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ORIGINAL ARTICLE

Are Women Taking Over Aortic Diseases? A Study of Morphological Changes in Surgically Treated Patients

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Abstract

Background/Aim: Aortic wall diseases requiring surgical intervention have become increasingly prevalent in recent decades. While cardiovascular diseases traditionally show a strong male predominance, less is known about the sex distribution and clinical characteristics in patients undergoing surgical treatment for aortic pathology. This study evaluated the epidemiological features, risk factors, comorbidities and histopathological findings in surgically treated aortic disease patients.

Methods: Ninety-two patients who underwent thoracic aortic surgery were analysed. Demographic, clinical and morphological data were collected for each patient and statistically evaluated.

Results: Atherosclerosis was the most common pathological finding in men, whereas aortic dissection predominated among women ($p < 0.01$). Hypertension was the most frequent comorbidity (75 %) and a positive family history was the commonest risk factor (31.5 %). Chest pain was the most prevalent presenting symptom, with significant variation in its frequency across different lesion types ($p < 0.01$).

Conclusion: Contrary to the well-known male predominance in cardiovascular disease, this study found no significant sex predominance among patients undergoing surgical treatment for aortic disease. Aortic dissection was significantly more frequent among women in this surgically treated cohort. These findings highlight the importance of recognising sex-specific patterns in advanced aortic pathology requiring surgical management.

Key words: Aorta; Atherosclerosis; Comorbidity; Chest pain; Aortic dissection.

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Introduction

In recent decades, aortic wall disease requiring surgical treatment has shown an increasing trend. McClure et al conducted a 12-year population-based retrospective cohort study.[1] The reported findings included a 4 % increase in the incidence of Stanford type A aortic dissection and a significant increase in aneurysms.[2] Treatment includes lifestyle and dietary measures, medical therapy and surgery, the latter permitting a definitive histopathological diagnosis. Surgical treatment typically involves reduction of the ascending aorta or replacement of part of the aorta, with or without the aortic valve, by a graft.[1, 3–8] Most researchers agree that cardiovascular diseases are more common in men. In some conditions, male sex is considered an independent risk factor.[7, 9] The present study examines the proportion of female patients among those undergoing aortic surgery and among patients treated for dissection.

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Methods

Study design

The study included 92 patients who underwent aortic surgery at the Institute of Cardiovascular Diseases of Vojvodina from January 2017 to December 2019. Procedures comprised aortic reduction, replacement of part of the aorta with a tubular graft or aortic valve replacement. Patient data were obtained from medical records and histopathological reports. Demographic and clinic-morphological data included age, sex, clinical symptoms, associated conditions and risk factors. Patients were classified into the following age groups: 20–29, 30–39, 40–49, 50–59, 60–69, 70–79 and 80–89 years. Associated conditions included hypertension (HTA), diabetes mellitus (DM), hyperlipoproteinaemia (HLP) and Marfan syndrome (MFS). Risk factors recorded were smoking (S), obesity (OB), family history (FHx) and statin use (Stat).

Patients were included if they had undergone aortic surgery, their aortic tissue had been submitted for histopathological analysis and the histological specimens were of adequate quality. Exclusion criteria were missing data in medical records or inadequate material for histological processing.

Histological processing of tissue samples

Surgically obtained tissue samples were examined macroscopically and processed using standard histological procedures. Sections were cut at a thickness of 5 µm and stained with haematoxylin and eosin (H&E). Histopathological lesions identified were mild, moderate and severe atherosclerosis (Figure 1a–c), aortic wall dissection (Figure 1d), aortitis (Figure 1e), mucoid degeneration (MD; Figure 1f) and cystic medial necrosis (CMN; Figure 1g).

