Original Article

The proximal extension of acute type A aortic dissection is associated with ascending aortic wall degeneration

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Background: Aortic root involvement during acute type A aortic dissection (ATAAD) may depend on ascending aortic wall degeneration. Surgical decision-making for extended resection of the aortic root is clinically made without histopathology. The aim of the study was to investigate whether the degree of degeneration of the ascending aortic wall found in patients with ATAAD is associated with the aortic root involvement.

Methods: Collectively, 141 consecutive patients undergoing ATAAD surgery at Tampere University Heart Hospital were investigated. The ascending aortic wall resected in surgery was processed for 11 different variables that describe medial and adventitial degeneration. In addition, atherosclerosis and inflammation were separately evaluated. Patients undergoing aortic root replacement were compared with those with supracoronary reconstruction of the ascending aorta with/without aortic valve surgery (root-sparing surgery) during a mean 4.9-year follow-up.

Results: Aortic root replacement together with the ascending aortic replacement was performed in 39% of the patients (n=55). The mean age for all patients was 65 years [standard deviation (SD 13)]. Many patients with aortic root replacement had moderate to severe aortic valve regurgitation (85.5%). Most of the patients with aortic root-sparing surgery included a supracoronary tube prosthesis (89.5%), while nine patients also had aortic valve replacement. The degree of mucoid extracellular matrix accumulation was more prominent in patients with aortic root replacement compared to patients with root-sparing surgery (2.1 SD 0.4 *vs.* 1.9 SD 0.4, P=0.04, respectively). During follow-up, there were 52 deaths among patients (log rank P=0.79).

Conclusions: Histopathology of the ascending aorta during ATAAD reveals distinctive aortic wall degeneration in patients with aortic root involvement *vs.* not. The degree of mucoid extracellular matrix accumulation assessed postoperatively is associated with the choice of surgical procedure in many patients.

Keywords: Mucoid extracellular matrix accumulation; acute type A aortic dissection (ATAAD); aortic root replacement

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Introduction

During emergency surgery for acute type A aortic dissection (ATAAD), the estimation of disease extension determines the surgical technique (1,2). Though a limited surgery including simple supracoronary reconstruction of the ascending aorta is considered suitable for many, the extension of the disease proximally encompassing the aortic root requires a conduit prosthesis or an aortic valve-sparing root operation (1,3,4); the aortic root represents a consistent anatomical structure. Traditionally, the estimation of aortic tissue degeneration and, hence, the extent of surgical extension that includes the ascending aorta alone or together with the aortic root is at the discretion of the surgeon. However, the extent of ATAAD is believed to depend in part on tissue degeneration of the aortic wall; the relation of ascending aortic wall degeneration with ATAAD and disease extension is controversial (1,5,6).

We have previously shown that the histology of the aortic wall reveals aortic degeneration that may require additional intervention after ATAAD surgery (7). Here, we hypothesize that ascending aortic wall degeneration is more prominent in patients who require aortic root replacement versus aortic root-sparing surgery with/without aortic valve surgery. The consensus statement on the surgical pathology of the aorta of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology was published to specify the nomenclature and diagnostic criteria of aortic degeneration (8). The consensus statement aids to investigate changes in the degenerative aortic wall that are relevant to the presence of ATAAD. As the emergency ATAAD surgery strategy includes the evaluation of tissue destruction, the objective of this study was to evaluate the plausible association of aortic wall degeneration and the extent of proximal aortic disease. We retrospectively investigated whether the presence of ascending aortic wall degeneration in ATAAD patients would differ in patients with proximal extension of surgery encompassing the aortic root compared to patients with aortic root-sparing surgery with/without aortic valve surgery. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-206/rc).

Highlight box

Key findings

- The degree of mucoid extracellular matrix accumulation in the ascending aortic wall is increased in patients with acute type A aortic dissection (ATAAD) selected to undergo aortic root reconstruction *vs.* a more limited surgical solution including aortic root-sparing surgery with or without aortic valve surgery.

