
Assessment of cardiovascular involvement in Connective Tissue Disease: Let's open Pandora's box

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Assessment of cardiovascular involvement in Connective Tissue Disease: Let's open Pandora's box

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ABSTRACT

Connective Tissue Disease (CTD) is characterized by autoimmune activation and systemic inflammatory response, affecting several internal organs. Cardiac involvement represents one of the most severe complications associated with higher rates of death and reduced life expectancy in this population. Cardiovascular abnormalities occurring in CTD encompass different aspects of cardiac disease, such as pericarditis, myocarditis, coronary artery disease, heart failure due to systolic and diastolic dysfunction and valvular disease. Considering the increased risk of cardiovascular disease (CVD) in CTD, early assessment and diagnosis of cardiovascular involvement is of utmost importance. However, CVD in CTD has often an atypical clinical presentation, and traditional diagnostic approaches such as transthoracic echocardiography have low sensitivity in the early stages. Cardiac magnetic resonance imaging can identify subtle morphological changes of the myocardium and contribute to earlier diagnosis of CVD in patients with CTD.

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Connective Tissue Disease (CTD) can affect a number of organs. CTD is characterized by impairment of adaptive immunity, such as the production of autoantibodies and autoreactive T cells.¹ Cardiovascular abnormalities in CTD are due to various pathophysiologic processes, such as myocardial/vascular inflammation, accelerated atherosclerosis, myocardial ischemia due to micro- or macro-vascular disease, abnormal coronary vasoreactivity and/or myocardial fibrosis.^{2,3} Patients may present with valvular, myocardial, pericardial inflammation, coronary artery disease, vasculitis, myocardial fibrosis, heart failure, as well as pulmonary arterial hypertension. Unfortunately, CVD in CTD may be asymptomatic or characterised by subtle, usually underestimated symptoms. When cardiac disease becomes clinically overt, it is indicative of advanced myocardial impairment and carries a poor prognosis,⁴ although early, aggressive application of targeted anti-rheumatic treatments may associate with significant reduction of disease-associated CVD mortality. The life expectancy in CTD still remains lower, compared with the general population,⁵ mainly due to CVD.⁶⁻¹⁰ Connective tissue diseases which are associated with cardiovascular involvement are: 1) Rheumatoid arthritis and the spondyloarthropathies; 2) Systemic lupus erythematosus; 3) Systemic vasculitides; 4) Inflammatory myopathies; 5) Systemic sclerosis; 6) Mixed Connective Tissue Disease (MCTD); and 7) Sarcoidosis (SRC).⁶⁻¹⁰

The most important reasons for "missing" early CVD in CTD include: a) atypical clinical presentation; b) ignorance of CTD pathophysiology by cardiologists; c) lack of sensitivity of the currently used diagnostic techniques in cardiology to detect cardiovascular lesions occurring in CTD. To promote early diagnosis, cardiologists must become familiar with CTD patients, rheumatologists must become familiar with the cardiovascular complications of these conditions, and better interaction between specialists should be introduced.

As regards the diagnostic approach, the exercise electrocardiogram (Ex-ECG) is commonly the first line of examination for diagnosing myocardial ischaemia. This method is inexpensive but has low sensitivity in females and many patients with myocarditis¹³ and is not useful for diagnosis of myocardial infarction in patients with left bundle branch block.¹² The current AHA/ACC guidelines recommend use of the Ex-ECG as the first test for evaluation of known or suspected coronary disease, only when the patient is able to exercise,¹⁴ which often is not the case for patients with CTD. Finally, while certain aspects of the Ex-ECG, such as exercise capacity and ST segment changes have prognostic value, the Ex-ECG is less accurate than alternative stress imaging technologies.¹⁴ Indeed, stress echocardiography has a higher sensitivity and specificity for detection of coro-

nary artery disease, especially in women that constitute the major group of people with CTDs.¹¹

Transthoracic echocardiography (TTE) is currently the cornerstone of identifying some causes of CVD. Stress echocardiography is the combination of TTE with a physical, pharmacological or electrical stress inducing higher pulse rate. If coronary stenosis is present, ischaemia of the left ventricular wall may occur, resulting in a transient worsening in the region of left ventricular wall contractility. Stress echocardiography may provide similar diagnostic and prognostic accuracy as radio-nuclide stress perfusion imaging, but at a substantially lower cost, without environmental impact, and with no biohazards for the patient and the physician. Among different types of stress tests of comparable diagnostic and prognostic accuracy, the semi-supine stress test is the most commonly used. Stress echocardiography is at present the most cost- and risk-effective imaging tool to achieve early non-invasive diagnosis of coronary artery disease.¹⁵

Stress myocardial perfusion scintigraphy (MPS) has been regarded as a clinically useful non-invasive imaging modality for diagnosing patients with suspected coronary artery disease.^{16,17} However, high radiation exposure, imaging artefacts and low spatial resolution that does not allow the detection of subendomyocardial/subepimyocardial and/or intramyocardial scars constitute serious limitations.¹⁸

Recently, cardiovascular magnetic resonance (CMR), a non-invasive, non-radiating, operator-independent technique has been more widely used as a cardiac imaging tool in CVD diagnosis. Currently, it is considered the gold standard for evaluation of left ventricular volume and mass, ejection fraction of atria and ventricles, detection of myocardial inflammation, myocardial infarction, evaluation of the aortic wall, detection of anomalous coronary arteries and coronary artery ectasia/aneurysm. Recently, the diagnostic capabilities of CMR have been extended to the evaluation of myocardial perfusion (stress perfusion CMR).

All the above applications may be of special interest to rheumatologists, because of the serious involvement of the cardiovascular system in the course of rheumatic diseases. CMR has already been successfully used in the evaluation of vasculitides, SLE, myositis, rheumatoid arthritis and scleroderma. Recently, a consensus report concerning applications of CMR in rheumatology has been published by specialists in cardiology and rheumatology.¹⁹ However, high cost, low availability and lack of expertise still remain serious obstacles for CMR becoming a routine method for the diagnosis of CVD complications in CTD.

In Greek mythology, Pandora was the first woman who dared to open a box containing all evils: the contents were released into the world, except for "Elpis" that lay

at the bottom of the box. "Elpis" translates to "Hope" or "Expectation". In cardiovascular rheumatology, by opening Pandora's box one can find some "Elpis" for better CVD management in patients with CTD. This can be achieved by promoting close collaboration between cardiologists and rheumatologists, utilising available knowledge and creating new knowledge and applications using advances in technology.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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