Quantification of Diffuse Myocardial Fibrosis and Its Association With Myocardial Dysfunction in Congenital Heart Disease

Craig S. Broberg, MD; Sumeet S. Chugh, MD; Catherine Conklin, RT; David J. Sahn, MD; Michael Jerosch-Herold, PhD

Background—The etiology of ventricular dysfunction in adult congenital heart disease (ACHD) is not well understood. Diffuse fibrosis is a likely common final pathway and is quantifiable using MRI.

Methods and Results—Patients with ACHD (n=50) were studied with cardiac MRI to quantify systemic ventricular volume and function and diffuse fibrosis. The fibrosis index for a single midventricular plane of the systemic ventricle was measured by quantifying T1 values for blood pool and myocardium. Results were compared to healthy volunteers (normal controls, n=14) and patients with acquired heart failure (positive controls, n=4). Patients studied (age, 37±12 years; female sex, 40%) included 11 with a systemic right ventricle (RV), 17 with tetralogy of Fallot, 10 with cyanosis, and 12 with other lesions. The fibrosis index was significantly elevated in patients with ACHD compared to normal controls (31.9±4.9% versus 24.8±2.0%; P=0.001). Values were highest in patients with a systemic RV (35.0±5.8%; P<0.001) and those who were cyanotic (33.7±5.6%; P<0.001). The fibrosis index correlated with end-diastolic volume index (r=0.60; P<0.001) and ventricular ejection fraction (r=−0.53; P<0.001) but not with age and oxygen saturation in patients who were cyanotic. Late gadolinium enhancement did not account for the differences seen.

Conclusions—Patients with ACHD have evidence of diffuse, extracellular matrix remodeling similar to patients with acquired heart failure. The fibrosis index may facilitate studies on the mechanisms and treatment of myocardial fibrosis and heart failure in these patients. (Circ Cardiovasc Imaging. 2010;3:727-734.)

Key Words: heart defects, congenital ■ endomyocardial fibrosis ■ gadolinium ■ ventricular dysfunction ■ heart failure ■ cyanosis

Heart failure in patients with adult congenital heart disease (ACHD) is an increasingly common and life-threatening complication for a substantial portion of patients,1–4 yet the etiology is not well understood, and treatment options are largely empirical. Myocardial fibrosis, or abnormal accumulation of extracellular material in the myocardium, is a common final pathway of a number of cardiovascular stresses,5–6 leading to diastolic dysfunction, systolic dysfunction, arrhythmia, and increased mortality, developments that all respond favorably to pharmacotherapy.7–12

Limited studies suggest a similar pathway in ACHD, although evidence for proven response to medical therapy is lacking. Therefore, fibrosis is an ideal pathological marker on which to focus attention.

Clinical Perspective on p 734

In the 1960s, clinicians observed that exercise performance after surgical repair of congenital defects was still below that of normal individuals and postulated the presence of a “myocardial factor” responsible for the persistent limitation.13 This important observation was likely the first to acknowledge that repair of the anatomic defect could not guarantee full restoration of cardiovascular function. Several years later, pathologists identified changes within the myocardium of patients with ACHD, including interstitial fibrosis, confirming the notion of the myocardial factor.14–16 Few studies have continued this line of investigation. Surgical samples in young patients with tetralogy of Fallot showed fibrosis in 65%;17 Recent interest has been revived by the use of late gadolinium enhancement (LGE) by MRI, which has demonstrated macroscopic fibrosis in both the right ventricle (RV) and the left ventricle (LV) in ACHD.18–22 However, the method is not conducive to quantify diffuse microscopic fibrosis.

The capacity to detect, quantify, and follow myocardial fibrosis offers tremendous advantage in efforts to study...
etiology and response to therapy. Quantification of T1 changes before and after gadolinium (Gd) administration during MRI has been successfully used to differentiate normal and abnormal hearts. We have further developed this method and used it to quantify myocardial extracellular volume fraction as a marker of extracellular matrix remodeling which we term the fibrosis index. The method is objective and independent of cardiac output, Gd dose, or imaging timing. It can be widely applied and serially obtained. We sought to apply this method for detection and quantification of fibrosis in patients with ACHD.

