Arrhythmogenic Right Ventricular Dysplasia: Ex Vivo and in Vivo Fat Detection with Black-Blood MR Imaging

**PURPOSE:** To assess electrocardiographically gated spin-echo (SE) and double inversion-recovery fast SE magnetic resonance (MR) imaging in the depiction of intramyocardial fat in cadaveric heart specimens and patients with arrhythmogenic right ventricular dysplasia (ARVD).

**MATERIALS AND METHODS:** A phantom was used to determine the effective in-plane spatial resolution of SE and fast SE MR imaging protocols. Two cadavers with proved ARVD were imaged with identical sequences with spectrally selected fat suppression. Contrast-to-noise ratios (CNRs) of intramyocardial fat in the right ventricle (RV) were compared by using analysis of variance and Student t test with Bonferroni correction. Eleven patients with ARVD and 10 control subjects underwent fast SE MR imaging. Two blinded readers semiquantitatively evaluated images for fat conspicuity and image quality.

**RESULTS:** Fast SE MR imaging achieved better spatial resolution but lower CNR than that of gated SE imaging. CNRs in cadaveric specimens were higher for double R-R than for single R-R fast SE sequences for all section thicknesses (P < .0001). Absolute CNR values were higher for fat-suppressed fast SE sequences than for those without fat suppression. Cadaveric specimens demonstrated fatty infiltration from epicardium toward endocardium of the RV free wall. Intramyocardial fat was detected in eight of 11 (73%) patients with ARVD and in no control subjects (P < .001).

**CONCLUSION:** Intramyocardial fat detection in ARVD was better with fast SE MR imaging alone and combined with fat suppression than with gated SE MR imaging. When fast SE imaging is applied in vivo, however, breath-holding constraints limit the spatial resolution for RV fat detection.

Initially described in 1977, arrhythmogenic right ventricular dysplasia (ARVD) is a rare and often familial disease characterized pathologically by fibrous and fatty replacement of the right ventricular (RV) myocardium (1–2). Patients generally present with arrhythmias of RV origin, which may lead to sudden death (1–3). Clinical diagnosis is based on criteria proposed by the European Society of Cardiology and by the International Society and Federation of Cardiology Working Group on Cardiomyopathies and Dysplasia (Table 1) (1,4). Magnetic resonance (MR) imaging is superior to other noninvasive imaging modalities in the assessment of ARVD because it provides both RV tissue characterization and functional information (5–13). The sensitivity, specificity, and accuracy of MR imaging are not well defined, however, because there is no standard with which MR imaging has been compared (12).

Previous studies report a wide variability in MR imaging sensitivity for detection of fatty replacement in the RV free wall (6–14). While only one series (6) reports 100% incidence...
of fatty replacement at MR imaging, other studies (7–11,14) report an incidence of 22%–70%. The importance of fat detection relative to other findings such as wall motion abnormalities or wall thinning has not been established, and fat can be present in the normal myocardium in small amounts. Thus, the importance of cine studies for wall motion abnormalities combined with black-blood MR imaging for fat detection has been emphasized in the diagnosis of ARVD (6–8,11–14).

In prior studies, an electrocardiographically (ECG) gated conventional T1-weighted spin-echo (SE) MR sequence has been used for identification of fat signal (6–11,14). In addition, all of these studies were conducted at single centers. Recently, a multicenter reader study showed that conventional gated SE MR images were not useful for reliable detection of RV fat signal when patients with definite ARVD were compared with (a) patients suspected of having ARVD and (b) healthy control subjects (15). Conventional T1-weighted ECG-gated SE MR images are susceptible to artifacts from respiratory motion and blood flow. A more recently described black-blood MR technique uses a breath-hold fast SE MR sequence with a dual magnetization preparation pulse (double inversion-recovery) (16). This pulse sequence provides excellent suppression of the blood pool signal and allows acquisition of high-spatial-resolution images of small cardiac structures, such as valve leaflets and the coronary vessel wall (17–19). Motion artifacts are greatly reduced by using this method instead of SE MR imaging. This may lead to improved RV evaluation in patients suspected of having ARVD.

The purpose of this study was to assess MR imaging with ECG-gated SE and double inversion-recovery fast SE sequences for depiction of intramyocardial fat in cadaveric heart specimens and in patients with ARVD.

### MATERIALS AND METHODS

Our institutional review board approved the study, including the clinical investigation of cadaveric specimens of ARVD, and informed consent was obtained for all living individuals prior to MR examination. Cadaveric specimens were used with the written consent of family members.

#### Study Components

**MR imaging phantom.**—For parameter optimization, a high-spatial-resolution test was performed by using an American College of Radiology MR phantom (J.M. Specialty Parts, San Diego, Calif) placed in a head coil.

**Cadaveric heart specimens.**—Two formalin-fixed heart specimens were obtained at autopsy of two women aged 18 and 35 years. Both women died of sudden cardiac arrest and had pathologically proved ARVD.