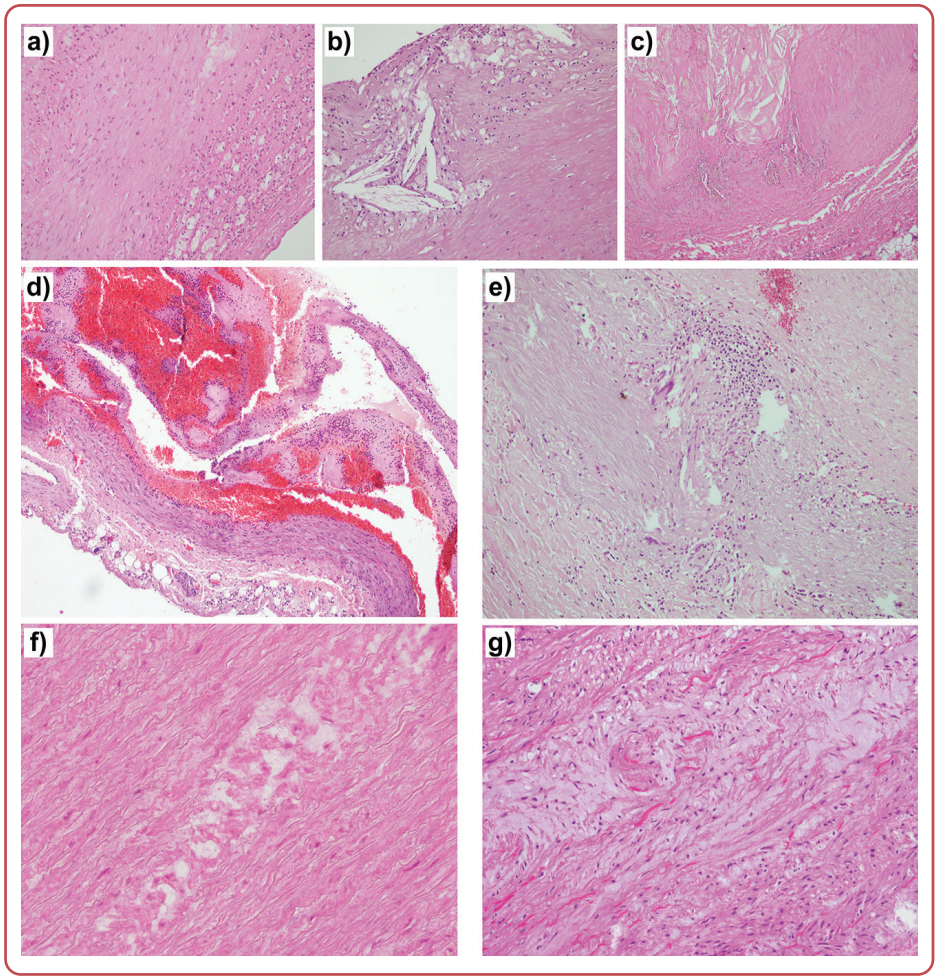


Figure 1: Histopathological lesions of the aortic wall (haematoxylin and eosin staining)
(a) Mild atherosclerosis, ×200; (b) moderate atherosclerosis, ×200; (c) severe atherosclerosis, ×100; (d) aortic wall dissection, ×100; (e) aortitis, ×200; (f) mucoid degeneration, ×400; (g) cystic medial necrosis and mucoid degeneration, ×200.

Statistical analysis

Categorical variables were presented as numbers and percentages. The Chi-square test and subsequent *post hoc* tests were performed to compare categorical variables. A p-value < 0.05 was considered statistically significant; *post hoc* tests adjusted the p-value using the Bonferroni correction method. Statistical analyses were performed with *StatSoft Statistica v.12.5*.

Results

Of the patients, 59.78 % were male and 40.22 % were female. Their mean age was 61.18 years; the youngest patient was 25 and the oldest was 84 years. The mean ages of men and women were 58.85 and 64.65 years, respectively. Most patients were aged 60–69 years, while the fewest were aged 20–29 years. Patients were classified into five groups according to the histopathological diagnosis. When multiple diagnoses were present, priority was given to the lesion that was morphologically dominant or clinically more urgent. The most common histopathological diagnosis was atherosclerosis and the least frequent lesion was CMN.

Atherosclerosis, including all stages, occurred significantly more frequently in men than in women (p = 0.005; Table 1). Among women, aortic wall dissection was the most common lesion (48.65 %), whereas each of the other lesions accounted for less than 20 %. Women predominated among patients with dissection (p = 0.005).

