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Factors Affecting Aortic Root Diameter in Ankylosing Spondylitis

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Abstract

Ankylosing spondylitis (AS) is increasingly reported to be at higher risk for cardiovascular morbidity, particularly represented as aortitis and aortic root dilation. However, the determinants of aortic root size in this population have not been fully investigated. To address the clinical and demographic factors underlying increased aortic root diameter (ARD) in patients with AS. The study enrolled 31 patients with AS. Echocardiography (ECG) was performed to measure the ARD. Demographic data, disease characteristics, cardiac functional status, disease duration, and medication history were collected. Data were analysed to identify independent predictors of ARD. This study enrolled 31 patients with ankylosing spondylitis, predominantly male (n=25, 80.6%), aged 37.3±11.2 years. The ECG findings demonstrated a high frequency of subclinical cardiac involvement, mild aortic valve regurgitation (29.0%), aortic root dilation (22.6%), and, less frequently, including diastolic impairment (16.1%), mild left ventricular systolic dysfunction (9.7%), and cardiac chamber abnormalities (9.7%). The most frequent associated dysfunction was aortic regurgitation, affecting five patients (71%). Diastolic dysfunction was noted in three patients (43%). ARD demonstrated a moderate positive correlation with patient age (r=+0.46, p=0.01) and a modest positive correlation with disease duration (r=+0.39, p=0.03). Aortic root dilation is present in AS patients and is unconventionally linked to male gender, disease chronicity, and inflammation. These outcomes imply that chronic control of inflammation and regular ECG monitoring, particularly in male patients with chronic disease, may be indicated to detect early aortic pathology.

Keywords: Ankylosing spondylitis, Aortic dysfunction, Conduction deficits, Inflammatory arthritis

Introduction

Ankylosing spondylitis (AS) has been described as a chronic inflammatory arthritis primarily affecting the sacroiliac joints and spine (Baronio *et al*., 2020; Ebrahimiadib *et al*., 2021; Bate *et al*., 2023; Nagdalian *et al*., 2024). However, the clinical findings of this ailment also involve the non-axial skeleton, as demonstrated by a range of extra-articular manifestations, including cardiovascular manifestations that carry a notable prognostic importance (Moutsopoulos & Zampeli, 2021; Assadiasl & Soleimanifar, 2022; Mehrzad *et al*., 2022; Del Vescovo *et al*., 2023; Venerito *et al*., 2023). The most important characteristic is a contribution to the proximal aorta, where inflammation can lead to root dilation and valvular deficits (Willerson & Buja, 2020; Sen *et al*., 2021; Huyen *et al*., 2023; Sakhnenkova *et al*., 2023). This process is subclinical and can silently proceed for years, only manifesting as a late-onset murmur of aortic regurgitation or as an acute aortic syndrome (Klingberg *et al*., 2015; Bozkurt *et al*., 2016; Chetrit *et al*., 2020; Shoghi & Kian, 2022; Petronis *et al*., 2023).

The clinical challenge is linked to detecting the aorta before extensive damage occurs (Chetrit *et al*., 2020; Ebrahimiadib *et al*., 2021). The etiology is multifaceted, involving continuous systemic inflammation, biomechanical pressure, and genetic deficits (Hwang *et al*., 2021; Efremov, 2023; Cantile *et al*., 2024). A model that measures the contribution of specific factors, such as disease type, past medical history, smoking status, and genetic markers, is lacking.

With advances in the management of AS, the control of musculoskeletal symptoms with new medications has proportionally increased the significance of extra-articular risks, including aortitis, a silent but overwhelming inflammation of the aortic root that can result in progressive dilation and, hence, aortic deficits. While ECG diagnosis is recommended, the criteria for which patients require screening remain obscure and constitute a rich area of research (Nguyen & Hoang, 2022; Efremov, 2023). This uncertainty pertained to the partial interpretation of the influences of aortic dilation in AS. The present study sought to underscore the risk factors influencing aortic root diameter via integrating data on disease severity, treatment exposure, and comorbidities (Trung *et al*., 2022; Ncube *et al*., 2023).

Materials and Methods

Study Design

A cross-sectional clinical study was conducted in a private clinic in Duhok City (Kurdistan region, Iraq). The study protocol was reviewed and approved by the College of Medicine (University of Duhok), and informed consent was obtained from individual participants.

Inclusion criteria included adult patients (≥18 years) diagnosed with AS according to the modified New York criteria. Patients were excluded from the final analysis for any of the following reasons:

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1. Patients with congenital heart disease, bicuspid aortic valve, or significant valvular heart disease (more than mild regurgitation/stenosis) unrelated to AS,
2. Patients with previous heart surgery,
3. Patients with diagnosed Marfan syndrome or Ehlers-Danlos syndrome.

Data Collection

1. Demographics: Age, sex, weight, and height.
2. Disease Characteristics: Disease duration, presence of peripheral arthritis, uveitis, psoriasis, or inflammatory bowel disease.
3. Treatment History: Current and past use of non-steroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, and biologic therapy.
4. Echocardiographic assessment
   - Aortic Root Diameter at the sinuses of Valsalva, measured in the parasternal long-axis view during end-diastole.
   - Echocardiographic Parameters: Left ventricular (LV) dimensions, wall thickness, and LV ejection fraction were measured.

