Prevalence of Myocardial Fibrosis Patterns in Patients With Systolic Dysfunction

Prognostic Significance for the Prediction of Sudden Cardiac Arrest or Appropriate Implantable Cardiac Defibrillator Therapy

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Background—Late gadolinium enhancement-cardiac magnetic resonance is increasingly performed in patients with systolic dysfunction. Numerous patterns of fibrosis are commonly reported among this population. However, the relative prevalence and prognostic significance of these findings remains uncertain.

Methods and Results—Three hundred eighteen consecutive patients referred for late gadolinium enhancement-cardiac magnetic resonance and a left ventricular ejection fraction <55% were followed up for the primary end point of sudden cardiac arrest or appropriate implantable cardiac defibrillator therapy. Late gadolinium enhancement images were blindly interpreted for the presence of 6 distinct pattern(s) of myocardial fibrosis in addition to signal threshold-based quantification of total fibrosis volume. The mean age and left ventricular ejection fraction of participants were 62.0±12.9 years and 32.6±11.9%, respectively. Any pattern of myocardial fibrosis was seen in 248 patients (78%) with ≥2 patterns present in 25% of patients. During follow-up (median of 467 days), 49 patients (15%) had a primary outcome. After adjustment for left ventricular ejection fraction, cardiomyopathy pathogenesis, and total fibrosis volume, the presence of a midwall striae pattern of fibrosis was an independent predictor of sudden cardiac arrest or appropriate implantable cardiac defibrillator therapy with a hazard ratio of 2.4 (95% confidence interval, 1.2–4.6; P<0.01); this finding is present in 30% of patients with nonischemic and 15% of patients with ischemic cardiomyopathy. Cumulative event rate was significantly higher among those with midwall striae, particularly among those with a left ventricular ejection fraction ≥35% (40% versus 6%; P=0.005).

Conclusions—Patients with systolic dysfunction frequently demonstrate multiple patterns of myocardial fibrosis. Of these, a midwall striae pattern of fibrosis is the strongest independent predictor of sudden cardiac arrest or appropriate implantable cardiac defibrillator therapy. (Circ Cardiovasc Imaging. 2014;7:593-600.)

Key Words: death, sudden, cardiac fibrosis magnetic resonance imaging

Systolic heart failure (HF) is an expanding health concern affecting ≥5 million people in the United States and contributing ≥37 billion dollars in annual healthcare expenditures.1,2 The capacity to identify patients at greatest risk of serious cardiovascular events, particularly those related to malignant ventricular arrhythmia and pump failure, is therefore of great importance. Risk stratification is largely based on the left ventricular ejection fraction (LVEF), a measure currently used to define candidacy for implantable cardiac devices.3 However, the solitary use of this metric has been challenged based on the evidence demonstrating only modest use for the prediction of life-threatening arrhythmias.4 Accordingly, alternate risk markers independent of LVEF are desirable.

Clinical Perspective on p 600

Cardiovascular magnetic resonance (CMR) has become a routinely performed imaging procedure among those with cardiomyopathy. Late gadolinium enhancement (LGE) routinely identifies patterns of hyperenhancement, a marker of fibrosis or other forms of interstitial expansion, related to underlying myocardial disease. These patterns have been useful in providing insight into the presence and burden of both ischemic5,6 and nonischemic myocardial injury7,8 in this
population. Efforts to characterize the latter has led numerous investigators to report nomenclature for signature patterns of hyperenancement, some considered pathognomonic for specific causes. Specifically, common disease associations include subendocardial hyperenancement is associated with ischemic cardiomyopathy (ICM), midwall striae hyperenancement with dilated non-ICM (NICM), midwall patchy hyperenancement with hypertrophic cardiomyopathy, subepicardial hyperenancement with myocarditis or sarcoidosis, right ventricular insertion site hyperenancement with pulmonary hypertension, and diffuse hyperenancement with amyloidosis. Indeed, within these respective cohorts, some patterns of hyperenancement have shown prognostic significance for the prediction of future cardiovascular events.

Recent studies support that specific patterns of hyperenancement may not be isolated to clinically defined patient cohorts. For example, midwall striae hyperenancement may be identified among those with ICM, subendocardial hyperenancement pattern may be seen among those with NICM, and right ventricular insertion site fibrosis seen among those without pulmonary hypertension. Therefore, although each hyperenancement pattern may represent a distinct myocardial remodeling process, these may not be unique to clinically defined patient cohorts. Accordingly, the identification of hyperenancement patterns by LGE imaging has the potential to provide an objective evaluation of myocardial disease burden independent of clinical bias. The relative prevalence and prognostic value of these hyperenancement patterns among a referral population with systolic dysfunction has not been previously examined.

