International Journal of Cardiology 171 (2014) 82–87

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Cardiovascular magnetic resonance imaging in asymptomatic patients with connective tissue disease and recent onset left bundle branch block

Sophie Mavrogeni [a,*], Petros P. Sfikakis [b], Georgia Karabela [c], Efthymios Stavropoulos [c], Georgios Spiliotis [c], Elias Gialafos [d], Stylianos Panopoulos [b], Vasiliki Bournia [b], Dionisia Manolopoulou [a], Genovefa Kolovou [a], George Kitas [e]

[a] Onassis Cardiac Surgery Center, Athens, Greece
[b] Rheumatology Unit, First Department of Propeudeutic and Internal Medicine, Laikon Hospital, Athens University Medical School, Athens, Greece
[c] Athens Naval Hospital, Athens, Greece
[d] Bioiatriki MRI Unit, Athens, Greece
[e] Arthritis Research UK Epidemiology Unit, University of Manchester, Manchester, UK

ARTICLE INFO

Article history:
Received 14 August 2013
Accepted 23 November 2013
Available online 4 December 2013

Keywords:
Connective tissue diseases
Cardiovascular magnetic resonance
LBBB
Myocarditis
Vasculitis
Myocardial infarction

ABSTRACT

Background–aim: Recent LBBB in connective tissue diseases (CTDs) is challenging, due to high incidence of underlying pathology that may remain undetected, due to limitations of imaging tests. We hypothesized that cardiovascular magnetic resonance (CMR) may be of diagnostic value in CTDs with recent LBBB and normal echocardiogram.

Patients–methods: 26 CTDs, aged 32 ± 7 yrs (19 F) and 26 controls without CTDs, aged 60 ± 4 yrs (10 F) with recent LBBB and normal echo were evaluated by CMR. The CTDs included 6 sarcoidosis (SRC), 4 systemic sclerosis (SSc), 6 systemic lupus erythematosus (SLE), 6 rheumatoid arthritis (RA) and 4 inflammatory myopathies (IM). CMR was performed by 1.5 T. LVEF, T2 ratio (oedema imaging) and late gadolinium enhancement (LGE) (fibrosis imaging) were evaluated. Acute and chronic lesions were characterised by T2 > 2 and positive LGE and T2 < 2 and positive LGE, respectively. According to LGE, lesions were characterised as diffuse subendo-, subepicardial/intramural not following and subendocardial/transmural following the distribution of coronaries, indicative of vasculitis, myocarditis and myocardial infarction, respectively.

Results: CTDs were younger ($p < 0.001$), with higher incidence of abnormal CMR (42.31 vs 30.77%, $p = NS$), including dilated cardiomyopathy (11.54%), diffuse subendocardial fibrosis (11.54%), myocardial infarction (7.69%) and acute myocarditis (11.54%) vs dilated cardiomyopathy (19.23%), myocardial infarction (7.69%) and acute myocarditis (3.85%), detected in non-CTDs.

Conclusions: In CTDs with recent LBBB, CMR documented acute and chronic cardiac pathology, particularly myocarditis. CMR should be considered as an adjunct to conventional diagnostic workup in both patient groups, more so in CTDs.

1. Introduction

Left bundle-branch block (LBBB) is the result of conduction delay or block in any site of the intraventricular conduction system, including the main left bundle-branch, each of the two fascicles, the distal conduction system of the left ventricle or, less commonly, the fibres of the bundle of His that become the main left bundle-branch. LBBB produces prolonged or abnormal QRS and abnormal ST complexes and usually appears in patients with heart disease, although in 12% of cases there is no clinically overt heart disease [1]. Epidemiological studies have identified that LBBB is associated with higher cardiovascular and all cause mortality, higher risk of high grade atrioventricular block and cardiac death, mainly in the form of sudden death [1–4]. The incidence of LBBB in the general population is 1–3% at age 65 yrs, while in people with heart failure it is much higher at around 30% [3]. Although recognition of LBBB on ECG is straightforward, identifying its aetiology and possible consequences for risk stratification still remains challenging. The altered cardiac activation in LBBB causes electrical and mechanical ventricular dyssynchrony, influences ischemia detection on ECG and affects both stress test and imaging modalities that are dependent on wall motion and thickening [5].