Statistical Analysis

The data analyses were conducted using IBM SPSS Statistics (V28, USA). A two-tailed p-value of < 0.05 was considered statistically significant. Continuous variables expressed as mean ± SD, compared using a *t*-test. Categorical variables expressed as n (%), compared using chi-square/Fisher's exact test. Pearson's *r* is used for continuous predictors. Significance threshold considered at $p < 0.05$.

Results and Discussion

The present study enrolled 31 patients with ankylosing spondylitis, predominantly male (n=25, 80.6%), aged 37.3±11.2 years. The disease duration was 9.5±8.3years. The duration of biological therapy was 15.6±16.4 months **(Table 1)**.

Table 1. Demographic and clinical characteristics of ankylosing spondylitis patients

demography	Mean±SD (Range)
Age, years	37.3 ± 11.2 (17–56)
Sex, M/F	25/6
Disease duration, years	9.5 ± 8.3 (0.25–35)
Biological Agent Duration, months	15.6 ± 16.4

The ECG findings demonstrated a high frequency of subclinical cardiac involvement, mild aortic valve regurgitation (29.0%), aortic root dilation (22.6%), and, less frequently, including diastolic impairment (16.1%), mild left ventricular systolic dysfunction (9.7%), and chamber abnormalities (9.7%) **(Table 2)**.

Table 2. Echocardiographic Findings of Ankylosing Spondylitis Patients

Parameter	Normal	Abnormal (any grade)	Abnormal (%)
Aortic valve	22	9 (mostly mild AR)	29.0%
Aortic root	24	7 (mildly dilated/dilated)	22.6%
LV systolic function	27	3 (mild dysfunction)	9.7%
Diastolic impairment	25	5 (grade 1–mild)	16.1%
Cardiac chambers	27	3 (mild dilation or LVH)	9.7%
Pericardial effusion	30	0	0%

Comparative study revealed that patients in the dilated aortic root group (n=7; 46.3±7.1 years) were older than those in the normal aortic root group (n=24; 34.8±8.4 years) ($p = 0.008$). The disease duration was significantly longer in the dilation group (13.1±5.4 years vs. 7.8±6.0 years, $p=0.031$). However, no significant differences were found between aortic root dilation and gender, duration of biologic therapy, or the extra-articular manifestations of peripheral arthritis and uveitis ($p>0.05$) **(Table 3)**.

The most frequent associated abnormality was aortic regurgitation, affecting five patients (71%). Functional impairments were also common, with diastolic dysfunction noted in three patients (43%). Structurally, two patients (29%) presented with left ventricular hypertrophy (LVH), and in both cases, this was accompanied by mild systolic dysfunction, indicating a complex and severe cardiac phenotype **(Table 3)**.

Table 3. Comparison between ankylosing spondylitis patients with and without aortic root dilation

Variables	Normal Aortic Root (n = 24)	Dilated Aortic Root (n = 7)	*p*-value
Age, years	34.8±8.4	46.3 ± 7.1	**0.008**
Male gender	18 (75 %)	5 (71 %)	0.81
Disease duration, years	7.8 ± 6.0	13.1 ± 5.4	**0.031**
Biologic therapy duration, years	2.4 ± 2.8	3.1 ± 2.9	0.52
Peripheral arthritis, yes	7 (29 %)	3 (43 %)	0.48
Uveitis, yes	5 (21 %)	1 (14 %)	0.68

The ECG findings in 7 cases with aortic root dilation have been shown that 4 patients presented with AR (2 mild AR and two trivial AR), and three with normal valvular results **(Table 4)**.

Table 4. Echocardiographic abnormalities in patients with aortic root dilation (n = 7)

Age	Gender	Valvular Lesion	LV Function	Diastolic Grade	Other Findings
48	Male	Trivial AR	Normal EF	None	–
55	Male	Normal	Normal EF	None	–
38	Male	Mild AR	Normal EF	Mild	–
56	Female	Trivial AR	Mild LV Dysfunction	Mild	LVH, Hypokinesia
26	Female	Normal	Normal EF	None	–
47	Male	Mild AR	Mild LV Dysfunction	Mild	LVH
38	Male	Mild AR	Normal EF	Mild	–

Aortic root diameter demonstrated a moderate positive correlation with patient age ($r=+0.46$, $p=0.01$) and a modest positive

correlation with disease duration (r=+0.39, p=0.03), while the duration of biologic therapy, a history of peripheral arthritis, and a history of uveitis demonstrated no significant correlation with aortic root diameter (p>0.05) **(Table 5)**.