**Patients and control subjects.**—Eleven patients (mean age, 36.9 years; age range, 16–58 years; six female patients with a mean age of 38.12 years and an age range of 25–46 years; five male patients with a mean age of 35.4 years and an age range of 16–58 years) with ARVD were examined prospectively with MR imaging at our institution. The diagnosis of ARVD for all patients was based on major and minor clinical criteria for ARVD (Table 1 [1–2]). MR imaging findings were not used as major or minor criteria for diagnosis of ARVD for these patients. In six of 11 patients (54%), the diagnosis was confirmed by means of tissue samples from endomyocardial biopsy. Two patients that received a diagnosis of ARVD on the basis of clinical criteria had negative results from endomyocardial biopsy of the septum for fibrofatty tissue. In the remaining three patients, endomyocardial biopsy was not performed, and diagnosis was assigned on the basis of clinical criteria. Ten control subjects that were matched according to age and sex (mean age, 32.7 years; age range, 25–41 years; four women with a mean age of 30.8 years and an age range of 25–41 years; six men with a mean age of 34.6 years and an age range of 25–40 years) underwent MR examination with an identical protocol. The control subjects were asymptomatic and had no evidence of ARVD on the basis of normal ECGs, electrocardiograms, and exercise stress test and physical examination findings.

**Imaging Protocol**

All studies were performed with a dedicated cardiovascular 1.5-T MR system

### TABLE 1

<table>
<thead>
<tr>
<th>Clinical Criteria for the Diagnosis of ARVD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criterion</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td><strong>Global and/or regional dysfunction</strong> and structural alterations</td>
</tr>
<tr>
<td><strong>Tissue characterization</strong></td>
</tr>
<tr>
<td><strong>ECG repolarization abnormalities</strong></td>
</tr>
<tr>
<td><strong>ECG depolarization and/or conduction abnormalities</strong></td>
</tr>
<tr>
<td><strong>Arrhythmias</strong></td>
</tr>
<tr>
<td><strong>Family history</strong></td>
</tr>
</tbody>
</table>

Note.—Diagnosis of ARVD requires fulfillment of (a) two major, (b) one major and two minor, or (c) four minor criteria.
MR imaging phantom.—To assess the blurring associated with fast SE imaging, a high-spatial-resolution test was performed by imaging the MR phantom in the transverse plane orthogonal to a resolution insert within the phantom. The insert contained three hole-array pairs, each with 31 small holes. The diameters of the array pairs were 1.1, 1.0, and 0.9 mm. Resolution was assessed for the SE, ECG-gated SE, and double inversion-recovery fast SE pulse sequences. T1-weighted SE images (repetition time [TR] msec/echo time [TE] msec, 300/14) were acquired, 14-cm FOV, 31.2-kHz bandwidth, and section thickness of 3, 5, and 7 mm. ECG-gated SE and double inversion-recovery fast SE sequences were then obtained with 28-cm FOV and section thicknesses of 3, 5, and 7 mm. An external triggering device (ECGplus; Bio-Tek Instruments, Winooski, Vt) with a frequency of 60 beats per minute (R-R interval of 1,000 msec) was used to simulate heart rate for the gated SE and fast SE sequences.

For the ECG-gated T1-weighted SE sequences (TR/TE, one heartbeat or R-R interval/TE), images were obtained with two signals acquired, 256 × 160 matrix, and 31.2-kHz bandwidth. The fast SE sequence was performed with a TR of one R-R interval and a short TE with a minimum value of 5 msec (hereafter, single R-R fast SE) or a TR of two R-R intervals and a TE of 30 msec (hereafter, double R-R fast SE). Thus, the resulting image data were acquired at end diastole for the double R-R interval and at end systole and/or early diastole for the single R-R interval.

With both single and double R-R intervals, imaging parameters were as follows: one signal acquired, 256 × 256 matrix, 62.5-kHz bandwidth, three-quarter rectangular FOV along the phase-encoding direction, and reconstruction with zero filling interpolation to 512 pixels. The fast SE sequence was also performed with four echo train lengths (ETLs) of 12, 16, 24, and 32. The imaging times for the double R-R fast SE sequence with these four ETLs were 36, 28, 20, and 16 seconds per imaging section, respectively. The imaging times for the single R-R fast SE sequence were half of these (18, 24, 10, and 8 seconds, respectively). The single R-R fast SE sequence was used with an increased matrix size of 384 × 256 in the frequency-encoding direction. In addition, the gated SE sequence was performed with a matrix size of 256 × 256 and 256 × 192 to simulate “clinical” spatial resolution limits.