What is known and what is new?

- The association of ascending aortic wall degeneration with ATAAD and disease extension is unsettled.
- Distinctive histopathological features of ascending aortic wall degeneration are present during ATAAD including proximal extension of the disease *vs.* those requiring local ascending aortic reconstruction during aortic root-sparing surgery with or without aortic calve surgery.

What is the implication, and what should change now?

- ATAAD includes aortic wall weakness that reflects the extension of the disease. Awareness of the features of the dissected aorta may facilitate follow-up of the patients after surgery for ATAAD.

Methods

Ethical statement and study design

After approval of the institutional review board (Ethical Committee of the Tampere University Hospital, Tampere, Finland, R23028), the need for informed consent was waived due to the retrospective nature of the cross-sectional study, and the study was conducted under the Declaration of Helsinki (as revised in 2013). ATAAD was preoperatively diagnosed using computed tomography (CT) and echocardiography. The largest diameter of the ascending aorta was retrospectively measured from CT images. The severity of aortic valve regurgitation included moderate to severe regurgitation graded as 2–3 out of 3. Surgery was done between December 2008 and August 2021.

Surgery

The decision on the extension of the resection and surgical technique during ATAAD was at the discretion of each operating surgeon. Whenever the aortic wall, including the sinotubular junction (STJ), was estimated as the reason for aortic regurgitation, STJ was tailored for a suitable graft in an aortic root-sparing fashion with/without aortic valve surgery (root-sparing surgery). When ATAAD included the root of the aorta, a complete resection of the dissecting and dilated ascending aorta was performed, including the root and the aortic valve. The aortic arch was entirely resected or a hemiarch reconstruction was performed depending on the involvement of aortic wall disease. The intimal tears were included in the resection if possible. The size of the graft was measured by the principal surgeon. The aortic wall sample was procured from the middle of the resected area of the ascending aorta in the vicinity of STJ.

Histology and immunohistochemistry

A minimum of six pieces of resected ascending aorta including all three aortic wall layers, i.e., the intima, the media, and the adventitia, were embedded in paraffin, cut to 4 µm thick sections and stained with hematoxylin and eosin, Verhoeff-van Gieson, Alcian Blue and periodic acid-Schiff. At least 18 sections (six stained with hematoxylin-eosin, six stained with Verhoeff-van Gieson stain and six with Alcian Blue and periodic acid-Schiff) were evaluated in each case.

Immunohistochemistry was done using the Ventana Lifesciences Benchmark XT© staining module for T and B lymphocytes, plasma cells, macrophages, and smooth muscle cells. Ventana Lifesciences Antibody Dilution Buffer© was used for dilution media. Immunohistochemistry was used to characterize the inflammatory infiltrate (CD3 as marker for T-lymphocytes, CD68 as macrophage marker and CD20 as B-lymphocyte marker).

Hematoxylin-eosin was used for overall evaluation, inflammation assessment and evaluation of smooth muscle cell nuclei. Verhoeff-van Gieson was applied in assessment of elastic fibers including laminal medial collapse. Alcian Blue and periodic acid-Schiff was used for mucoid extracellular matrix accumulation assessment and fibrosis evaluation. The presence of ascending aorta atherosclerosis was categorized as mild, moderate, severe, atherosclerosis with plaque disruption including surface thrombus, and calcific atherosclerosis was reported. The pattern of ascending aorta inflammation was defined as granulomatous including giant cells, lymphoplasmacytic, mixed inflammatory and suppurative.