In this study, we evaluate the prevalence of all recognized patterns of myocardial hyperenancement among patients referred to CMR with reduced systolic function. We evaluate the capacity of each respective hyperenancement pattern to predict the occurrence of sudden cardiac arrest (SCA) or appropriate implantable cardiac defibrillator (ICD) therapy.

**Methods**

**Study Population**

Three hundred eighteen consecutive patients with systolic dysfunction referred for LGE-CMR between April 2008 and April 2012 were studied. Systolic dysfunction was defined as a LVEF ≤55% because this value corresponds to the lower limit of the 95% confidence interval (CI) in healthy subject. Using the World Health Organization definitions of cardiomyopathy, patients were stratified into the 2 subcohorts of ICM and NICM. This was based on the review of invasive catheterization images and medical records. All patients with obstructive coronary artery disease (>70% stenosis of ≥1 epicardial coronary vessel) or a clinical history of previous myocardial infarction were categorized as having ICM. Any patient clinically suspected to have hypertrophic cardiomyopathy, restrictive cardiomyopathy (sarcoidosis or amyloidosis), or arrhythmogenic right ventricular cardiomyopathy at referral was excluded.

Patients were excluded if standard contraindications to LGE-CMR existed, inclusive of a glomerular filtration rate of ≤30 mL/min per 1.73 m². The study was approved by the Health Sciences Research Ethics Board at Western University, London, Ontario, and all participants gave both verbal and written informed consent.

**CMR Imaging Protocol**

Cardiovascular MRI was performed using a 3T MRI scanner (TIM Trio or Verio; Siemens, Erlangen, Germany) equipped with a 32-channel cardiac coil. Cardiac function was assessed in sequential short-axis views at 10-mm intervals from the atroventricular annulus to the apex using a standard SSFP-based cine pulse sequence. Typical imaging parameters were slice thickness 6 mm, gap 4 mm, TE 1.3 ms, flip angle 50°, matrix 256×205, iPAT 2, temporal resolution 28 to 38 ms. Ten to 15 minutes after intravenous administration of gadolinium-contrast (0.15–0.2 mmol/kg; Gadovist; Bayer, Inc), LGE imaging was performed using a phase-sensitive inversion recovery gradient echo pulse sequence in identical imaging planes. Typical imaging parameters were slice thickness 6 mm, gap 4 mm, TR 500 ms, TE 3.9 ms, flip angle 20°, matrix 256×205, segments 13 to 21, iPAT 2. The inversion time was optimized to null normal myocardium, as previously described.

**CMR Image Analysis**

Quantitative image analysis for cine and LGE images was performed using commercially available software (CMR42; Circle Cardiovascular Inc, Calgary, Alberta, Canada). Cine images were examined by a blinded and experienced core laboratory to determine LV and right ventricular end-systolic volumes and end-diastolic volumes, in addition to LV mass by semi-automated endocardial and epicardial contour tracing. Short-axis images were processed using a segment-based quantification of total hyperenancement volume using a signal threshold versus reference mean technique with a >5 SD cutoff, as previously described. The largest contiguous region of homogeneously nulled (black) myocardium is served as the reference region. Visual scoring of all LGE fibrosis patterns was performed using the consensus of 2 experienced readers in accordance with 6 patterns, as shown in Figure 1. These patterns were predefined based on the previously published classification and using the authors' experiences. These were (1) subendocardial based, (2) midwall striae, (3) midwall patchy, (4) subepicardial, (5) right ventricular insertion point, and (6) diffuse. Patterns were required to be visually identified on contiguous or orthogonal slices and also be seen on both magnitude and phase-corrected image reconstructions (to ensure not related to inaccurate TI prescription). Examples of hyperenancement pattern assignments are shown in Figure 2.

**Follow-Up and Clinical Events**

Clinical follow-up was initiated from the time of CMR imaging. The primary composite clinical outcome was SCA or appropriate ICD therapy for sustained ventricular tachycardia/ventricular fibrillation. Criteria used for appropriate ICD therapy were as previously described, and SCA was defined as death occurring within 1 hour of symptom onset based on a modified Hinkle–Thaler system. Patients were also followed up for the composite secondary outcome of HF admission or non–sudden cardiac death. Non–sudden cardiac death was defined as death that occurred after 1 hour of symptom onset but within the same admission. Among patients who had ≥1 clinical event during follow-up, the time of first clinical event was used for analysis of event-free survival. Follow-up was performed by a scripted telephone interview, review of all medical records, and a blinded review of all device interrogations.