Methods

Patient Selection

Consecutive patients with ACHD referred for MRI at our institution were studied according to accepted clinical standards, including the use of Gd. Specifically, though not exclusively, we focused on 3 diagnostic subgroups: (1) patients with a systemic RV (L-transposition of the great arteries or D-transposition with prior atrial redirection surgery) (n=11); (2) repaired tetralogy of Fallot (n=17); and (3) cyanotic heart disease, including Eisenmenger syndrome (n=10). These conditions were targeted because systemic ventricular dysfunction is a known complication in each, they are commonly referred for MRI, and fibrosis has been shown by LGE in all 3. Additional patients with other congenital abnormalities with an assumed increased likelihood of diffuse fibrosis (n=12) also were included. In addition, we studied patients with dilated or ischemic cardiomyopathy with visible replacement fibrosis (positive controls, n=4) and healthy volunteers (normal controls, n=14). Groups are summarized in Table 1. The protocol was approved by the Institutional Review Board, and healthy volunteers signed informed consent before participation.

MRI Protocol

Patients were studied using either a 1.5-T (Philips Achieva) or a 3-T (Philips Intera) scanner, depending solely on scanner availability. Short-axis images through the heart were obtained to quantify RV and LV volume and function using established methods. Phase velocity flow mapping through the aorta and pulmonary artery were used as confirmation of ventricular stroke volumes. Measurements of T1 were made using a Look-Locker technique (a gradient echo sequence with a nonslice selective inversion pulse initially after the R wave followed by segmented gradient echo acquisition for 21 cardiac phases over 2 to 3 cardiac cycles) (temporal resolution, 40 ms; slice thickness, 8 mm; repetition time, >3 R-R intervals) for a single midventricular plane. This type of sequence often is used for determination of optimal nulling for delayed enhancement (inversion time scout). This same Look-Locker acquisition was repeated, using the same midventricular plane, and at various intervals 3 to 25 minutes after injection of Gd-diethylenetriamine penta-acetic acid (Omniscan, 0.15 mmol/kg), interwoven during the LGE portion of the study. LGE was studied in the usual manner 10 to 20 minutes after Gd administration. Total scan times were typically 50 to 90 minutes, depending on the clinical questions addressed. Scans were done according to clinical need, not purely for study purposes.

Fibrosis Index Quantification

For each T1 sequence, the endo- and epicardial borders of the systemic ventricle were traced (Figure 1A) and divided into 6 standard segments (Mass CMR software; Medis; Leiden, The Netherlands). We did not study the subpulmonic ventricle in any patient. The signal intensity versus time curve for each segment and blood pool was used to determine a segmental T1 through exponential fitting (Figure 1B) and its reciprocal R1. This was done for each Look-Locker acquisition. The slope of the linear relationship between R1 for myocardium versus blood from all R1 measurements before and after Gd administration defined the partition coefficient for Gd, or \( \lambda \) (Figure 1C), and values for all 6 myocardial segments were averaged. To obtain the myocardial volume of distribution of Gd, or extracellular volume fraction, the partition coefficient was.
multiplied by \((1 - \text{hematocrit}/100)\), which we refer to as the fibrosis index.

**LGE**

Areas of late enhancement (unrelated to sites of expected surgical intervention, such as a ventricular septal defect patch) were identified and categorized by location. To determine whether the presence of LGE influenced the fibrosis index, we quantified the area of LGE within the midventricular plane used for the fibrosis index, expressed as a percentage of total myocardial area in the plane (% area LGE). In this quantification, we included any enhancement in the RV-LV junction that overlapped with the region of interest drawn for the fibrosis index.

**Statistical Analysis**

Results are presented as mean±SD. One-way ANOVA was used to compare fibrosis index values for all ACHD subgroups and both positive and normal controls, with Tukey post hoc analysis (SPSS version 11.0). Age, systemic ventricular ejection fraction (EF), and end-diastolic volume index (EDVi) also were compared in the same manner. Student \(t\) test was used to compare patients with versus without LGE. Pearson correlation coefficient was used to correlate the fibrosis index with age, oxygen saturation in patients who were cyanotic, ventricular volumes, EF, and % area of LGE. To test whether the association of EDVi, EF, and age with the fibrosis index varied among diagnostic groups, an interaction between fibrosis index and diagnostic group was included in linear regression models. Nonparametric methods (Kruskal Wallis test with follow-up Mann-Whitney comparisons and Spearman correlation coefficients) were used to assess the sensitivity of the results to standard parametric assumptions. One-way ANOVA for repeated measures was used to detect a possible association between mean fibrosis index and the index in specific myocardial segments.