Quantification of medial degeneration

The aortic specimens were assessed as a part of routine surgical pathology evaluation according to guidelines of The Society for Cardiovascular Pathology and The Association for European Cardiovascular Pathology (8,9) by two experienced cardiovascular pathologists (I.K., T.P.). The assessed features included overall medial degeneration, mucoid extracellular matrix accumulation, elastic fiber loss/fragmentation, elastic fiber thinning, elastic fiber disorganization, smooth muscle cell nuclei loss, laminal medial collapse, smooth muscle cell disorganization, medial fibrosis, vasa vasorum medial thickening, and adventitial fibrosis. All features were assessed for grade (absent, mild, moderate, and severe) and distribution (focal, multifocal, and extensive). The worst present grade/distribution was reported and semi-quantified on a scale of 0–3 (8).

Follow-up protocol

Documentation of mortality and morbidity was available for all patients. Follow-up consisted of physical examination, CT, and echocardiography three months after surgery, and yearly CT thereafter. The mean follow-up for the patients was 4.9 years [standard deviation (SD) 4]. Morbidity after surgery included documentation of aortic reoperation due to reverse aortic remodeling that included proximal or distal aortic reoperations encompassing new aortic dissection or rupture, or increased aortic aneurysm observed by CT or echocardiography. The aortic aneurysm included an aortic diameter greater than 5.0–5.5 cm wide or aortic growth greater than 1 cm in a year. The criteria was adjusted to the presence of Marfan syndrome, sex, patient size, and symptoms according to The Yale Center criteria (10).

Statistical analysis

Continuous variables were expressed as means with SD and compared using the Mann-Whitney *U* test. Categorical variables were presented as numbers and percentages and were compared using χ^2 or Fisher's exact tests. To seek clinical relevance associated with immunohistochemistry in ATAAD surgery, patients were divided into two groups according to aortic root replacement or aortic root-sparing surgery with/without aortic valve surgery. Unadjusted survival was investigated using Kaplan-Meier analysis with logarithmic rank tests. Multivariable binary logistic regression analysis was performed to analyze the association of extent of mucoid extracellular matrix accumulation adjusted for clinically relevant confounders with aortic root involvement. These confounders included the presence and location of entry tear, aortic valve regurgitation, age, male sex, presence of bicuspid aortic valve and aortic diameter. The predictive value of the extent of mucoid extracellular matrix accumulation alone and together with the clinically relevant parameters using a receiver operating characteristic (ROC) curve were analyzed for the association between the decision-making for the aortic root replacement *vs.* aortic root-sparing surgery. All analyzes were performed with IBM

Table 1 Patient demographics

Variables	All patients (n=141)	Aortic root replacement (n=55)	Aortic root-sparing (n=86)	P value
Age, years	65 (13.1)	65 (10.9)	65 (14.4)	0.63
Sex				
Female	48 (34.0)	17 (30.9)	31 (36.1)	0.59
Male	93 (66.0)	38 (69.1)	55 (64.0)	
Hypertension	83 (58.9)	31 (56.4)	52 (60.5)	0.73
Diabetes	8 (5.7)	4 (7.3)	4 (4.7)	0.71
Hypercholesterolemia	19 (13.5)	7 (12.7)	12 (14.0)	>0.99
Arthritis	2 (1.4)	0	2 (2.3)	0.52
Asthma	10 (7.1)	6 (10.9)	4 (14.0)	0.19
CAD	14 (9.9)	6 (10.9)	8 (9.3)	0.78
Cerebrovascular stroke	3 (2.1)	1 (1.8)	2 (2.3)	>0.99
Previous CABG	7 (5.0)	4 (7.3)	3 (3.5)	0.43
Previous AVR	7 (5.0)	3 (5.5)	4 (14.0)	>0.99
Previous aortic dilatation	17 (12.1)	7 (12.7)	10 (11.7)	>0.99
Previous aortic operation	9 (6.4)	2 (3.7)	7 (8.2)	0.48
BAV	9 (6.4)	8 (14.6)	1 (1.2)	0.002
Connective tissue disorder	7 (5.0)	2 (3.7)	5 (5.8)	0.71
Aortic diameter, mm	50 (9.2)	49 (9.8)	51 (8.1)	0.17
AR	97 (68.8)	47 (85.5)	50 (58.2)	<0.001

Data are presented as mean (SD) or n (%). CAD, coronary artery disease; CABG, coronary artery bypass graft surgery; AVR, aortic valve replacement; BAV, bicuspid aortic valve; AR, moderate to severe aortic valve regurgitation; SD, standard deviation.