**Statistical Analysis**

This study was adequately powered (80%) to detect a disparity of the primary outcome between 2 groups at a 2-sided α of 0.05, for a hazard ratio of 2. Initially, univariate analysis was performed to highlight predictors that were statistically significant to be included in the multivariable model. This was done using the Cox proportional hazards method and reported as hazard ratios with 95% CI. This was followed up by a Cox proportional multivariable regression analysis with significant predictor variables forced into the model. The model was selected using forward stepwise process for entry at P ≤0.05 and removal at P > 0.10 significance. All tests were 2 sided with a level of statistical significance set at P ≤ 0.05. Kaplan–Meier method was used to generate survival curves for those with and without mid wall striae hyperenancement using the log-rank test. Subgroup analysis was planned a priori to examine for the primary outcome in patients.
with an LVEF>35%. Post hoc analysis was performed for primary outcome using a more stringent definition of systolic dysfunction using a LVEF≤50% in keeping with the 2013 ACCF/American Heart Association Guideline for Management of Heart Failure. Baseline clinical and CMR characteristic were also compared for patients with and without a pattern of midwall striae fibrosis as a post hoc analysis. All statistical analyses were performed using PASW (SPSS version 21.0).

Results

Baseline Characteristics and CMR Measurements

A total of 318 consecutive patients were enrolled. On the basis of clinical referral criteria, we categorized as 149 (47%) patients having ICM and 169 (53%) patients having NICM. Additional baseline clinical characteristics are presented in Table 1.

The mean LVEF of the population was 32.6±11.9% (Table 2). Overall, 248 patients (78%) had any fibrosis identified by blinded visual interpretation. The respective prevalence of hyperenhancement patterns among the entire population, and among those with clinically defined ICM or NICM, is shown in Table 2. Overall, subendocardial (48%) and midwall striae (18%) were the most frequently identified hyperenhancement patterns. A total of 77 patients (24%) were found to have ≥2 patterns of fibrosis, this occurring in 27 (19%) patients with ICM and 50 (29%) patients with NICM. Examples of patients with combined patterns of fibrosis are shown in Figure 2.

Quantitative analysis of total hyperenhancement, performed using the signal threshold versus reference mean–based >5 SD technique, showed a mean total hyperenhancement of 14.8±15.5% for all patients. Those categorized as ICM had significantly higher hyperenhancement volume versus those with NICM (19.4±17.8 versus 13.9±14.9%; P=0.02; Table 2).

Primary Outcome

During follow-up (median of 467 days; interquartile range, 1406 days; range, 16–1422 days), the primary outcome was observed in 49 patients (15.4%). This consisted of 10 patients with SCA and 39 appropriate ICD therapies. Of these 49 patients, 27 were categorized as having ICM (8 SCA/19 appropriate device therapies) and 22 as NICM (2 SCA/20 appropriate device therapies).

By univariable Cox proportional hazard analysis, the only baseline clinical characteristics associated with the primary outcome were LVEF (HR=1.11, 95% CI 1.02 to 1.21 per 1% reduction; P=0.01).
outcome were ICM pathogenesis, history of previous ventricular arrhythmia, and current use of Digoxin (Table 1). Non–LGE-CMR variables showed that LVEF was modestly but significantly lower among those having the primary outcome (27.3±11.3% versus 33.6±11.7%; \( P =0.001 \); Table 2). Both the presence of any hyperenhancement (3.8; 95% CI, 1.4–10.8;
and total hyperenhancement volume (1.02; 95% CI, 1.01–1.03; \( P=0.008 \)) were predictive for the primary outcome. Among individual hyperenhancement patterns, midwall striae was uniquely found to be the predictive for the primary outcome (2.7; 95% CI, 1.2–4.6; \( P=0.01 \)). At the end of follow-up, event-free survival was 62% and 87% among those with versus without midwall striae hyperenhancement, respectively. Kaplan–Meier analysis showed that event-free survival was significantly shorter among those with midwall striae hyperenhancement (log-rank, \( P=0.004 \); Figure 3).