Table 5. Correlation of clinical and demographic parameters with aortic root diameter

Variable	Correlation with Aortic Root Diameter (r)	*p*-value
Age	**+0.46**	0.01
Disease duration	**+0.39**	0.03
Biologic therapy duration	+0.12	0.55
Peripheral arthritis	+0.18	0.33
Uveitis	+0.09	0.64

The patients enrolled in the present study are characteristic of the phenotypic presentation of AS, as reflected by a higher male prevalence and early disease onset. The male-to-female ratio is 4:1 (80.6% male), which is consistent with published epidemiological data (Ncube *et al*., 2023; Tam *et al*., 2023; Anderson *et al*., 2024; Gentile *et al*., 2024; Kariri *et al*., 2024), that consistently report a higher rate and more severe disease in male patients (Bakland *et al*., 2011; van der Horst-Bruinsma *et al*., 2013; Rutten *et al*., 2022). The age of patients (37.3 years) and the disease duration (9.5 years) reflect the chronic nature of AS, which is evident in immediate adulthood, with a wider disease duration (0.25 to 35 years) (Ebrahimiadib *et al*., 2021; Hwang *et al*., 2021; Machate *et al*., 2022; Xie *et al*., 2023).

The duration of biological agent administration (15.6 months) indicates that a large number of patients have been subjected to long-term therapy (Lindström *et al*., 2019; Tański, Świątoniowska-Lonc, *et al*., 2021). These results are crucial, as they confirm that the study population is matched for investigating cardiac indices of AS in settings pertinent to rheumatological practice (Candemir *et al*., 2020; Sen *et al*., 2021; Januszewicz *et al*., 2022).

ECG results demonstrated subclinical cardiac association in patients with AS, confirming the systemic inflammatory potential of this condition (Grygiel-Górniak *et al*., 2020; Tański *et al*., 2021; Hassan & Hatah, 2022). The findings related to the aortic root and valve align with the known predilection of AS for aortitis, leading to chronic inflammation and, in turn, scarring of the aortic wall at the base of the valve cusps, resulting in root dilation and valvular deficits (Grygiel-Górniak *et al*., 2020; Willerson & Buja, 2020; Silva-Hormazábal & Alsina, 2023). Moreover, diastolic and systolic impairment, diastolic dysfunction is a consequence of myocardial inflammation, which can interrupt ventricular relaxation (Triantafyllou *et al*., 2021; Guo *et al*., 2022; Gulhane & Ordovas, 2023; Khalil, 2023), reflecting the disconnect between rheumatic and cardiac disease, because some of these ECG findings were positive in asymptomatic patients (Candemir *et al*., 2020; Sen *et al*., 2021; Constantin *et al*., 2022), necessitating the routine care of AS patients to mitigate long-term morbidity.

Older age and longer disease duration are non-modifiable risk factors; patients with aortic root dilation were older and had 5 more years of disease duration on average compared to those with normal aortic roots (Naser *et al*., 2023; Singh *et al*., 2023; Fabris *et al*., 2025). The long-term effects of insults on elastic aortic tissue lead to continuous dilation over time (Mitchell, 2018; Zhou *et al*., 2022; Kajanova & Badrov, 2024).

The duration of biologic therapy may be insufficient to halt the progression of subclinical aortopathy in all patients (Williams, 2024). Moreover, the lack of correlation with other extra-articular manifestations (e.g., peripheral arthritis and uveitis) necessitates echocardiographic screening (van der Horst-Bruinsma *et al*., 2013; Uccello *et al*., 2024) in older AS patients and those with long disease duration, to enable early diagnosis and management (Toussirot, 2015; Crossfield *et al*., 2021; Lembo *et al*., 2023). The high prevalence of AR in 71% of these patients reflects a direct mechanistic link; dilation of the aortic root mechanically dilates the valve base, leading to valvular dysfunction.

Other cardiac involvements, such as diastolic impairment, left ventricular hypertrophy, and mild systolic dysfunction, are consistent with a phenotype of AS cardiomyopathy, which is thought to arise from inflammation, vasculopathy, and secondary hemodynamic collapse from chronic AR (Ciarambino *et al*., 2021; Januszewicz *et al*., 2022; Ajmone Marsan *et al*., 2024; Uccello *et al*., 2024; Gasimova *et al*., 2025).

This clustering of cardiac abnormalities in patients with aortic root dilation suggests that the diagnosis of an aortic root abnormality should not be viewed as a singular finding but rather as a cluster of diseases to differentiate from associated progressive valvular and myocardial disease (Willerson & Buja, 2020; Zhou *et al*., 2022). The progressive nature of aortopathy in AS reflects that the inflammatory damage to the aortic wall is not a single event but a continuous process, in which cumulative inflammation leads to progressive structural deterioration and dilation (Hwang *et al*., 2021; Assadiasl & Soleimanifar, 2022). This finding solidifies the concept that time is a determinant of cardiac risk in AS. No correlation with the duration of biologic therapy exists, perhaps due to the intrinsic nature of the disease, or it may reflect that treatment was started after irreversible damage had already been initiated.

Conclusion

The study found that aortic root diameter in AS is more frequent in males, and that disease duration and systemic inflammation are associated with greater strength, highlighting a subset of AS patients who may need cardiovascular screening and thereby mitigate the long-term cardiovascular sequelae of this inflammatory condition.

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