SPSS Statistics version 28.0 (IBM Corporation, Armonk, NY, USA) with P<0.05 as the significance criterion.

Results

Patient characteristics

Resection of the ascending aortic wall was performed for 141 consecutive patients who underwent ATAAD surgery and obtained for histology. All patients experienced the onset of symptoms leading to surgery for ATAAD in less than 2 weeks. Patient demographics are shown in *Table 1*. There were 55 patients with aortic root replacement and 86 with aortic root-sparing surgery with/without aortic valve surgery. Altogether, there were 48 female patients (34.0%). The mean age for all patients was 65 years (SD 13). Eight patients were diabetics, and hypercholesterolemia was equally represented in both groups. Only seven patients had a connective tissue disorder such as Marfan syndrome. A bicuspid aortic valve was present in nine patients (6.4%), of which all but one had aortic root replacement. Previous surgery such as coronary artery bypass grafting, aortic valve or aortic surgery was present in both groups. A history of aortic dilation prior to ATAAD was rarely recorded among patients (12.1%). The largest aorta diameter was 49 (SD 9.8) in patients with aortic root-sparing and 51 (SD 8.1) in patients with aortic root replacement (P=0.17, missing cases =3). Taken together, most of the patients with aortic root replacement had severe to moderate aortic valve regurgitation (85.5%).

Operative technique

The operative details are shown in *Table 2*. A little more than a third of all patients received an aortic valve prosthesis together with replacement of the aortic root and

Table 2 Chosen surgical techniques based on surgical evaluation during acute type A aortic dissection

Variables	All patients (n=141)	Aortic root replacement (n=55)	Aortic root-sparing (n=86)
Intimal tear			
Ascending aorta	73 (51.8)	32 (58.2)	41 (47.7)
Aortic arch	19 (13.5)	6 (10.9)	13 (15.1)
Unknown	49 (34.8)	17 (30.9)	32 (37.2)
Graft replacement of root and ascending aorta			
Mechanical conduit	16 (11.3)	16 (29.1)	0
Biological conduit*	39 (27.7)	39 (70.9)	0
Graft replacement of ascending aorta			
Mechanical valve + supracoronary prosthesis	2 (1.4)	0	2 (2.3)
Biological valve + supracoronary prosthesis	7 (5.0)	0	7 (8.1)
Supracoronary prosthesis	77 (54.6)	0	77 (89.5)
Distal extension			
Ascending aorta	91 (64.6)	37 (67.3)	54 (62.8)
Hemiarch	38 (27.0)	16 (29.1)	22 (25.6)
Total arch	12 (1.4)	2 (3.6)	10 (11.6)

Data are presented as n (%). *, includes one aortic valve-sparing root replacement David-operation.

ascending aorta (n=55, 39.0%). Aortic root replacements included either mechanical or biological conduit prosthesis (29.1% and 70.9%, respectively). One patient had an aortic root replacement with an aortic valve-sparing strategy (David-operation). Most patients with either aortic root replacement (n=37, 67.3%) or aortic root-sparing surgery (n=54, 62.8%) had only the ascending aorta replaced by a straight supracoronary tube prosthesis of the ascending aorta with a distal anastomose at the level of the brachiocephalic artery. Altogether, there were 38 patients with hemi-arch replacements (27.0%) and 12 total arch replacements (1.4%). Nine patients with a supracoronary aortic replacement had also aortic valve replacement; these patients were also included in the aortic root-sparing group. In 19 patients, the entry tear was situated in the aortic arch, while there were 73 patients with entry tears in the ascending aorta. There were 49 unreported or unknown sites of entry tears. In addition, coronary artery bypass grafting was performed in 21 patients.