Analysis of histopathological lesions by age showed that their frequency was highest among patients aged 60–69 years and lowest in the youngest group, aged 20–29 years, in which only two cases of mucoid degeneration were recorded (Table 2). No statistically significant association was found between patient age and the occurrence of histopathological lesions (p = 0.64).

Of the associated conditions analysed, HTA was the most common, occurring in 69 patients (Table 1). HLP and DM were less frequent, while MFS was not recorded. No statistically significant difference was found in the distribution of individual comorbidities between lesion groups.

Of the recorded risk factors, positive family history was the most common (30 subjects) and obesity the least common (Table 1). Statistical analysis of these risk factors did not reveal a statistically significant difference between the diagnostic groups.

Table 1: Distribution of sex, associated conditions and risk factors by histopathological lesion

Variable	Histopathological diagnosis					Total	p-value
	Atherosclerosis	Dissection	Aortitis	Mucoid degeneration	Cystic medial necrosis		
Overall n (%)	29 (31.52)	28 (30.43)	12 (13.04)	18 (19.57)	5 (5.43)	92	-
Sex							
Male n (%)	24 (44.72)	10 (18.18)	6 (10.90)	11 (20.00)	4 (7.27)	55	0.005
Female n (%)	5 (13.51)	18 (48.65)	6 (16.22)	7 (18.92)	1 (2.70)	37	
Comorbidities							
HTA n (%)	22 (31.88)	19 (27.54)	9 (13.04)	15 (21.74)	4 (5.80)	69	0.820
DM n (%)	5 (33.33)	4 (26.67)	2 (13.33)	3 (20.00)	1 (6.67)	15	0.990
HLP n (%)	12 (42.86)	7 (25.00)	4 (14.29)	5 (17.86)	0 (0.00)	28	0.360
OB n (%)	8 (53.33)	4 (26.67)	1 (6.67)	1 (6.67)	1 (6.67)	15	0.290
Risk factors							
Stat n (%)	11 (44.00)	6 (24.00)	5 (20.00)	3 (12.00)	0 (0.00)	25	0.170
S n (%)	11 (37.93)	5 (17.24)	5 (17.24)	7 (24.14)	1 (3.45)	29	0.360
FHx n (%)	8 (26.66)	4 (13.33)	5 (16.66)	9 (30.00)	2 (6.66)	30	0.120

Values are n (%) except for totals and P-values. Percentages in the overall row use the total sample; other percentages are calculated within the corresponding row. HTA: arterial hypertension; DM: diabetes mellitus; HLP: hyperlipoproteinaemia; OB: obesity; Stat: statin treatment; S: smoking; FHx: family history.

Table 2: Distribution of histopathological diagnoses by patient age

Age group (years)	Atherosclerosis			Dissection	Aortitis	Mucoid degeneration	Cystic medial necrosis	Total
	Mild	Moderate	Severe					
20-29, n (%)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (100.00)	0 (0.00)	2
30-39, n (%)	0 (0.00)	0 (0.00)	0 (0.00)	1 (33.33)	1 (33.33)	1 (33.33)	0 (0.00)	3
40-49, n (%)	0 (0.00)	1 (12.50)	0 (0.00)	2 (25.00)	1 (12.50)	3 (37.50)	1 (12.50)	8
50-59, n (%)	3 (14.29)	4 (19.05)	1 (4.76)	6 (28.57)	3 (14.29)	3 (14.29)	1 (4.76)	21
60-69, n (%)	3 (7.89)	6 (15.79)	5 (13.16)	10 (26.32)	5 (13.16)	6 (15.79)	3 (7.89)	38
70-79, n (%)	1 (6.25)	3 (18.75)	1 (6.25)	6 (37.50)	2 (12.50)	3 (18.75)	0 (0.00)	16
80-89, n (%)	0 (0.00)	1 (25.00)	0 (0.00)	3 (75.00)	0 (0.00)	0 (0.00)	0 (0.00)	4

Percentages are calculated within each age group.

