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SUBCLINICAL CARDIOVASCULAR DISEASE AND HEALTH RELATED QUALITY OF LIFE IN RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Akademisk avhandling

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Title

Subclinical Cardiovascular Disease and Health Related Quality of Life in Patients with Radiographic Axial Spondyloarthritis

Abstract

Background: Radiographic axial spondyloarthritis (r-axSpA) is a chronic inflammatory rheumatic disease mainly affecting the axial skeleton. Increased risk of cardiovascular disease (CVD) related comorbidities significantly contributes to mortality and burden of disease in r-axSpA. The increased CVD risk is not fully explained by traditional CVD risk factors, and little is known about sex differences in CVD risk profiles. Moreover, the association of disease related variables and subclinical signs of CVD on ultrasound remain to be comprehensively investigated. Additionally, studies investigating factors related to health-related quality of life (HRQoL) acknowledge that r-axSpA patients have lower HRQoL than the general population. However, constancy in study methods and comparison to general population controls, especially stratified by sex are limited.

Objectives: To study the impact of r-axSpA on HRQoL (*Paper 1*) and identify novel ultrasound markers of subclinical CVD (Papers 2-4) in patients with r-axSpA, overall, stratified by sex, and compared to controls.

Materials and methods: *Paper 1:* The Short Form-36 (SF-36) questionnaire was used to assess HRQoL in patients with r-axSpA from Western Sweden (n=210, females 42.4%). Each patient was compared to 5 age- and sex-matched persons from the SF-36 Swedish normative database (n=1055). *Papers 2-4:* Ultrasound was used to (i) assess bilateral common carotid arterial (CCA) stiffness by calculation of β -stiffness index and circumferential 2D strain (*Paper 2*); (ii) measure mean bilateral carotid intima media thickness (cIMT) and investigate its relationship with biomarkers of inflammation (*Paper 3*); and (iii) assess the mean thickness of the epicardial adipose tissue (EAT) deposit and its associations with traditional CVD related risk factors (*Paper 4*). Papers 2-4 used a well characterized patient group from Northern Sweden ('Backbone cohort', n=155, female 31.0%). The control group for paper 2 included 46 age- and sex- matched persons from the local population, with no traditional CVD risk factors. The control group for papers 3 and 4, was derived from the Umeå region Swedish CArdioPulmonary bioimaging Study (SCAPIS) recall study (n= 400, females 51.0%). All results were presented stratified by sex. Uni- and multi-variate regression analysis methods were used to evaluate associations with disease and demographic variables. All studies were of cross-sectional design.

Results: *Paper 1:* Patients exhibited significantly lower HRQoL compared to controls ($P<0.001$). Upon stratification by sex, both sexes scored significantly lower physical compared to the mental HRQoL scores. Multivariable logistic regression analysis found that patients with a longer disease duration, worse physical function (assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI), high disease activity (measured by the Ankylosing Spondylitis Disease Activity Score (ASDAS)), or who lived alone had significantly lower physical HRQoL. Lower mental HRQoL was associated with fatigue, high ASDAS and living alone. Some differences in sex were also found. *Paper 2:* Patients had higher mean bilateral CCA β -stiffness index, and lower 2D CCA circumferential strain, compared to controls. Multivariate linear regression analysis found that several disease related parameters, in addition to age, were related to 2D circumferential strain (R^2 0.33), whereas only age was related to β -stiffness index (R^2 0.19). *Paper 3:* Linear regression analysis, with various adjustment models, showed that patients had increased cIMT compared to controls. White blood cell (WBC)- and monocyte- count were the only inflammatory biomarkers associated with cIMT. This association was only seen in male patients and remained after adjustments. *Paper 4:* Mean EAT was thicker in r-axSpA patients overall and stratified by sex compared to controls. No difference in mean EAT was found between the sexes. The both models for cholesterol levels were borderline significantly associated with EAT thickness in male patients.

Conclusion: Patients with r-axSpA have decreased HRQoL and increased subclinical indicators of CVD compared to controls. By modifying factors, such as ASDAS-CRP and fatigue, HRQoL may be improved in patients with r-axSpA. Additionally, ultrasound methods are non-invasive, and easily obtainable, offering additional insights into factors influencing the risk of CVD in r-axSpA patients. Although studies are required to validate novel ultrasound methods, these techniques represent a powerful approach to detect, monitor, and help manage CVD related comorbidities.

Keywords

Radiographic axial spondyloarthritis, health related quality of life, cardiovascular disease, ultrasound, common carotid artery, intima media thickness, epicardial adipose tissue

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