Perioperative findings, histology, and immunohistochemistry

As shown in *Table 3* and *Figures 1,2*, the extent of mucoid extracellular matrix accumulation was more prominent in patients with aortic root replacement compared to those with aortic root-sparing surgery [2.1 (SD 0.4) *vs.* 1.9 (SD 0.4), P=0.04, respectively].

ROC analysis and adjusted multivariable binary logistic regression analysis

The predictive value of the extent of mucoid extracellular matrix accumulation alone to identify those patients that require aortic root surgery was not significant as assessed by ROC analysis [area under the curve (AUC) 0.556, standard error (SE) 0.066, 95% confidence interval (95% CI): 0.427–0.686, P=0.40]. However, the predictive value of the extent of mucoid extracellular matrix accumulation together with clinically relevant variables, such as presence and location of intimal tear, aortic valve regurgitation, age, male sex, presence of bicuspid aortic valve and aortic diameter, to identify patients with aortic root replacement was significant, as assessed by ROC analysis (AUC 0.783, SE 0.052, 95% CI: 0.682–0.885, P<0.001). According to the adjusted multivariable binary logistic regression analysis, the extent of mucoid extracellular matrix accumulation [odds ratio (OR): 9.981, 95% CI: 1.832–54.363, P=0.008]

Table 3 Histopathological findings based on the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology guidelines (9)

Variables	All patients	Aortic root replacement	Aortic root-sparing	P value
Overall medial degeneration, n	141	55	86	>0.99
Severity	2.4 (0.6)	2.4 (0.7)	2.4 (0.6)	0.92
Mucoid extracellular matrix accumulation	141 (100.0)	55 (100.0)	86 (100.0)	>0.99
Extent	2.0 (0.4)	2.1 (0.4)	1.9 (0.4)	0.04
Severity	2.0 (0.6)	2.0 (0.6)	2.0 (0.6)	0.95
Elastic fiber fragmentation and/or loss	141 (100.0)	55 (100.0)	86 (100.0)	>0.99
Extent	2.0 (0.5)	2.0 (0.4)	1.9 (0.5)	0.31
Severity	2.0 (0.7)	2.0 (0.8)	1.9 (0.6)	0.34
Elastic fiber thinning	86 (61.0)	35 (63.6)	51 (59.3)	0.72
Extent	1.0 (0.9)	1.1 (0.9)	1.0 (0.9)	0.51
Severity	0.9 (0.8)	0.9 (0.9)	0.9 (0.8)	0.89
Elastic fiber disorganization	112 (79.4)	47 (85.5)	65 (75.6)	0.20
Extent	1.3 (0.8)	1.4 (0.8)	1.3 (0.9)	0.38
Smooth muscle cell nuclei loss	122 (86.5)	45 (81.8)	77 (89.5)	0.21
Type	1.4 (0.7)	1.3 (0.8)	1.5 (0.7)	0.11
Extent	1.7 (0.9)	1.5 (0.9)	1.8 (0.9)	0.08
Laminal medial collapse	78 (55.3)	26 (47.3)	52 (60.5)	0.17
Type	0.7 (0.7)	0.5 (0.6)	0.8 (0.7)	0.053
Extent	0.9 (0.9)	0.8 (0.9)	1.0 (0.9)	0.18
Smooth muscle cell disorganization	31 (22.0)	16 (29.1)	15 (17.4)	0.15
Extent	0.3 (0.7)	0.5 (0.8)	0.3 (0.6)	0.10
Medial fibrosis	19 (13.5)	6 (10.9)	13 (15.1)	0.62
Extent	0.3 (0.7)	0.2 (0.6)	0.3 (0.8)	0.46
Severity	0.3 (0.7)	0.2 (0.7)	0.3 (0.7)	0.49
Foreign body giant cell reaction	3 (2.1)	0	3 (3.5)	0.28
Vaso vasorum medial thickening	22 (15.6)	12 (21.8)	10 (11.6)	0.15
Adventitial fibrosis	26 (18.4)	6 (10.9)	20 (23.3)	0.08
Atherosclerosis				
Mild	45 (31.9)	16 (29.1)	29 (33.7)	0.59
Moderate	42 (29.8)	21 (38.2)	21 (24.4)	0.09
Severe	21 (14.9)	5 (9.1)	16 (18.6)	0.15
Atherosclerosis with plaque disruption and surface thrombus	1 (0.7)	0	1 (1.2)	>0.99
Calcific atherosclerosis	9 (6.4)	4 (7.3)	5 (5.8)	0.74
Inflammation				
Granulomatous/giant cell pattern	5 (3.5)	1 (1.8)	4 (4.7)	0.65
Lymphoplasmacytic pattern	24 (17.0)	8 (14.5)	16 (18.6)	0.65
Mixed inflammatory pattern	3 (2.1)	1 (1.8)	2 (2.3)	>0.99
Suppurative pattern	5 (3.5)	1 (1.8)	4 (4.7)	0.65