**Results**

Fifty patients with ACHD were studied (age, 37±12 years; range, 18 to 71; female sex, 20). In addition to the target subgroups (Table 1), we studied 4 patients with pressure overloading (3 with coarctation of the aorta and 1 with bicuspid aortic stenosis), 5 with volume loading (systemic atioventricular valvular regurgitation or shunts), 2 with single ventricle Fontan palliation, and 1 with prior Rastelli repair. In addition, we studied 4 positive controls and 14 normal controls. Positive controls were significantly older. From the entire group (including controls), 25 studies were performed at 3.0 T and 43 at 1.5 T, with no overall difference in the fibrosis index between them \((P=0.40)\), including no differences between them for normal controls specifically. Fibrosis index values for all groups are shown (Table 2). Overall comparisons among groups was highly significant (ANOVA \(P<0.0001\)). The fibrosis index was significantly elevated in patients with ACHD compared with normal controls \((31.9\pm4.9\% \text{ versus } 24.8\pm2.0\%\); \(P=0.001\)) and was comparable to the mean fibrosis index in positive controls \((36.2\pm5.7\%\); \(P=0.1)\). Values were highest in patients with systemic RV \((35.0\pm5.8\%\); \(P=0.001\) versus normal controls) and who were cyanotic \((33.7\pm 5.6\%\); \(P<0.001\) versus normal controls). The fibrosis index correlated with EDVi \((r=0.60; 95\% \text{ CI}, 0.42 \text{ to } 0.73; P<0.001)\) (Figure 2) and EF \((r=-0.53; 95\% \text{ CI}, -0.68 \text{ to } -0.34; P<0.001)\) (Figure 3) but not with age \((r=0.11; 95\% \text{ CI}, -0.13 \text{ to } 0.34; P=0.37)\).

There was no evidence that the association of EDVi, EF, and age with the fibrosis index varied among diagnostic groups; therefore, the data for the patients with ACHD were pooled. Results were similar when using nonparametric procedures. As mean±2 SD for the control group was 28.8%, we defined an abnormal fibrosis index as any value ≥29%.

**Subgroup Differences**

Of the 11 patients with systemic RV, 10 had abnormal fibrosis index values. There was a positive relationship between EDVi (morphological RV) and the fibrosis index \((r=0.65; P=0.03)\) and a nonsignificant trend with EF \((r=-0.40; P=0.2)\). There was no association with age. Two patients had severe tricuspid regurgitation, including the patient with the highest value of 46% who had an EF of 45%. There was no association with tricuspid valve regurgitant fraction (estimated by stroke volume comparisons).

All patients with tetralogy had been repaired, and none were cyanotic. The mean fibrosis index for the LV was higher than for normal controls \((29.2\pm3.4\%\), although this did not reach statistical significance \((P=0.051)\). The value was abnormal in 9 of the 17 patients. The patient with the highest fibrosis index (value of 38%) had severe LV dysfunction (EF, 30%). Overall, there was no correlation with LV EDVi or EF as seen in the other subgroups. There was also no correlation between the fibrosis index (for the LV) and RV size or function. We did not measure the fibrosis index for the RV. There was a nonsignificant correlation between the pulmonary valve regurgitant fraction and the fibrosis index \((r=0.44; P=0.086)\). Patients with an abnormal fibrosis index \((n=9)\) compared with those with normal values \((n=8)\) more often had moderate-to-severe pulmonary regurgitation \((P=0.02, \text{ Fisher exact test})\) and fewer prior cardiac surgeries (range, 1 to 3 surgeries; \(P=0.034\) by \(\chi^2\) test). We found no significant differences in prior shunt placement, age at time of shunt placement, or age at time of repair.

To determine the influence of the RV on septal fibrosis in tetralogy of Fallot, we compared fibrosis index values of the 6 segments of the myocardial wall in all 17 patients, using a random effects model. Range of fibrosis index measures for the patients with tetralogy of Fallot by segment were as follows: anterior, 21.7 to 37.1; anterior-septal, 23.7 to 39.5; inferior-septal, 21.1 to 41.5; inferior, 24.9 to 40.8; lateral 23.1 to 34.9; and posterior, 23.5 to 33.2%. Similar ranges for