Table 3: Frequency of symptoms by histopathological diagnosis

Variable	Atherosclerosis	Dissection	Aortitis	Mucoid degeneration	Cystic medial necrosis	Total	p-value
CP	8 (27 %)	23 (82 %)	3 (25 %)	6 (33 %)	1 (20 %)	41	< 0.01
D	0	3 (10 %)	0	1 (5 %)	0	4	0.29
P	4 (13 %)	3 (10 %)	0	3 (16 %)	0	10	0.56
E	0	1 (3 %)	1 (8 %)	1 (5 %)	0	3	0.65
SOB	3 (10 %)	3 (10 %)	4 (33 %)	5 (27 %)	1 (20 %)	16	0.25
W	6 (20 %)	5 (18 %)	5 (41 %)	5 (27 %)	2 (40 %)	23	0.47
V	0	1 (3 %)	0	2 (11 %)	1 (20 %)	4	0.14
N&V	2 (6)	4 (14 %)	0	0	0	6	0.26
T	0	2 (7 %)	0	0	0	2	0.32
F/C	1 (3 %)	1 (3 %)	0	0	0	2	0.81
HA	0	1 (3 %)	0	1 (5 %)	0	2	0.70

Values are n (%) of patients with the corresponding diagnosis, except for totals and p-values. CP: chest pain; D: dizziness; P: palpitations; E: oedema; SOB: shortness of breath; W: weakness; V: vertigo; N&V: nausea and vomiting; T: tingling and pain in the right arm; F/C: fever and/or chills; HA: headache. Symptoms may overlap.

Review of medical records showed that 28 of the 92 patients were asymptomatic at admission and during hospitalisation before undergoing aortic surgery (Table 3). Chest pain was the most common symptom, occurring in 41 patients, including 23 patients with aortic dissection. A highly statistically significant difference was found in the occurrence of chest pain according to the histopathological lesion ($p < 0.001$).

Discussion

Male sex is considered one of the constitutional risk factors for cardiovascular disease (CVD). A higher frequency of CVD in males has been reported in animal models and more men than women underwent surgery in the present cohort.[10–12] Several authors, including Sciomer et al, argue that current guidelines require revision because the importance of CVD in women is often neglected.[13] A substantial proportion of patients in this cohort, 40.22 %, were women, who accounted for a higher proportion of dissections. Humphries et al emphasise the association between diabetes and CVD and the greater importance of this comorbidity in women than in men.[14]

Dissection was the second most common histopathological lesion of the aortic wall in this cohort. The largest number of patients were aged 60–69 years and older age is considered a risk factor for aortic wall dissection. Although male sex is commonly described as a principal risk factor for aortic dissection, 64.29 % of dissections in the present cohort occurred in women. McClure et al found that dissection was more common in men but that women had higher hospital mortality.[1] A study comparing patients with Stanford type A aortic dissection in Belgium and Japan reported differences in sex distribution: women accounted for 48.8 % of patients in Japan and

28.7 % in Belgium.[15] These findings suggest that geographical, socioeconomic and other factors may influence the differing proportions of aortic dissection between the sexes.

Atherosclerosis was the most common histopathological lesion in this cohort. The highest frequency of lesions occurred among patients aged 60–69 years, consistent with reports of a low prevalence at younger ages.[4, 8, 16]

Aortitis also occurred most frequently in patients older than 60 years, with giant cell arteritis accounting for the largest proportion of histopathological findings. This is consistent with the study by Gonzalez-Gay et al, which describes a more frequent occurrence of this lesion in older age.[17] In the present study, lesion prevalence did not differ significantly between the sexes.