Data are presented as mean (SD) or n (%). SD, standard deviation.

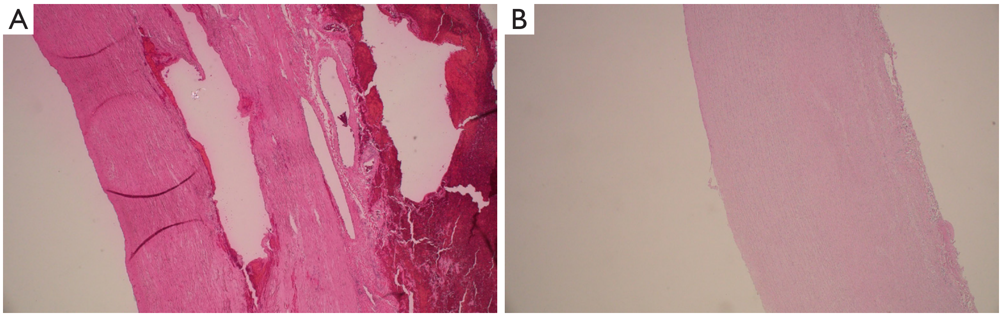

Figure 1 Representative histology (hematoxylin and eosin, 40× magnification) of ascending aorta during acute type A aortic dissection in a patient undergoing. (A) Histology of ascending aorta in a patient with aortic root replacement. Note dissection tear inside the media layer. (B) Histology of ascending aorta in a patient with aortic root-sparing surgery.

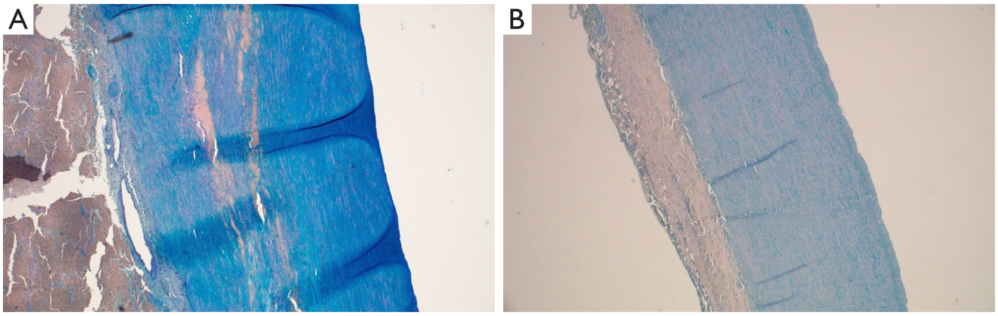

Figure 2 Representative immunohistochemistry (Verhoeff-Van Gieson, 40× magnification) of ascending aorta during acute type A aortic dissection in a patient undergoing. (A) Immunohistochemistry of ascending aorta in a patient with aortic root replacement showing extensive mucoid extracellular matrix accumulation within the media layer. (B) Immunohistochemistry of ascending aorta in a patient with aortic root-sparing surgery showing mild focal mucoid extracellular matrix accumulation.

was a significant factor related to patients with aortic root replacement.