**Secondary Outcome**

The secondary outcome of HF admission or non–sudden cardiac death was observed in 52 patients; 42 being HF admission and 10 being non–sudden cardiac death. Of these patients, 25 had ICM (22 HF admissions/3 non-SCA) and 27 belonged to the NICM cohort (20 HF admissions/7 non-SCA). All clinical and cardiac MRI baseline characteristics, including hyperenhancement patterns and volumes, were comparable between both groups, with the exception of LVEF (27.2±11.4% versus 33.6±11.7%; \( P=0.001 \)). LVEF was significantly associated with HF admission or non–sudden cardiac death (hazard ratio, 0.95; 95% CI, 0.93–0.97; \( P=0.00005 \)).

No patient was lost to follow-up with 7 patients undergoing cardiac transplantation during the follow-up period and 13 patients with non–sudden cardiac death (combination of sepsis, accidental death, transplant complications, cancer, or refusal to disclose cause). Patients receiving transplantation were censored at the time of surgery.

**Subgroup Analysis**

Subgroup analysis was performed for patients with a LVEF>35% and continued to demonstrate a higher occurrence of the primary outcome among those with versus without midwall striae hyperenhancement (40% versus 6%; \( P=0.005 \)). Corresponding Kaplan–Meier survival analysis showed a statistically significant difference in event-free survival (log-rank test, \( P=0.009 \); Figure 4). A higher occurrence of the primary outcome also persisted for patients with a pattern of midwall striae fibrosis when analysis was restricted to patient fulfilling a more stringent definition of systolic dysfunction (LVEF≤50%; Table I in the Data Supplement). On post hoc analysis, patients presenting a pattern of midwall striae fibrosis showed a greater incidence of left bundle-branch block and had higher left ventricular end-diastolic volume, left ventricular end-systolic volume, right ventricular end-systolic volume, and lower LVEF and right ventricular EF. No patients with a pattern of midwall striae fibrosis had a LVEF>50% (Tables II and III in the Data Supplement).

### Table 3. Univariable Analysis of all HE Patterns for the Prediction of Sudden Cardiac Arrest or Appropriate Implantable Cardiac Defibrillator Therapy

<table>
<thead>
<tr>
<th>Event (n=49)</th>
<th>No Event (n=269)</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any HE, n (%)</td>
<td>Yes</td>
<td>45</td>
<td>203</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>4</td>
<td>66</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Subendocardial HE, n (%)</td>
<td>Yes</td>
<td>27</td>
<td>125</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>22</td>
<td>144</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Midwall striae HE, n (%)</td>
<td>Yes</td>
<td>15</td>
<td>42</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>34</td>
<td>227</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Midwall patchy HE, n (%)</td>
<td>Yes</td>
<td>8</td>
<td>27</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>41</td>
<td>242</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>RV insertion site HE, n (%)</td>
<td>Yes</td>
<td>10</td>
<td>41</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>39</td>
<td>228</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Subepicardial, HE, n (%)</td>
<td>Yes</td>
<td>7</td>
<td>27</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>42</td>
<td>242</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Diffuse HE, n (%)</td>
<td>Yes</td>
<td>2</td>
<td>7</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>47</td>
<td>262</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Total HE, per 1% LV mass</td>
<td></td>
<td></td>
<td>1.02</td>
<td>1.01–1.03</td>
</tr>
</tbody>
</table>

HE indicates hyperenhancement; LV, left ventricular; and RV, right ventricular.
Discussion

The performance of LGE-CMR in patients with systolic dysfunction offers the potential for risk stratification according to tissue-based markers of myocardial disease. This study identifies that this population commonly exhibits ≥1 disease pattern, despite a single clinical referral diagnosis. Although the pathophysiology of individual fibrosis patterns remains speculative, the presence of certain patterns seems to be independently predictive for relevant cardiovascular outcomes. Specifically, the presence of a midwall striae pattern of hyperenhancement identifies patients at an elevated risk of SCA or appropriate ICD therapy after adjustment for both referral clinical diagnosis and LVEF. Importantly, this marker is predictive of this primary outcome among those currently not considered eligible for ICD therapy.

