Cardiac imaging in rheumatic diseases

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The majority of the imaging techniques in cardiology could be applied in rheumatic diseases (RDs), such as echocardiography, single-photon emission computed tomography (SPECT), radionuclide ventriculography, angiography, cardiovascular MRI and CT. Inflammatory pericardial involvement is the most common cardiac manifestation in various forms of RD. Echocardiography is the gold standard for diagnosis of pericardial abnormalities, demonstrating location and amount of pericardial effusion. Cardiac MRI and CT can be used to assess the features of pericardial effusions and pericardial structures. In patients with valvular heart disease in RD, transoesophageal echocardiography is a superior method and offers reliable information about valve morphology, the severity of the disease and left ventricular (LV) function. In addition, cardiac MRI is a valuable tool for the evaluation of valvular stenosis and regurgitation severity. Myocardial involvement in RD is demonstrated by abnormalities in LV size and function, indicating myocardial inflammation. In these patients Doppler echocardiography and myocardial tissue imaging can provide essential diagnostic information. Both LV angiography and cardiac MRI can provide reliable information on LV size, function and mass. In patients with coronary disease associated with RD, LV ejection fraction and ventricular wall motion can be assessed by echocardiography, radionuclide ventriculography, gated SPECT and MRI. Three-dimensional (3D) echocardiography is considered superior to 2D echocardiographic techniques. Stress echocardiography is the most used method for detection of myocardial ischaemia. The only accurate visualization of the coronary arteries is by selective coronary arteriography, which remains the gold standard. Although new non-invasive techniques have been developed, including CT and MRI angiography, some limitations apply.

Introduction

In patients with rheumatic diseases (RDs), cardiovascular involvement is common, may have serious consequences, and can contribute to worsening of patients outcome (Table 1) [1]. Incidence and prevalence of cardiovascular diseases (CVD) in RD have recently been largely increased due to both the improved biochemical and cardiology imaging techniques. CVD can be diagnosed in more than 50% of the patients with systemic lupus erythematosus (SLE) [2], and is the cause of nearly 40% of deaths in rheumatoid arthritis (RA) patients [3]. Patients with RA are more likely to have myocardial infarction and sudden death, and are prone to serious systemic complications. Systemic sclerosis (SSc) is frequently associated with pulmonary hypertension and/or systemic hypertension, which can lead to subsequent complications.

The majority of the imaging techniques in cardiology could be also applied in RD, with variable diagnostic accuracy. These include echocardiography, single-photon emission computed tomography (SPECT), radionuclide ventriculography, angiography, cardiovascular MRI and CT. Imaging techniques are essential in the early detection of CVD in RD, having significant therapeutic implications and improving patients long-term outcome.

Involvement of pericardium

Inflammatory pericardial involvement is the most common cardiac manifestation in various forms of RD [2, 3]. In RA, pericardial effusion is seen in 2–10% of the patients as chronic, asymptomatic pericardial effusion, while tamponade and constrictive pericarditis are rare (0.5%) [2]. In patients with SLE, symptomatic pericardial effusion has been reported in 6–50%, clinically significant pericarditis and pericardial thickening are described in <30%, while post-mortem pericardial lesions range from 60–80%. In SSc, pericardial involvement is seen in 70% of the patients, mostly as small pericardial effusion [4].

Echocardiography is the most widely used imaging technique in the evaluation of suspected pericardial disease. Transthoracic echocardiography represents the gold standard for diagnosis of pericardial abnormalities, demonstrating the location and amount of even minimal pericardial effusion. The echocardiographic features of pericardial effusion are the pericardial layer separation with an echo-free space and the decrease in the parietal pericardium motion. If tamponade develops, which is a rare complication of RD, a several echocardiographic signs can be appreciated such as diastolic compression of right heart chambers, lack of inspiratory collapse of the dilated inferior
vena cava and the swinging of the entire heart [5] (Fig. 1). Doppler echocardiographic patterns of tamponade include marked respiratory variations of right and left ventricular (LV) inflow and pulmonary and hepatic venous flow velocities. Echocardiography is also very instrumental if combined pericardial and valvular pathology is observed (Fig. 2).