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<th>Table 2. Fibrosis Index</th>
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<tr>
<td><strong>Mean±SD</strong></td>
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<tr>
<td>Normal control</td>
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<tr>
<td>Systemic RV</td>
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<td>Cyanosis</td>
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Results of the fibrosis index by subgroup. Omnibus \(P<0.0001\). Tukey method used for follow-up comparisons.
normal controls were as follows: anterior, 20.6 to 29.3; anterior-septal, 18.7 to 29.9; inferior-septal, 21.4 to 29.5; inferior, 21.6 to 31.5; lateral, 19.6 to 27.1; and posterior, 19.6 to 26.3%. ANOVA for repeated measures indicated that in patients with tetralogy, there was a significant variation of the means of the fibrosis index among segments \((P < 0.009)\). In normal controls, the same test did not indicate any significant variation among segments \((P > 0.127)\). The largest values for the fibrosis segment in patients with tetralogy were observed in the inferior segments. Post hoc paired comparisons confirmed that among the 6 myocardial segments, the inferior segment had higher fibrosis index values compared with all other segments \((P < 0.05\) with Bonferroni correction) except the inferior-septal segment. Relative to the anterior segment, this difference of fibrosis index only amounted to a trend \((P = 0.1)\). Therefore, the septum was not disproportionately affected compared to other myocardial segments.

In the 10 patients cyanosis (mean oxygen saturation, 80±4%), 9 had abnormal values. There was a strong correlation between the fibrosis index and systemic EDVi \((r = 0.72; \ P = 0.019)\) and EF \((r = -0.86; \ P < 0.001)\). There was no correlation of the fibrosis index with resting oxygen saturation (mean, 80±4%) or age. Even after exclusion of patients with cyanosis from the rest of the cohort, relationships of the fibrosis index with EDVi and EF remained significant for the remaining patients \((r = 0.493 \text{ and } r = -0.451\) respectively; \(P = 0.001)\).

Ten of the 12 other patients with ACHD had abnormal fibrosis coefficient values, including all 3 with coarctation, 5 with volume loading, and both with Fontan palliation. One patient with a prior surgical repair of a ventricular septal defect was normal, as was a patient with bicuspid aortic valve stenosis.

LGE

Of the total ACHD cohort, 2 patients (1 cyanotic and 1 systemic RV) had poor LGE data from difficulty nulling and were not included. Of the remaining cohort, LGE was present in the systemic ventricle in 27 (56%) patients, specifically 5 of 10 transposition, 12 of 17 tetralogy, 5 of 9 cyanotic, and 5 of 12 other ACHD. The most common LGE finding was enhancement at the RV-LV junction, and in 12 patients (7 with tetralogy), this was the only area of enhancement present. The majority of other positive LGE findings involved small portions of septum or papillary muscle. Only 1 patient had transmural enhancement consistent with a small myocardial infarction known from a perioperative coronary embolism. There was no difference in the fibrosis index between patients with and without LGE \((31.2 \pm 4.8\% \text{ versus } 33.2 \pm 5.1\%; \ P = 0.17)\). All patients with acquired heart disease had visible LGE within the plane selected for the fibrosis index.

The % area LGE in patients with ACHD was significantly lower than the amount seen in acquired heart disease \((3.0 \pm 2.8\% \text{ versus } 14.1 \pm 6.3\%; \ P < 0.001)\). For all patients with ACHD, there was no correlation between the fibrosis index and % area LGE \((r = 0.22)\) (Figure 4). In 5 patients, the LGE findings were not present in the plane used for LGE. Even excluding these patients, there was no relationship between % area LGE and the fibrosis index \((r = 0.27)\).

Discussion

Patients with ACHD show evidence of myocardial extracellular matrix expansion causing an enlargement of the volume of distribution of Gd, namely the fibrosis index. We found a relationship between this index and ventricular volume and systolic function across a subset of patients with ACHD. This finding is congruous with histopathologic studies demonstrat-
ing diffuse fibrosis in ACHD. Together with other data showing neurohormonal activation, exercise intolerance, and mortality similar to patients with acquired heart failure, our findings provide additional evidence that ACHD is a form of progressive heart failure with a pathological process similar to other etiologies.