An expanding literature supports a significant association between the presence of myocardial fibrosis by LGE imaging and clinically relevant cardiovascular outcomes.6,8,14,15,26–29 These investigations have examined a range of cardiomyopathy states but only few have focused on the prediction of arrhythmic among those with systolic dysfunction. Among patients with idiopathic NICM, 3 studies to date have reported an association between midwall striae hyperenhancement and future arrhythmic events.7,16,30,31 The first such description was provided by Assomull et al where, among 101 patients, this pattern of fibrosis was identified in 35%. In these patients, there was a higher rate of a composite end point inclusive of all-cause mortality, cardiovascular hospitalization, SCA, and sustained ventricular tachycardia. A similar but smaller study by Nazarian et al found that this pattern of fibrosis to be the strongest predictor of inducible ventricular tachycardia at electrophysiology study, remaining statistically significant after adjusting for LVEF. Most recently, a large cohort study of 472 patients with idiopathic NICM, reported by Gulati et al described a 30% prevalence of midwall striae hyperenhancement and an association with all-cause mortality, the primary outcome, and SCA. Overall, these studies suggest the potential of this marker to identify patients with idiopathic NICM at risk for future arrhythmic events reliably.

Although prognostic relevance has not been examined, previous studies have described the occurrence of midwall striae hyperenhancement among those with ICM.17 Furthermore, additional studies have commented on the presence of multiple hyperenhancement patterns (inclusive of subendocardial injury) among those with NICM.16,19 Therefore, it seems that patterns of hyperenhancement are not isolated to specific cardiomyopathy states but rather reflect common pathophysiologic end points of myocardial disease. Indeed, in the current study, we identify that one
quarter of patients will show ≥2 patterns of hyperenhancement. Of all patterns, midwall striae hyperenhancement is most significantly associated with future arrhythmic events, a relationship that was found to be independent of both clinically defined pathogenesis and LVEF. Mechanisms for the development of nonischemic fibrosis in patients with cardiomyopathy remain poorly understood. Postulation is that multiple contributory factors interact to establish such phenomena, including genetic predisposition, microvascular ischemia, abnormal modulation of immune and metabolic responses, as well as contributions from the renin–angiotensin–aldosterone system.7,33,34 The prevalence of specific patterns seems elevated among certain cohorts (ie, midwall striae in patients with idiopathic NICM) and most likely reflects a relative dominance of pathophysiological contributors. However, some of these patterns are likely to reflect a culmination of maladaptive remodeling and may not be directly related to the inciting insult itself.

**Limitations**

Site and test referral bias must be considered because this study was performed at a single tertiary care referral center as part of a prospective clinical outcomes registry of patients referred for CMR. Also, the primary outcome was a composite of SCA or appropriate ICD therapy. Appropriate ICD therapy is considered a meaningful surrogate of life-threatening arrhythmia but should not consider equivalent to SCA. Finally, our study was not aimed at evaluating patterns among patients with known nonischemic cardiomyopathies, such as cardiac sarcoid, amyloid, or hypertrophic cardiomyopathy. Accordingly, the prognostic use of hyperenhancement patterns in these distinct referral populations is not addressed within this study.

**Conclusions**

Patients with systolic dysfunction commonly exhibit ≥1 pattern of myocardial fibrosis. However, within this referral population, the presence of a midwall striae pattern of fibrosis identifies those at significantly higher risk of SCA or appropriate ICD therapy independent of LVEF, cardiomyopathy pathogenesis, total fibrosis volume, and other fibrosis patterns. Such patients have poorer event-free survival, particularly among those not currently considered eligible for ICD therapy by LVEF criteria alone.

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We thank Linda Marziali, Kris Carter (RN), Kim Krueger (RMT), and John Butler (RMT) for their important contributions to this work.

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**Disclosures**

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**References**


**CLINICAL PERSPECTIVE**

Cardiac resonance imaging is increasingly performed for the evaluation of patients with systolic dysfunction. Imaging investigators have increasingly associated signature fibrosis patterns with specific cardiomyopathy subtypes, numerous studies now showing respective prognostic significance for the prediction of future cardiovascular events among clinically defined cohorts. However, it is recognized that these fibrosis patterns do not seem to be exclusive to such clinical cohorts and may indeed be multiple within a single individual. This is suggestive that a combined pathological state exists in a significant number of patients with heart failure. In this study, we explored the prevalence and prognostic significance of all currently described myocardial fibrosis patterns among a population of patients with heart failure referred for cardiac resonance imaging. Our findings confirm a significant prevalence of combined myocardial fibrosis patterns among this referral population. Furthermore, our results identified that the presence of a midwall striae pattern of fibrosis was the strongest predictor of future arrhythmic events, this being independent of cardiomyopathy pathogenesis and left ventricular ejection fraction.
Prevalence of Myocardial Fibrosis Patterns in Patients With Systolic Dysfunction: Prognostic Significance for the Prediction of Sudden Cardiac Arrest or Appropriate Implantable Cardiac Defibrillator Therapy