Pericardial thickening resulting from fibrosis or calcification can be presented as a small echo-free space or a single dense band of echoes. Since the pericardium is the most echogenic structure in the image, sensitivity and specificity of transthoracic echocardiography for pericardial thickening is low. Doppler assessment of diastolic flow patterns and the respiratory changes in these patients can provide compelling evidence for pericardial constriction and rule out the diagnosis of restrictive cardiomyopathy and cardiac tamponade [6].

Both cardiac MRI and CT in RD can also be used to assess the size and location of pericardial effusions, although they tend to overestimate the amount of fluid in comparison with echocardiography [7] (Fig. 3). Pericardial effusion is hypodense in comparison with the myocardium, with radiodensity ranging from 10–40 Hounsfield units, depending on the protein content (fibrin) and admixture of blood. If the amount of blood in the pericardium is small, differentiation from fibrosis (chronic constrictive pericarditis), which displays about the same density, may be impossible [8].

MRI is useful in patients with loculated or complex configurations of pericardial effusions, which can be often found in RD. MRI has an advantage over CT in differentiating small pericardial effusions from pericardial thickening. However, MRI cannot distinguish between chronic pericardial thickening and calcifications. CT and MRI diagnosis of constrictive pericarditis is established only if the findings of systemic venous hypertension are confirmed, such as dilated superior and inferior vena cava, ascites, hepatomegaly and pleural effusion. MRI has high diagnostic accuracy for the definitive non-invasive diagnosis of constrictive pericarditis and its separation from restrictive cardiomyopathy. Both the increased pericardial thickness and alterations in the heart structures can contribute to the diagnosis with sensitivity of 88%, specificity 100% and accuracy of 93% [9]. Furthermore, MRI could quantify functional abnormalities, namely LV systolic and diastolic dysfunction, which may be associated with pericardial diseases [10].

### Involvement of heart valves

Echocardiography is superior and the most frequently used technique for the evaluation of the patients with valvular heart disease in RD. This method offers the non-invasive and reliable

| Table 1. Heart diseases in major rheumatic diseases |
| Pericardium | Valves | Myocardium | Coronary arteries |
| RA | +++ | + | + | ++/+++
| SLE | ++++ | +++ | +++ | ++/+++++
| APLA | ++++ | ++ | -- | --/+
| SS | ++++ | ++ | -- | --/+

RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; APLA, antiphospholipid antibody syndrome; +, rare; ++, low incidence; ++++, medium incidence; ++++, high incidence.
involvement about valve morphology, the severity of valve stenosis or regurgitation, and the impact of valvular lesion on LV size and function.Transoesophageal echocardiography is considered to be more sensitive than transthoracic echocardiography in revealing valve abnormalities in RD [11]. The haemodynamic data are derived from Doppler echocardiography, and valvular regurgitation can be assessed by colour flow imaging of regurgitant jet.

Valvular disease can be frequently diagnosed in SLE, as valvular thickening, vegetations and valvular insufficiency. As the most typical lesion, the Libman–Sacks endocarditis (atypical verrucous endocarditis) is described, echocardiographically characterized by vegetations usually <10 mm in diameter, which vary in shape, have irregular borders, and have various echodensities (Fig. 4). Lesions are easily echocardiographically detected and are usually attached to the basilar portion of the aortic and mitral valve leaflets. The verrucae are near the edge and in only 3–4% of the patients haemodynamically significant. Echocardiographic anatomical abnormalities were reported in 40–50% of these cases, with much higher sensitivity for transoesophageal echocardiography in 50–60% patients [2].

Valvular involvement in RA patients can be also confirmed by echocardiography, which usually reveal aortic valve lesions in 5–14% and mitral valve abnormalities (thickening and prolapse) in 5–35% of the patients, depending on the imaging technique applied [6].