We used a technique for assessing diffuse fibrosis based on changes of T1 after Gd administration. Gd-contrast-based changes in myocardial R1 accurately reflect Gd concentration and relative distribution volume with good reproducibility and correlate with histological evidence of fibrosis even in the absence of LGE. The methodology avoids the necessity of defining “normal” myocardium for nulling, as is done with LGE imaging. However, reliance on T1 alone as an indicator of extracellular remodeling requires consistency in Gd dosing and timing of postcontrast image acquisition. The method used here overcomes this by measuring the myocardial partition coefficient for Gd-based contrast whereby the R1 changes in myocardium are normalized by the R1 changes in the blood. Correcting for hematocrit to account for changes in plasma Gd concentration gives the fibrosis index, a measure of extracellular volume fraction. Increased extracellular volume implies the presence of diffuse interstitial fibrosis. The normal range in our study agrees with other estimates of the extracellular myocardial volume. Our data cannot exclude the possibility that replacement fibrosis (or frank myocyte necrosis) contributed to the observed findings. However, elevation of the fibrosis index was not explained by visible LGE and was found diffusely across wall segments. Although the presence of LGE will raise the fibrosis index, as we found in positive controls, the patients with ACHD had fibrosis index values far greater than what could be explained by visible LGE alone (Figure 4), and 21 patients had no LGE in the selected plane despite an elevated fibrosis index. These findings are consistent with the interpretation that diffuse microscopic fibrosis is present.

The amount of LGE seen in target subgroups was generally consistent with previous reports. Although degree of LGE in patients with tetralogy and D-transposition correlates with adverse clinical variables, the clinical relevance of LGE in patients with Eisenmenger syndrome remains undetermined. One possible reason for this finding may be the difficulty of quantifying LGE when the fibrotic change may be much more diffuse, as has been described in cardiac amyloidosis. Indeed, difficulty nulling may reflect the diffuse nature of extracellular myocardial change, and nulling with shorter inversion times would effectively suppress the evidence of diffuse fibrosis.

Our use of positive controls specifically included patients with visible fibrosis on LGE, including patients with both ischemic and nonischemic cardiomyopathy. We recognize that not all patients with nonischemic cardiomyopathy will necessarily have visible fibrosis by LGE; therefore, we also made comparisons on patients with idiopathic cardiomyopathy from our previous study. We identified 7 patients (5 men; age, 59 ± 16 years) with reduced LV function (LV EF, 32 ± 14%) and quantified the fibrosis index for each. The fibrosis index (mean, 31.4 ± 4.6%) was significantly higher than normal controls in the present study (P < 0.001), but not different from our ACHD cohort or positive controls (P = 0.78 and P = 0.16, respectively). There were significant correlations within this group between the fibrosis index and EDVi and EF (r = 0.51 and r = −0.59, respectively), and the index did not increase with age. These confirmatory findings also support the similarities between ACHD and acquired heart failure.

**Specific Subgroup Considerations**

Extracellular remodeling was present in all 3 diagnostic subgroups (although less so in tetralogy of Fallot), despite likely differences in the pathogenesis of myocyte dysfunction in each, such as volume and pressure loading, abnormal ventricular geometry, previous cardiopulmonary bypass, or chronic myocardial ischemia. The finding that diffuse interstitial fibrosis is present to some degree in all 3 groups underscores this as a common final pathway and invites further study into specific inciting mechanisms in each subgroup.

We found comparatively less fibrosis in the tetralogy group, which generally had less evidence of heart failure. Although systolic dysfunction is more common in the RV in

![Figure 4](http://circimaging.ahajournals.org/) Relationship between fibrosis index and the % area LGE (area of positive late enhancement/total area of myocardium in the selected plane) for patients with ACHD. There was no correlation, and many patients with a significantly elevated fibrosis index had little or no detectable LGE. By comparison, patients with acquired heart disease had area LGE values of 16% to 20% (data not shown). Dotted line is the upper limit of normal.
this group, we measured fibrosis in the LV. LV dysfunction is increasingly common and has prognostic significance,\textsuperscript{40,41} although very little is known about its etiology. In practical terms, it is harder to reliably demarcate the thin-walled RV. In this limited subgroup, we found no evidence of interventricular interaction that might explain the development of fibrosis in the LV through electromechanical or neurohormonal coupling with the RV. However, the finding of more-severe PR in patients with higher LV fibrosis does suggest a role of RV loading.

Other patients included those with pressure loading. All patients with coarctation were previously repaired and did not have restenosis at the time of the study. The patient with bicuspid valve stenosis had moderate stenosis, although the fibrosis value was not elevated as we would have expected. The patient was asymptomatic, and it is possible that fibrosis had not yet occurred in response to the load.