Understanding the pathophysiologic background of LBBB is very important, due to its frequent association with various cardiovascular diseases [5,6]. Left ventricular (LV) dilatation, reduced LV ejection fraction (EF) [5–7], septal perfusion defects [8–10], even in the absence of coronary artery disease and/or structural adaptation of the left ventricle could be some of the reasons of LBBB development [10,11]. There is also

* Corresponding author at: 50 Esperou Street, 175-61 P.Faliro, Athens, Greece. Tel./fax: +30 210 98 82 797.
E-mail address: soma13@otenet.gr (S. Mavrogeni).

0167-5273/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ijcard.2013.11.059

evidence that bundle branch defects and sudden cardiac death are more common in patients with connective tissue diseases (CTDs), compared to the general population [12]. However, there are no detailed data about the pathophysiology of recent onset LBBB and possible clinical implications in CTDs.

Cardiovascular magnetic resonance (CMR) imaging is a non-invasive, non-radiating technique that performs both function and tissue characterisation, and has already been used in Cardiology and recently in the evaluation of CTDs [13–19]. However, the capability of CMR to detect the pathophysiologic background of new onset LBBB in patients with CTDs and normal echocardiographic studies has never been evaluated. We hypothesized that CMR, using the combination of T2-weighted images (oedema imaging) and late gadolinium enhanced (LGE) images (fibrosis imaging) may be useful for assessing the pathophysiologic background of new onset LBBB in such patients. A combination of T2 > 2 with positive LGE was considered as indicative of acute myocardial lesion and a combination of T2 < 2 with positive LGE of chronic myocardial lesion [15,16].

2. Patients–methods

2.1. Patients

Twenty-six consecutive patients with CTDs, aged 32 ± 7 yrs (19 F/7 M) and 26 patients without evidence of known CTD (non-CTDs), aged 60 ± 4 yrs (10 F/16 M), served as controls, were evaluated by CMR. All subjects had recent onset of asymptomatic LBBB (documented in the previous 15–45 days, without any known history or symptoms of heart disease) and had already had normal echocardiographic study. Patients of both groups with LBBB and known history of coronary artery disease, heart failure, renal failure, diabetes mellitus, thyroid disease, history of cardiac medication or other drugs that could possibly induce conduction delay or block and/or known contraindications to CMR were excluded. The CTD population included 6 sarcoidosis (SRC), 4 systemic sclerosis (SSc), 6 systemic lupus erythematosus (SLE), 6 rheumatoid arthritis (RA) and 4 inflammatory myopathies (IM). All CTDs and non-CTDs gave written consent forms and the study was approved by the hospital's ethics committee. The clinical characteristics of patients with CTDs are shown in Table 1.

2.2. Methods

2.2.1. Cardiovascular magnetic resonance imaging

All patients underwent CMR on a 1.5 Tesla scanner (Signa CV/i, GE Medical Systems) using ECG-triggered steady-state, free precession breath-hold cines (echo time (TE)/repetition time (TR) 1.6/3.2 ms, flip angle 60) in long-axis planes and sequential 8 mm short-axis slices (3 mm gap) from the atrio-ventricular ring to the apex. STIR T2-weighted images (triple inversion recovery; TE: 60 ms, TR: 2 × R–R interval, TI: 170 ms, slice thickness 20 mm, flip angle: 180, pixel size 2.3 × 1.3 mm) were acquired in short-axis planes for oedema imaging. Finally, late gadolinium enhancement (LGE) images were acquired 10 min after intravenous gadolinium–DTPA (Schering; 0.2 mmol/kg) in identical short-axis planes using an inversion-recovery gradient echo sequence for fibrosis detection. Inversion times were adjusted to null normal myocardium (typically 320–440 ms; pixel size 1.7 × 1.4 mm). Ventricular volumes and function were measured for both ventricles using standard techniques and analysed using specialized software (MEDIS, Leiden, NL) [20–23]. A left ventricular ejection fraction (LVEF) <55%, was considered abnormal [20–23].