In SSc, nodular thickening of the mitral valve could be seen in 38% of the patients, while in only a few cases mitral and tricuspid vegetations are reported [12]. In patients with antiphospholipid syndrome, heart valve abnormalities are the most common cardiac manifestations and could be presented as vegetations, thickening and valvular dysfunction [13]. Mitral valve thickening is found on echocardiography in 63% of the patients, followed by the aortic (32%) and tricuspid valve thickening in 8% of the patients [14]. Ankylosing spondylitis is associated with aortic root and valve disease [15]. Aortic valve thickening is predominantly echocardiographically manifested as nodularities, usually single, homogeneously echoreflectant, with well-defined borders, located on any portion of the three cusps. Mitral valve thickening could also be common and is predominantly localized to the basal anterior mitral leaflet.

Cardiac MRI is a valuable tool for evaluation of valvular regurgitation severity and quantification of the effects of valvular lesion on LV volumes, function and mass [10]. The accepted MRI method for qualitative assessment of severity of valvular regurgitation is based on the dark signal extending from the diseased valve into the receiving chamber during a variable time period of the cardiac cycle. For the valve stenosis evaluation, signal loss distal to an abnormal valve is appreciated, but could not be used as an accurate parameter because it is dependent on MRI settings. Non-invasive quantitative assessment of blood flow can be performed by velocity-encoded cine MRI, not yet available for clinical use. Furthermore, in the absence of a cardiac shunt, any discrepancy between stroke volumes in a patient with regurgitation will identify the regurgitant LV volume. Disadvantage of this method is that only patients with a single regurgitant valve can be assessed although combination with velocity-encoded cine MRI allows assessment and quantification of multivalvular disease [10].

**Involvement of myocardium**

The myocardium is frequently affected in RD by means of different immunological mechanisms. In RA, myocardium was involved in 19% of the cases on post-mortem study by Lebowitz [16]. Although myocarditis is not usually associated with RA, secondary amyloidosis could cause cardiomyopathy and atrioventricular conduction abnormalities [17]. Acute or chronic congestive heart failure due to SLE and acute myocarditis are not common, the latter could be initial clinical presentation of the disease. Acute myocarditis has been reported in 8–25% of these patients, but due to introduction of steroid therapy decreased to 5% [18]. In SS, myocardial involvement can manifest as incipient cardiomyopathy that could progress to ventricular dysfunction and heart failure [4].

Echocardiography is considered an accurate tool for the assessment of LV size and function, which are indicative of myocardial inflammation and/or dysfunction. 2D echocardiography could be of limited value, but Doppler echocardiography and myocardial tissue imaging can provide essential diagnostic information. The analysis of impaired myocardial relaxation, decreased compliance and increased filling pressure, are important clues in revealing LV diastolic dysfunction [2].

LV angiography demonstrates LV volumes and function and is routinely used in the assessment of these patients. LV angiography using technetium 99m-labelled red cells can be used to evaluate LV function, but has largely been replaced by echocardiography and recently MRI [10]. CT is not considered the tool of choice for the assessment of LV function in RD due to radiation and application of contrast media.

Cardiac MRI is superior to other techniques in assessment of LV size, function and mass because it is non-invasive, has high spatial resolution, high reproducibility and low interobserver and intraobserver variability. The results are comparable to SPECT and the method is more accurate than 2D echocardiography and radionuclide ventriculography [10]. Myocardial fibrosis, which is considered as a non-specific finding, is demonstrated as a low signal intensity area on T2-weighted images and as a delayed enhanced region after contrast administration. Inflammatory oedema consistent with myocarditis, could be seen as multiple focal areas of increased myocardial signal intensity on T2-weighted images, and early and late gadolinium enhancement images [19] (Fig. 5). Similar to this, increased gallium-67 citrate uptake may be indicative of a myocardial interstitial inflammation [20].

