Cardiovascular Magnetic Resonance, Fibrosis and Prognosis in Dilated Cardiomyopathy

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Background: Non-ischemic dilated cardiomyopathy (DCM) is associated with significant morbidity and premature mortality. Accurate risk stratification of patients with non-ischemic dilated cardiomyopathy (DCM) in the era of device implantation is problematic. Previous studies have shown that approximately 30% of patients with DCM have mid-wall fibrosis as detected by late gadolinium-enhancement (LGE) cardiovascular magnetic resonance (CMR); see figure 1. Myocardial fibrosis may be associated with increased susceptibility to arrhythmia and progression of heart-failure.

Hypothesis: We speculated that fibrosis in DCM might predict outcome. We tested this hypothesis in a prospective longitudinal study comparing the clinical outcomes in DCM patients according to the presence or absence of mid-wall fibrosis with a pre-defined primary outcome measure of the assessment of death and hospitalization for cardiovascular causes.

Methods: Consecutive patients diagnosed with DCM (N =63, 45 Male) and an EF of <40% were recruited. All patients had previously had a normal coronary angiogram and had no CMR evidence of prior myocardial infarction. The patients were divided into 2 groups according to the presence or absence of mid-wall fibrosis and followed prospectively for 534 ± 318 days. Event data was collected and recorded by communication with patients, their cardiologists and general practitioners at regular intervals. Medical records were reviewed for recruited patients following attendance at outpatient clinics or hospitalization. Follow-up was complete. The pre-defined primary end-point was a composite of all-cause death and hospitalization for a cardiovascular event.

Statistical analysis: Continuous data are expressed as mean ±SD. The baseline characteristics of the two groups were compared with the use of independent sample t-tests for continuous variables and chi-square or Fisher’s tests for categorical variables where appropriate. Survival estimates and cumulative event rates were compared by the Kaplan–Meier method. The time to first event for each end-point was recorded for each patient. The log-rank test was used to compare the Kaplan-Meier survival curves in the two groups. The hazard ratio was calculated using a Cox regression model with computed 95% confidence intervals (CI). Multivariate analysis was also performed using 3 covariates known to affect the end-points, namely age, left ventricular (LV) ejection fraction (EF), and right ventricular (RV) EF. The duration of follow up was computed using the date of entry into the study (day of the CMR scan) to the date of the first end-point reached. For patients who did not reach an end-point, follow up data was collected to the time of their last clinical follow up. A p value of <0.05 was deemed significant.

Results: Mid-wall fibrosis was present in 26 patients (41%). There were no baseline differences in age, left ventricular and right ventricular size and function between the two groups. In addition, the proportion of patients on treatment with beta blockers, ace inhibitors and spironolactone were comparable. The presence of mid-wall fibrosis was associated with a higher rate of death and hospitalization (hazard ratio [HR] 2.5, p=0.03, see figure 2). Multivariate analysis demonstrated mid-wall fibrosis as the sole significant predictor of death/hospitalization (HR 2.4, p=0.048).

Conclusions: This is the first study to evaluate the prognostic significance of detecting myocardial fibrosis in DCM. Patients with myocardial fibrosis had a higher incidence of the predetermined endpoint of all-cause mortality and hospitalization, and this finding persisted after correction for baseline patient differences in LV/RV volumes/function and age. These findings have potentially important implications for the risk stratification of DCM patients and further studies are required to establish whether LGE-CMR can be used for refinement of patients groups selected for device therapy.

Figure 1: Late gadolinium enhancement patterns in DCM in vertical long axis (a, c) and short axis (b, d). A patient without late enhancement is shown in a), b) and a patient with marked mid-wall enhancement is shown in c), d). The enhancement pattern (arrows) is distinct from that associated with coronary artery disease because of endocardial sparing and non-coronary territory distribution.

Figure 2: Analysis of subset of patients with LV ejection fraction (EF) <40%. a) Kaplan-Meier survival estimates for the primary endpoint of all-cause mortality or hospitalization for a cardiovascular cause. b) same data adjusted for baseline differences in age, LVEF and RVEF.