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Supplemental Material
Supplemental Table 1. Results of multivariable analysis for the prediction of Sudden Cardiac Arrest or Appropriate ICD therapy in patient with an LV EF ≤ 50%

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Event n=47</th>
<th>No event n=244</th>
<th>Adjusted Hazard ratio</th>
<th>95% Confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-wall striae HE, n (%)</td>
<td>15</td>
<td>42</td>
<td>2.1</td>
<td>1.1 to 4.1</td>
<td>0.024</td>
</tr>
<tr>
<td>LVEF, per unit</td>
<td>1.0</td>
<td>0.9 to 1.0</td>
<td></td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Total HE, per 10% LV mass</td>
<td>1.0</td>
<td>1.0 to 1.0</td>
<td></td>
<td></td>
<td>0.035</td>
</tr>
</tbody>
</table>

Abbreviations used: HE= hyperenhancement, LVEF= Left ventricular ejection fraction

* Ischemic cardiomyopathy was no longer significant on univariate analysis.

Supplemental Table 2. Clinical baseline patient characteristics, presented for the total population and for those with and without midwall striae

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>With Midwall Striae (N=57)</th>
<th>Without Midwall Striae (N=261)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.8±12.0</td>
<td>59.1±13.1</td>
<td>0.70</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>45 (79)</td>
<td>188 (72)</td>
<td>0.285</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>23 (40)</td>
<td>130 (50)</td>
<td>0.195</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>12 (18)</td>
<td>59 (22)</td>
<td>0.799</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>24 (42)</td>
<td>143 (55)</td>
<td>0.082</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>28 (49)</td>
<td>102 (39)</td>
<td>0.162</td>
</tr>
<tr>
<td>H/O revascularization, n (%)</td>
<td>13 (23)</td>
<td>64 (24)</td>
<td>0.784</td>
</tr>
<tr>
<td>QRS interval (msec)</td>
<td>137.6±35.4</td>
<td>130.5±42.6</td>
<td>0.12</td>
</tr>
<tr>
<td>LBBB, n (%)</td>
<td>31 (54)</td>
<td>98 (38)</td>
<td>0.019*</td>
</tr>
<tr>
<td>H/O vent. arrhythmia, n (%)</td>
<td>7 (12)</td>
<td>27 (10)</td>
<td>0.668</td>
</tr>
<tr>
<td>NYHA class 3-4, n (%)</td>
<td>32 (56)</td>
<td>115 (44)</td>
<td>0.098</td>
</tr>
<tr>
<td>GFR (mL/min)</td>
<td>75.8±25.7</td>
<td>76.3±22.1</td>
<td>0.877</td>
</tr>
<tr>
<td>Etiology (referral diagnosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>24 (42)</td>
<td>128 (49)</td>
<td>0.342</td>
</tr>
</tbody>
</table>

Continuous data are expressed as mean ±SD, categorical data as n (%).
* P value calculated by two sample t-test or Mann Whitney U test for continuous variables or Fischers exact or Chi-square test for categorical variables.

Abbreviations used: LBBB=left bundle-branch block; NYHA = New York Heart Association; H/O = history of; Vent. = Ventricular
Supplemental Table 3. Baseline cardiac magnetic resonance imaging characteristics of study population in those with and without midwall striae

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>With Midwall Striae (N=57)</th>
<th>Without Midwall Striae (N=261)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV (mL)</td>
<td>279.7±86.6</td>
<td>222.6±76.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVESV (mL)</td>
<td>206.2±81.2</td>
<td>151.6±70.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>25.4±10.1</td>
<td>34.2±11.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVEDV (mL)</td>
<td>145.2±53.2</td>
<td>132.6±47.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVESV (mL)</td>
<td>87.4±49.0</td>
<td>68.4±39.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>42.6±16.3</td>
<td>50.0±15.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any HE, (n)</td>
<td>57 (100)</td>
<td>190 (73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total HE (%LV mass)</td>
<td>14.3±13.6</td>
<td>14.5±15.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Continuous data are expressed as mean ±SD, categorical data as n (%).
Abbreviations used: SD= Standard Deviation; LVEDV= Left ventricular end diastolic volume; LVESV= Left ventricular end systolic volume; LVEF= Left ventricular ejection fraction; RVEDV= Right ventricular end diastolic volume; RVESV= Right ventricular end systolic volume; RVEF= Right ventricular ejection fraction; HE= hyperenhancement.