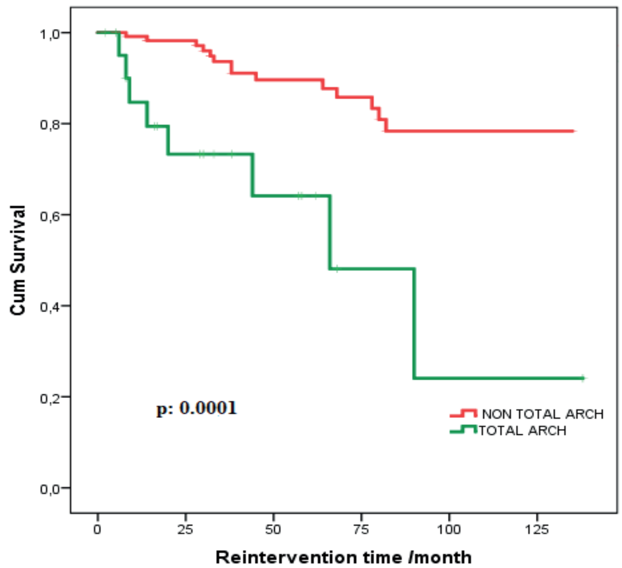

Figure 1. Kaplan-Meier plot of the incidence of total arch replacement and development of reintervetion

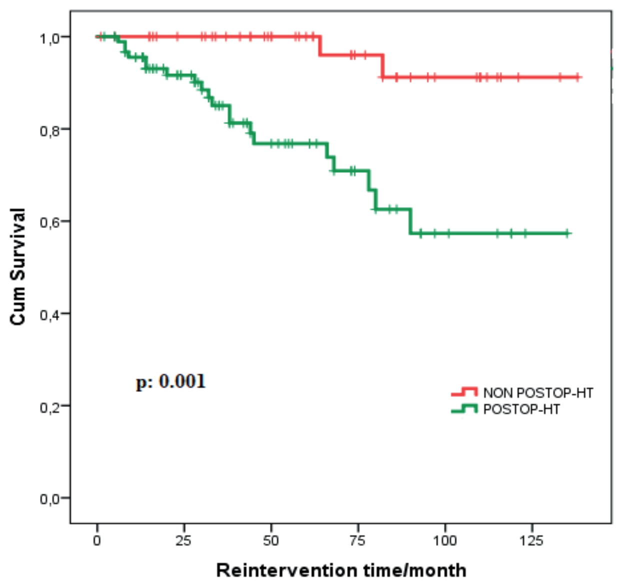

Figure 2. Kaplan-Meier plot of the incidence of postoperative HT and reintervention

DISCUSSION

Dr. Crawford, one of the pioneers in aortic surgery, stated that "No patient should be considered cured of the disease", which is a saying that remains valid today [6]. Other studies have reported a high risk of late aortic events not only in patients with residual dissected aorta but also in those who have anatomically normal aortas without any dissection after the initial emergency surgery [7]. In our patients presenting with TAAD, the main objective was the resection of the primary intimal tear zone. In our study, we anticipated recovery following the total resection of the aortic arch. Nevertheless, we observed that the need for reinterventions persisted in the patients.

Research on reintervention is increasing in patients who have undergone surgery after the diagnosis of TAAD with increasing survival rates. In most TAAD patients, dissection after surgical repair extends beyond the left subclavian artery, and repairing the ascending aorta does not remove all dissected aortic segments [8]. The rate of reintervention due to late distal aortic events following proximal TAAD repair ranges from 6% to 15% [7,9]. At our center, the reintervention rate in TAAD patients who underwent surgery was found to be 15.5%, which is consistent with the literature.

Younger age at first operation was a strong risk factor for late aortic reinterventions [10,11]. Rylski et al. investigated the early and mid-term results of surgical repair of the aortic arch in patients operated on with TAAD [9]. The fact that the patients were under 45 years of age and the dissected aortic arch was not completely resected had no effect on reintervention. Dohle et al. indicated that dissected aortic involvement and age were risk factors for reintervention during the follow-up period in patients who underwent proximal aortic repair with the diagnosis of TAAD [12]. In our study, it was seen that the age difference between those with and without reintervention was statistically significant. However, due to the insignificant results in the multivariate analysis, we cannot claim that younger age is a risk factor for reintervention, as in the study of Kirsch et al. [5].

The effect of the surgical procedure on reintervention in the future was discussed in the 2022 AHA guideline, and it was shown that the procedure should be supported with hemiarch with repair of ascending aortic surgery [2]. It was shown in our study that there was a significant statistical relationship between the Bentall procedure performed for the repair of the ascending aorta and the reintervention group. Although the relationship between Bentall procedure and reintervention was significant in univariate analysis, the relationship lost its meaning with multivariate analysis.