**Clinical Implications and Future Directions**

The importance of our data lies not only in demonstration of diffuse fibrosis, but also in the potential application of the fibrosis index as a tool for future studies. The quantification of diffuse fibrosis serially over time has tremendous implications for both therapeutic and mechanistic studies.

Therapeutically, studies of specific medications known to attenuate or reverse fibrosis can use this method for detecting change noninvasively in specific patient groups. To date, studies generally have not succeeded in showing a favorable impact of these drugs using clinical end points.\textsuperscript{42,43} An exception to this was the report that patients with tetralogy with restrictive RV physiology randomized to lisinopril versus placebo for 6 months had a favorable increase in LV EF.\textsuperscript{44} This report is interesting in light of our data, which suggest a possible rationale for the findings, namely, that restriction is known to be associated with fibrosis, and fibrosis should improve with angiotensin-converting enzyme inhibitor therapy. Small studies with surrogate end points such as the fibrosis index will be easier to fund and coordinate. These in turn can provide important pilot data to support larger multicenter studies with hard clinical end points, including exercise capacity, arrhythmia, or even mortality, which are tremendously lacking in the field.

Mechanistically, the identification of key inciting events that trigger fibrogenesis as well as their biochemical pathways will manifest differences between subgroups and be the key to prevention. Using the fibrosis index in either humans or animal models coupled with biomarkers of inflammation, neurohormonal activation, or collagen deposition, we may demonstrate to what extent fibrogenesis is induced by pressure loading, myocardial ischemia, cardiopulmonary bypass, or microvascular thrombosis. In addition, the method can be applied to other patient groups susceptible to ventricular dysfunction.

**Limitations**

Our study uses an approach that is relatively novel. Only a single midventricular slice was quantified, and analysis is time consuming. The fibrosis index measures extracellular volume, which may be increased from processes other than fibrosis (e.g., acute inflammation, infiltrative processes). The relation between the partition coefficient of Gd (on which the fibrosis index is based) and collagen volume fraction (the gold standard for quantifying fibrosis) has only been tested ex vivo,\textsuperscript{28} which by necessity uses a different method of Gd diffusion. Obtaining histological confirmation was not feasible here, although correlation between histology and T1 measurements has been demonstrated.\textsuperscript{25} Only systolic function was measured, although diastolic function would be expected to correlate with fibrosis. Further study will be required for additional validation. The method requires exclusion of patients with pacemakers or implantable cardioverter-defibrillators. Because the need for pacing or arrhythmia may be associated with myocardial fibrosis, this selection bias may exclude patients with more extreme fibrosis. Our study has limited power, and thus the lack of association/correlation does not necessarily mean that an association would not be found with a larger sample size, which is especially relevant for tests involving the 4 positive controls.

**Conclusions**

In congenital heart disease, it is becoming increasingly evident that protection of the myocardium should be given as much attention as the hemodynamics early on in a patient’s life for both preservation of ventricular function and improved survival. This study demonstrates that remodeling of the extracellular matrix, or myocardial fibrosis, which can be quantified serially and noninvasively, is associated with adverse ventricular enlargement and declining ventricular function across different forms of congenital heart disease. The data confirm that myocardial fibrosis is a common final pathway leading to myocardial dysfunction and opens further possibilities for much-needed research into both etiology and treatment of these patients.

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**CLINICAL PERSPECTIVE**

There is growing recognition that progressive myocardial dysfunction in patients with congenital heart disease contributes substantially to clinical heart failure, arrhythmia, and mortality. MRI with late gadolinium enhancement has been used to demonstrate areas of replacement fibrosis in several subgroups of congenital heart disease, confirming that myocardial fibrosis is a likely final common pathway in these patients. However, late enhancement identifies dense replacement fibrosis and is not as amenable to detecting smaller amounts of diffuse, microscopic fibrosis. To quantify myocardial fibrosis, we used a modified Look-Locker sequence to quantify a “fibrosis index” based on T1 times for a single short-axis plane of the systemic ventricle before and after administration of gadolinium-based contrast. In 50 patients with congenital heart disease, the fibrosis index was significantly elevated in patients compared with normal controls and especially elevated in patients with a systemic right ventricle and those with cyanosis. The fibrosis index correlated with end-diastolic volume index and ventricular ejection fraction but not with age. Values for patients with congenital heart disease were largely similar to patients with cardiomyopathy. The findings lay the groundwork for further investigation on pathophysiology and treatment of heart failure specifically in congenital heart disease.
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