Delayed-Enhanced Cardiovascular Magnetic Resonance in the diagnosis and management of Cardiac Sarcoidosis

Chapter 10

Summary

When we set out to formally evaluate the value of contrast-enhanced cardiovascular magnetic resonance (CMR) for the diagnosis and management of cardiac sarcoidosis (CS) little was known of the prevalence of cardiac sarcoidosis in The Netherlands.

In **Chapter 2** we reviewed contrast-enhanced CMR in the diagnosis and management of CS. The aim of this review was to provide relevant clinical and pathophysiological background on CS, whilst introducing cardiovascular magnetic resonance imaging (CMR) as a technology, and detailing its past, current and future role in the management of CS. **Chapter 3** details the prevalence of cardiac involvement in patients with pulmonary sarcoidosis (PS) assessed at two University Medical Centres in The Netherlands. We reviewed the findings in 101 consecutive patients who either presented to us with symptoms of cardiac involvement, or were screened for CS during 1998 -2004. Sixteen of the 19 (84%) patients who presented with cardiac symptoms and 3 of the 82 (4%) who were screened for cardiac involvement were diagnosed with CS (adapted Japanese 1993 criteria). Once PS patients developed CS, their prognosis became grim, with 4 deaths (20%), and 9 cardiac devices implants (47%). The CS patients who presented with cardiac failure or ventricular arrhythmias had significant morbidity and a mortality rate of 25% during a mean follow up of 15 months. In contrast, PS patients diagnosed with asymptomatic, small, focal scar fared well. Our study was the first to systematically evaluate cardiac involvement in patients with sarcoidosis in The Netherlands, and at that stage the largest published to employ CMR. **Chapter 4** reported the additional value of gadolinium-enhanced CMR to standard assessment with electrocardiography, Doppler-echocardiography, and ^{201}thallium scintigraphy for cardiac involvement in 55 patients with PS.

Of the 55 patients evaluated, standard evaluation diagnosed cardiac involvement in 13 while CMR diagnosed myocardial scarring in an additional 6 (11%) patients. The extent of delayed enhancement correlated with disease duration, ventricular dimensions and function, severity of mitral regurgitation and the presence of ventricular tachycardias. Patients in whom cardiac involvement was only diagnosed with CMR had less focal myocardial scarring and functional impairment compared to patients diagnosed with standard assessment. CMR provided an accurate estimation of the extent of cardiac involvement, and may have reveal signs of early infiltration that were not detected by standard assessment. The extent of LGE related to severity of cardiac involvement and may therefore have prognostic implications

Chapter 5 evaluated the accuracy of gadolinium-enhanced CMR in the diagnosis of cardiac sarcoidosis.

In 2005 the diagnosis of CS was made according to the guidelines of the Japanese Ministry of Health and Welfare (1993). CMR had not been incorporated in the guidelines, and the diagnostic accuracy of CMR for the diagnosis of CS had not yet been evaluated. We performed an analysis of the 12-lead ECGs, 24-hours ambulatory

ECGs, echocardiograms, thallium scintigrams and gadolinium-enhanced CMR studies in 58 biopsy proven PS patients assessed for CS. The diagnostic accuracy of CMR for CS was determined with modified Japanese guidelines as gold standard. Twelve of the 58 patients were diagnosed with CS (21%). The sensitivity and specificity of CMR were 100%, and 78%, the PPV and NPV 55% respectively 100%, with an overall accuracy of 83%. The combination of ECG and CMR had a sensitivity and specificity of 100% and 96%, and PPV and NPV of respectively 86%, and 100%, with an overall accuracy of 97%.

Late gadolinium enhancement (LGE) accurately delineates myocardial necrosis or focal fibrosis. The pattern of LGE in ischemic and non-ischemic myocardial disease is different, and might be helpful in distinguishing CS from ischemic disease. The pattern of LGE in CS has been reported to be patchy, multi-segmental, not related to coronary artery territories, while predominantly involving the mid myocardial and subepicardial layers. In **Chapter 6** we reviewed the value of delayed contrast-enhanced CMR (DECMR) in differentiating patients with CS from those with coronary artery disease and recent myocardial infarctions. The DECMR studies of 30 patients with CS were compared to those performed in 30 consecutive infarct patients, who had been managed with primary coronary interventions, and 10 healthy controls. Two experienced blinded observers classified patients by assessing the distribution of LGE. Gadolinium CMR was helpful in differentiating patients with CS from patients with ischemic heart disease and previous myocardial infarctions. In a subgroup of ischemic patients the pattern of LGE was atypical, and suggestive of non-ischemic etiology. Cardiac involvement in sarcoidosis is reported in up to 30% of patients. Left ventricular involvement demonstrated by DECMR has been well validated. We sought to determine the prevalence and distribution of RV LGE in patients diagnosed with PS. In **Chapter 7** Right ventricular involvement in CS demonstrated with CMR. We prospectively evaluated 87 patients diagnosed with PS with contrast-enhanced cardiac magnetic resonance for RV involvement. Right ventricular enhancement was present in 16% of patients diagnosed with PS, and in 48% of patients with LV enhancement. The presence of RV enhancement correlated with pulmonary arterial hypertension, RV systolic dysfunction, hypertrophy and dilation. More extensive LV enhancement correlated with RV involvement. Right ventricular enhancement may result from direct infiltration and resulting scar, or pulmonary hypertension. Previous studies associated impaired systolic RV function and RV enhancement with ventricular tachy-arrhythmias. We demonstrate RV enhancement with cardiac magnetic resonance to be mostly multi-focal, involve the septum and correlate with increased RV volumes, hypertrophy and impaired systolic function. Finally in **Chapter 8** we present the long-term follow up of 84 consecutive biopsy proven pulmonary sarcoidosis patients after baseline DECMR. Biventricular LGE at presentation was the strongest, independent predictor of adverse outcome during long-term follow up. Small asymptomatic LV myocardial scar of < 8% of LV mass carried a favorable long-term outcome. RV delayed enhancement correlates with systolic RV dysfunction and predicts ventricular tachy-arrhythmias as well as all cause death during follow up. This is the first pro-

spective study to detail the prognostic relevance of right ventricular involvement in pulmonary sarcoidosis, and reports on improved long-term outcomes when cardiac sarcoidosis is managed according to current guidelines.