Aortic reoperations and survival

Altogether, five patients with aortic root replacement (9.1%) and 16 patients with aortic root-sparing surgery were reoperated (18.6%). Aortic reoperations included six aortic root operations, of which three patients had reconstruction of the distal aorta as well; five patients with root-sparing surgery required reoperation for proximal root replacement and one patient with a biological root replacement required a reoperation for a second root replacement due to root pseudoaneurysm. The extent of elastic fiber fragmentation and/or loss was increased in the five patients needing reoperations after root-sparing surgery as compared to those without need of reoperations for the aortic root [2.40 (SD 0.55) *vs.* 1.87 (SD 0.49), P=0.027]. Fifteen patients underwent distal aortic reoperation encompassing six endografts of the descending aorta, five frozen elephant trunk prostheses, and four reconstructions of the aortic arch that initially had aortic root-sparing surgery. The 30-day mortality was found in 31 of 141 patients (22%). During follow-up, 52 patients died (*Figure 3*, logarithmic rank P=0.79).

Discussion

This study shows that the degree of mucoid extracellular matrix accumulation in the ascending aortic wall is increased in patients selected to undergo aortic root reconstruction *vs.* a more limited surgical solution such as aortic root-sparing surgery.

The decision to replace the aortic root during ATAAD is based on visualization of the intimal flap in the Valsalva sinus, the presence of aortic valve regurgitation that is not amenable to a root-sparing aortic surgery, and the

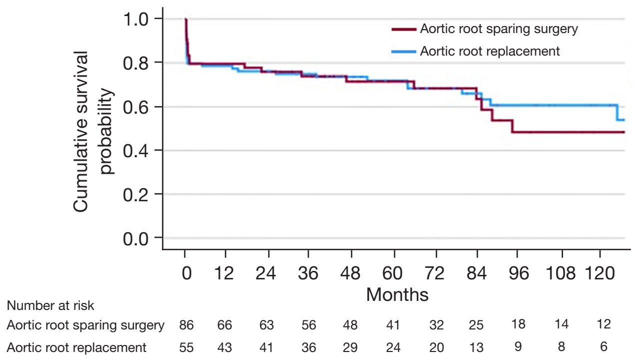

Figure 3 Survival probability of patients undergoing surgery for acute aortic type A dissection including ascending aortic replacement with aortic root (aortic root replacement, blue line) compared with patients operated only for the ascending aorta (aortic root-sparing surgery, red line). Time-dependent outcome according to Kaplan-Meier estimation. Log rank P=0.79.

involvement of the coronary artery ostia (11,12). Although risk factors that complicate the outcome of ATAAD surgery, such as circulatory malperfusion, pericardial tamponade, strokes, and comorbidities also affect surgical decision-making, surgery for the aortic root is generally recommended also during annuloaortic ectasia, and genetic predispositions such as Marfan syndrome (13). The degree of degeneration of the tissue of the ascending aortic wall is thought to reflect the extension of the disease, including the aortic root (14). This study shows that decision-making regarding aortic root resection was consistent with the degree of ascending aortic wall degeneration investigated histologically after surgery, but the extent of mucoid extracellular matrix accumulation alone cannot predict the need for aortic root replacement.

The consensus statement on the surgical pathology of the aorta of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology offered an important tool to retrospectively analyze the quality of aortic wall histopathology (8), and therefore it was possible to analyze whether aortic wall histology differed in the extended form of aortic dissection encompassing the need for aortic root surgery compared to patients with restricted aortic surgery with aortic root-sparing surgery.