Mucoid degeneration and cystic medial necrosis are histopathological entities for which contradictory findings have been reported. Some studies suggest that changes in the aortic media may underlie the development of more severe, macroscopically apparent lesions, such as aneurysms and dissections.[3, 4, 18–20] Homme et al reported cystic medial degeneration in 51 % of patients with aortic dissection, whereas other reports have described CMN in only a few patients with severe aortic disease.[21] Differences in reported prevalence may partly reflect inconsistent definitions and the difficulty of distinguishing ageing from pathological change. Terminological inconsistency is a major obstacle to comparing studies. Erdheim introduced the term medionecrosis in 1930, after which terminology continued to vary. The Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology subsequently proposed a unified nomenclature for non-inflammatory degenerative aortic lesions. The consensus uses medial degeneration as an overarching term and describes specific alterations, including mucoid extracellular matrix accumulation (MEMA), elastic fibre fragmentation and/or loss and smooth muscle cell nuclear loss, rather than relying on older labels such as CMN.[3] Age-related changes may contribute to medial degeneration, but the observation of MD in the youngest age groups in this study is difficult to explain solely by ageing. MD and CMN are therefore regarded here as pathological changes requiring further investigation to determine whether they predispose to more severe disease or are incidental findings. Larger studies and consistent terminology are needed to clarify the nature and origin of these lesions.[3, 4, 18–21]

The prevalence of HTA in the general adult population of Serbia was 42.7 % in the PAHIS study. In the present study, 75.9 % of patients with atherosclerosis had HTA.[22] HLP was also most frequent among patients with atherosclerotic lesions, consistent with its role in atherogenesis.[6, 8] Atherosclerosis is an important macroangiopathic complication of long-standing diabetes, with earlier and more pronounced atherosclerotic plaque formation. A Danish national study reportedly found an association between DM and inflammatory processes in the aortic wall, whereas Chowdary and colleagues reported contrasting findings.[5, 9, 23]

Of the 92 respondents in this surgically selected cohort, 31.5 % had consumed cigarettes for many years. The literature states that there are about 4000 substances in tobacco smoke with a toxic effect on the endothelium of blood vessels.[8, 9, 24] A PDAY study of 100 young men aged between 15 and 34 who died in trauma showed that smokers had more than twice as many advanced atherosclerotic lesions and fewer early lesions compared with non-smokers, which implies that smoking accelerates the progression of early and intermediate lesions into atheromas, fibroatheromas and complicated changes.[25]

The effects of statins on serum lipid levels and the prevention of atherogenesis are well established. Studies have also examined their effects on atherosclerotic lesions, particularly proteins involved in macrophage apoptosis, including p53, Bcl-2 and Bcl-xL. Statin use is thought to be associated with increased macrophage survival, potentially resulting in more early lesions, fewer later lesions (types IV and V) and greater plaque stability.[26, 27] A higher frequency of early lesions could lead statin exposure to be interpreted as a risk marker, whereas fewer late lesions and plaque stabilisation could suggest a protective association. In this study, 37.9 % of patients with atherosclerotic lesions received statins. No statistically significant association was found between statin use and the severity of atherosclerotic lesions. This question requires further investigation in a larger sample.

Chest pain was the most common symptom reported during hospitalisation and preoperative assessment and occurred most frequently in aortic dissection, with a statistically significant

difference between lesion groups. A major diagnostic challenge is aortic dissection without typical pain, as symptoms and physical findings may vary. Marroush et al collated reports of painless aortic dissection to assist earlier diagnosis of this time-critical condition.[28] They found that these cases most often presented with a left-sided neurological deficit, followed by dyspnoea and a lower-extremity deficit. Almost 20 % of patients with dissection in the present cohort had no pain. These findings support greater attention to neurological findings when painless aortic dissection is suspected and consideration of whether existing diagnostic protocols adequately address such presentations.

Conclusion

Aortic diseases represent a substantial clinical burden. Although male predominance is traditionally reported, women represented a substantial proportion of this surgically treated cohort and aortic dissection was significantly more frequent among women. Painless aortic dissection can complicate timely diagnosis because the absence of typical symptoms may delay recognition and management. These findings highlight the importance of considering sex-specific patterns and atypical presentations among patients requiring aortic surgery.

Ethics

The use of tissue material and review of medical records for research were approved by the Ethics Committee of the Institute of Cardiovascular Diseases of Vojvodina (Decision No: 3674-1/9, dated 11 December 2019).

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None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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