**Involvement of coronary arteries**

In SLE, risk of developing coronary artery disease (CAD) is 4–8 times higher than in controls, while in the middle-aged women with long-standing disease and a long period of corticosteroid intake the risk is increased 50-fold than in the
matching age group [2]. In patients with RA, risk of CAD is
2–3-fold increased in comparison with the general population.
In addition, silent ischaemia and sudden cardiac death are more
likely to be experienced by RA patients [1].

For assessment of LV ejection fraction and ventricular wall
motion in CAD, radionuclide ventriculography, echocardi-
ography, gated SPECT and MRI could be used. According to
American Heart Association/American College of Cardiology
(AHA/ACC) Task Force on Practice Guidelines in CAD, radio-
nuclide ventriculography should be used for serial measurements
of LV ejection fraction [21]. Gated SPECT myocardial perfusion
nuclear imaging is preferred for simultaneous assessment of
myocardial perfusion and function [22].

2D echocardiography is suggested for routine assessment of LV
ejection fraction in patients with CAD in RD. 3D echocardio-
graphy is superior to both quantitative and qualitative 2D
echocardiographic techniques and correlates well with measure-
ments made using cardiac MRI. Tissue Doppler imaging study
[23] revealed that early diastolic velocities and mitral E/A ratio are
lower in patients with CAD in comparison with the controls.
Recently, a new global index of left ventricular function (TEI
index), was introduced by Turiel et al. [14] aimed to assess systolic
and diastolic LV function, and was confirmed to be higher in
patients with RA and SS compared with control subjects.

Stress echocardiography is a useful method for detection of
myocardial ischaemia and for risk stratification of patients with
suspected or known CAD. Stressors include exercise, pharmaco-
logical agents and pacing. In patients with LV dysfunction and
documented CAD, stress echocardiography can differentiate
viable from scarred myocardium. In patients who are unable to
eexercise, pharmacological stressors can be used: sympathomimetic
agents (dobutamin) or vasodilatatators (dipyridamole or adeno-
sine). This technique is important to differentiate myocardial
stunning from necrosis, and it is considered safe, relatively
inexpensive and easy to perform.

Cardiac MRI pharmacological stress test is well-established to
identify ischaemia-induced wall motion abnormalities. Dobutamine MRI has greater sensitivity than dobutamine
echocardiography (86 vs 74%) and specificity (86 vs 70%) [24].

The diagnostic accuracy of adenosine stress cardiac MRI varies
significantly according to the MRI parameter evaluated.

Ischaemic territories can be identified with high sensitivity and
specificity by using intravenous gadolinium for a first-pass
perfusion, when perfusion abnormalities were confined to the
subendocardium. Dark areas of low perfusion could be identified
visually or using computer analysis (Fig. 6). Usually, both stress
and rest myocardial perfusion scans are used and are comparable
with myocardial perfusion reserve using flow wire probe, positron
emission tomography (PET) and SPECT [22]. More simple
approach is to assess stress myocardial perfusion only during
vasodilatation, and using late gadolinium enhancement to define
areas of non-viability.

Severity of stenotic coronary lesion could be measured by
coronary flow reserve and direct visualization of coronary artery
tree. Coronary flow reserve could be estimated with the
combination of coronary flow assessment by Doppler and
vasodilatator stress, which increases accuracy of this technique
[14]. Determination of coronary flow by cardiac MRI in humans
has been only reported to identify stenosis of the left anterior
descending artery [10].

The most accurate visualization of the coronary arteries is by
selective coronary arteriography, which remains a gold standard.
Although new non-invasive techniques have been developed,
including CT and MRI angiography, some limitations apply.
Coronary angiography using 64-slice CT scanners, does not
dentify all coronary segments (88%), and has sensitivity of
88–100%, and specificity of 85–97% per patient. Angiography
with MRI has even lower diagnostic accuracy than multislice CT
angiography [25]. However, neither of the techniques is an
alterative to selective coronary angiography and neither is
recommended for screening asymptomatic patients, including
those at high risk [26].

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