2.2.2. Cardiovascular magnetic resonance analysis

CMR scans were analysed independently by two experienced interpreters blinded to clinical data. Scans were reviewed with assessment of ventricular volumes and function using the images from SSFP sequence. T2 ratio was calculated by measuring the ratio of myocardial to skeletal muscle signal intensity from STIR T2W images [18]. Finally LGE images were assessed for subendocardial or transmural enhancement in the distribution of a coronary artery compatible with myocardial infarction [19] for midwall or subepicardial enhancement, compatible with myocarditis [18] and for diffuse subendocardial fibrosis compatible with vasculitis [17]. Patients were further sub-classified into acute (T2 ratio > 2) or non-acute (T2 ratio < 2) stage [18,19]. A combination of T2 > 2 with positive LGE was considered indicative of an acute and a combination of T2 < 2 with positive LGE of a chronic myocardial lesion [15,16]. According to location and morphology of LGE, CTD patients were categorized as follows: (a) diffuse subendocardial LGE, indicative of subendocardial vasculitis; (b) subepicardial or intramural LGE, not following the distribution of coronary arteries, indicative of myocarditis; and (c) subendocardial or transmural LGE, following the distribution of coronary arteries, indicative of myocardial infarction. Scans with completely normal range volumes and function with no LGE/T2 abnormalities were considered normal.

2.2.3. Image analysis

In T2W, the signal ratio was measured from the region of interest covering the left ventricular myocardium as well as a skeletal muscle in the same slice. To assess the contrast-enhanced images (LGE), all short-axis slices from base to apex were inspected visually to identify areas of normal (completely nulled) myocardium. Mean signal intensity and standard deviation (SD) were derived and a threshold of 0.4 SD exceeding the mean was used to define areas of LGE. Summing the planimetered areas of LGE in all short-axis slices yielded the total volume, which was also expressed as a proportion of total LV myocardium (% LV). The LGE analysis was performed by one experienced reader and reviewed and confirmed by a second expert reader with both of the independent readers blinded to patient's identity and clinical profile. Any discrepancies in the analysis between the two readers were then adjudicated by a senior reader with >10 yrs of CMR experience, also blinded to the patient's identity and clinical profile (SM, GK, GK). Cine images were used for the evaluation of left ventricular ejection fraction (LVEF). Left ventricular endocardial borders were outlined on the end-systolic and end-diastolic short-axis view images covering the entire LV. Papillary muscles were considered as myocardium. Left ventricular ejection fraction was calculated as follows: LVEF Ό [(volume at end-diastole − volume at end-systole) / volume at end-diastole]. The MRI-MASS, Medis, Leiden, The Netherlands software was used and the readers were blinded to the clinical data.

2.2.4. Statistical analysis

All measurements were expressed as mean ± SD. Statistical significance of the differences was investigated using unpaired Student's *T*-test. Correlation between variables was sought with Pearson's correlation coefficient. Categorical values were compared using chi-square test. Statistical significance was considered for $p < 0.05$.

Table 1
Clinical characteristics of patients with CTDs at the time of CMR evaluation.

Patient characteristics	SRC (N = 6)	SSc (N = 4)	SLE (N = 6)	RA (N = 6)	IM (N = 4)
Age (yrs)	35 ± 8	28 ± 3	35 ± 8	31 ± 8	27 ± 5
Sex (F/M)	3/1	3/1	5/1	5/1	3/1
Diabetes	0	0	0	2	0
Dyslipidaemia	1	0	1	1	0
Smoking	0	1	0	0	0
Hypertension	1	0	1	0	0
CRP mg/l; mean, SD (normal range 0–5)	8.3 ± 2.3	7.0 ± 1.8	11.3 ± 3.2	10.2 ± 4.0	11.5 ± 4.0
ESR, mm/h; mean, SD (normal range 0–10)	17.8 ± 2.7	20.5 ± 6.4	19.0 ± 14.8	18.3 ± 5.2	20.5 ± 6.4
Family history of IHD (%)	0	0	0	0	0
Disease duration;(yrs)	2.0 ± 0.5	4.0 ± 1.0	3.0 ± 1.5	4.0 ± 2.0	2.0 ± 1.0
ACE/AT-II, n	1	1	1	1	0
b-Blockers, n	0	0	0	0	0
Statins, n	0	0	1	1	0
Current prednisone, n	3	0	0	0	2
Current NSAID, n	0	0	2	3	0
Current non-biologic DMARDs, n	2	3	4	4	2
Current biologic DMARD (infliximab), n	0	0	0	2	0