Anticoagulation with vitamin-K antagonist is recommended by guidelines after use of metallic prosthetic valves [13]. In the study of Vendramin et al. on the false lumen patency of oral anticoagulation after TAAD repair, patients were also examined in terms of reintervention, and the effect of oral anticoagulation was not found to be significant [14]. Larsson et al. investigated the effect of the use of anticoagulation on false lumen patency in their study, and patients who underwent reintervention were also examined in the same study, and no significant difference was found in reintervention between patients with oral anticoagulation [15]. Although the relationship between reintervention and anticoagulation was statistically significant in our study, it was found that anticoagulation had no effect on reintervention in the multivariate evaluation.

Rylski et al. investigated the reasons for reintervention and compared the results of open surgery and endovascular repair in reintervention [16]. Reintervention indications were determined as aneurysmal degeneration with a maximum aortic diameter of ≥5.5 cm, growth rate of >1 cm/year, suture line aneurysm, malperfusion syndrome secondary to compression of the true aortic lumen, penetrating aortic ulcers, and the presence of continuity between the true and false lumen in the descending aorta [16]. In this study, the relationship between ascending aortic replacement and total arch replacement and reintervention in the first surgical procedure was found to be statistically significant.

In patients treated for TAAD, false lumen diameter of >22 mm in the proximal descending aorta, false lumen size (>70% of total aortic area), persistence of the false lumen at the inner curvature, late aneurysmal degeneration, and adverse aortic event are accepted as risk factors [17]. In addition, the presence of single intimal tear, tear >10 mm in diameter, tear localization in the arch or in the descending thoracic aorta, and elliptical configuration of the true lumen were also considered predictive for the development of undesirable aortic events and the need for aortic repair [17,18]. In our study, the complete excision of the intimal tear forms the basis of the operating procedures. We believe that the intimal damage in the aortic arch, which necessitates total arch replacement, and the configuration change in the aortic arch after repair, support the idea that plays a role in the development of undesirable aortic events.

In their study, Iida et al. examined the conditions and consequences of TEVAR procedure performed for residual aortic dissection after TAAD [19]. They showed that after total arch surgery and elephant trunk procedure in the first operation of 52.8% of the patients, >55-60mm distal aortic diameter, >5mm aortic diameter enlargement in 6 months, postoperative true lumen stenosis and intimal tear in the descending thoracic aorta were the cause of reintervention. Total arch surgery repair was found to be a factor affecting reintervention in our study. Together with the studies, we believe that the incomplete closure of the false lumen orifice, possible intimal tear in the left subclavian artery or descending aorta may cause this situation.

Hypertension has been a known risk factor for aortic aneurysm and TAAD. Larsoon et al. also stated in the same study that the use of beta-blockers and tight blood pressure control should be considered [15]. We know that DeBakey et al. showed the relationship between postoperative blood pressure control and the progression of aneurysmal disease in the long term [20]. Zierer et al. supported the same claim and also stated that elevated systolic blood pressure in long-term follow-up was associated with late reintervention [10]. They declared in the report that the effect of beta blocker use is important on reintervention. In their study, Squizzato et al. associated the use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers or calcium channel blockers with a slower growth rate in the supraaortic vessels, depending on the artery segment [21]. Our study shows that incomplete or irregular antihypertensive treatment after TAAD makes patients the number one candidate for reintervention in the later period.

Our study has some limitations. The main limitation is the retrospective analysis of our study. All data about patients were scanned retrospectively from hospital information systems. Our study is the product of a single-center study. The fact that there is more than one surgical team in this center and that the surgical teams do not act with a common consensus is another limitation. The fact that more than half of the patients apply to our hospital due to referral from an external center may cause a lack of continuity of follow-up in external centers after discharge. As a result of these situations, the measurement of aortic diameters and false lumen diameters were not possible. In addition, a comprehensive analysis for the diagnosis, follow-up and screening of connective tissue diseases could not be indicated.

Expanding the diagnosis and screening for connective tissue diseases, providing easy and priority access to health services for TAAD patients in the postoperative period, and expanding the studies comprehensively will undoubtedly strengthen the available data. We believe that the conditions that cause reintervention and the relationships between them will be revealed more clearly with multicenter large series studies.

CONCLUSION

It is observed that the need for reintervention increases in total arch repair independent of proximal aortic repair. In the postoperative period, strict systolic blood pressure of the patients should be monitored, and we think that the regulation of antihypertensive treatments, especially beta blockers, should be given as much importance as the patients.

Ethics Committee Approval: The study protocol was approved by the İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (date: 18.01.2022, no: 2022.01-02). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: Individual informed consent was waived due to the retrospective design.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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