Previously, ATAAD was histopathologically described as encompassing weaknesses in the congenital *vs.* acquired aortic wall (15) or including mixed subgroups *vs.* degenerative (16). The nomenclature and definitions can overlap between subgroups, as many degenerative aortic walls were described as to be free of severe or moderate atherosclerosis compared to mixed aortic walls with atherosclerosis and degeneration (16). Indeed, according to the definitions, the congenital form of aortic disease during ATAAD did not include obvious atherosclerotic lesions, while these were evident in the acquired form of aortic wall weaknesses (15). The common denominator for both congenital and degenerative subgroups was increased mucoid extracellular matrix accumulation compared to acquired and mixed subgroups (15-17). Unfortunately, these previous studies did not report the extent of the disease or surgical techniques used during ATAAD, but the involvement of the aortic root disease phenotype may have been more prevalent during the congenital and degenerative forms of aortic wall weaknesses.

Mucoid extracellular matrix accumulation may well describe not only the severity of weakness of the aortic wall, but also the extent of the disease involvement. Mucoid extracellular matrix accumulation was more prominent in patients with root replacement in our study and in both congenital and degenerative subgroups of weaknesses of the aortic wall compared to patients with aortic root-sparing surgery, acquired and mixed aortic wall subgroups. Interestingly, Marfan syndrome was statistically equally represented in patients with root replacement and root-sparing surgery, which is also observed in aortas from patients previously classified as degenerative *vs.* mixed (16). Marfan syndrome may not have been diagnosed in some patients prior to ATAAD. We also speculate that many patients with Marfan syndrome may have had aortic surgery before developing ATAAD.

The association of the extent of mucoid extracellular matrix accumulation of the ascending aorta is significantly increased in those aortas that were surgically operated for both the ascending aorta and the aortic root as compared with a limited solution of aortic root-sparing surgery. The presence and location of the intimal tear, moderate to severe aortic valve regurgitation, age, male sex, the presence of bicuspid aortic valve and increased aortic diameter are all part of the decision-making for the extent of surgery encompassing the aortic root. In case the aortic root appears not to be involved during ATAAD, careful inspection of the quality of aortic tissue is performed during surgery, and the decision to replace the aortic root is made according to clinical judgment to ensure blood circulation in the true lumen. This study suggests that the extension of ATAAD appears to be determined by a chronic process associated with mucoid extracellular matrix accumulation prior to the acute clinical presentation of ATAAD. Even if the confounders, i.e., presence and location of intimal tear, aortic valve regurgitation, age, male sex, presence of bicuspid aortic valve and aortic diameter were considered, the extent of mucoid extracellular matrix accumulation was a significant factor related to patients with aortic root replacement.

Limitations

This initial study is an example of a contemporary cross-sectional study cohort from real life. The limitations of this study include the small number of patients with a relatively short follow-up. Aortic wall histology is only obtained from patients undergoing surgery. The decision to undergo aortic root surgery together with the ascending aorta for ATAAD depends on the discretion of the surgeon. Postmortem investigation data is not available. There were 49 unreported or unknown sites of entry tears, and many entry tear locations are difficult to confirm once the ascending aorta is transected during ATAAD. On the other hand, the entry tear alone may not always determine the distal site of anastomose during surgery for ATAAD (18).

Conclusions

Specific histopathological features of the aortic wall were present during ATAAD including proximal extension of the disease *vs.* those who required local ascending aortic reconstruction during aortic root-sparing surgery. Understanding the features of the dissected aorta may facilitate follow-up of the patients in the future. The evaluation of the quality of ascending aorta degeneration with ATAAD using the consensus statement on the surgical pathology of the aorta of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology suggests that local histology of the ascending aorta is associated with proximal disease extension during ATAAD. This study confirms that ATAAD includes aortic wall weakness that reflects the extension of the disease.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-206/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. After approval of the institutional review board (Ethical Committee of the Tampere University Hospital, Tampere, Finland, R23028), the need for informed consent was waived due to the retrospective nature of the study and the study conforms to the Declaration of Helsinki (as revised in 2013).

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