Heart specimens.—During imaging, the heart specimens were placed on a transmit-receive extremity coil in a sealed plastic bag, which was wrapped in a temperature pad that was connected to a heating circulator (Model 801A; Polyscience, Niles, Ill) outside of the imager. Specimens were warmed to 37°C, and temperature was monitored continuously during imaging with a fiberoptic temperature probe (UM18; FISO Technologies, Sainte-Foy, Quebec, Canada). Imaging parameters were identical to those used for the MR phantoms described earlier. In addition, imaging was repeated with spectrally selective fat suppression for both single and double R-R fast SE sequences.

All SE and fast SE sequences were performed in a plane equivalent to an in vivo transverse plane. The high-spatial-resolution SE sequence (512 × 256 matrix, 14-cm FOV) was used as the reference for subsequent pulse sequence comparisons. From these images, three section positions with areas of increased intramyocardial signal intensity in the RV free wall, which corresponded to fatty changes, were chosen for subsequent pulse sequence comparisons.

Patients and control subjects.—MR imaging was performed by using ECG gating with fiberoptic leads (MR Equipment, Bay Shore, NY) and a dedicated phased-array surface coil. The parameters of the black-blood double inversion-recovery fast SE MR images for fat detection were based on imaging findings described earlier for the MR phantom and cadaveric optimization. Images were obtained by using breath-hold techniques to reduce respiratory motion. Fast SE images were obtained in a transverse plane from the diaphragm to above the level of the RV outflow tract with 4–5-mm section thickness and 5-mm spacing. Image reception was performed by using two anterior elements of a cardiac phased-array coil; posterior elements were switched off to avoid wrap-around aliasing artifacts with a reduced FOV of 24–28 cm. The remaining sequence parameters were similar to those used for phantom and specimen measurements: TR/TE, double R-R/30; 62.5-kHz bandwidth; ETL of 24–32; 256 × 256 matrix; and three-quarter rectangular FOV in the phase-encoding direction. Imaging time was dependent on heart rate and ranged from 8–20 seconds per section. Nine to 18 sections were obtained. Anterior saturation bands were routinely placed to decrease artifacts from the chest wall. Spectrally selective fat-suppressed fast SE imaging was also performed.

Image Analysis

MR imaging phantom.—The high-spatial-resolution test was performed by visually inspecting the smallest grid pattern that could be distinguished in both frequency- and phase-encoding directions at MR imaging. Assessment was performed independently by three readers, who had 10 (D.A.B) and 2 (E.C., H.T.) years of experience in cardiac MR imaging studies. If there was a discrepancy, majority opinion was used. No further statistical analysis of the measured resolution was performed.

Heart specimens.—Qualitative analysis of the high-spatial-resolution SE MR images was performed by two radiologists (E.C., D.A.B) and one pathologist (E.R.R.). Comparison of MR imaging and histologic findings was performed by means of consensus, and these results were used as the standard of reference. Quantitative image analysis was performed with a dedicated postprocessing workstation (Advantage Windows v4.0; GE Medical Systems) by one radiologist (E.C.). The contrast-to-noise ratio (CNR) (20) of high intramyocardial signal intensity (ie, higher than myocardial signal intensity) in the RV free wall that corresponded to fatty replacement was evaluated for all gated SE and fast SE MR sequences.

CNR was calculated in the three sections obtained with each pulse sequence as follows: A region of interest with an area of 0.1–0.2 cm² was placed within the zone of high intramyocardial signal intensity. A second region of interest of identical size was placed within the free wall of the left ventricular myocardium. The difference between the mean signal intensities of both regions of interest was divided by the SD of the signal intensity measured outside the specimen (noise region of interest, 1 cm²).

Patients and control subjects.—Fast SE MR images were evaluated by two independent readers (E.C., H.T.) who were blinded to whether images belonged to patients with ARVD or to control subjects. Images were shown to the readers in random order. The conspicuity of high signal intensity changes in the RV myocardium was rated as 1, definitely not present; 2, indeterminate because of...
technical reasons or only present on a single section; or 3, definitely present in at least two contiguous sections (21). Differences in the location of the high signal intensity within the RV free wall were resolved by means of consensus.

For overall image quality, a rating scale of 1–4 was used: 1, very good depiction of RV and left ventricular myocardium with complete blood suppression and no motion artifacts; 2, blood suppression possibly incomplete but allows a good and clear delineation of the RV free wall with minor or no motion artifacts; 3, fair blood suppression with free RV wall identified but incontinuously defined with minor degradation due to motion artifacts; and 4, poor blood suppression with RV free wall identified vaguely or not identified and major degradation due to motion artifacts.

**Statistical Analysis**

All statistical analyses were performed by using STATA 7.0 software (StataCorp, College Station, Tex). Continuous data were expressed as mean ± SD. Continuous variables such as CNR values within groups were analyzed by means of repeated-measures analysis of variance. Bonferroni correction was applied to Student t test results for multiple comparisons of section thickness and ETL. Differences in categorical variables between patients with ARVD and control subjects (a) for all individuals together as one group and (b) separately for female and male groups were also assessed with the χ² test. A two-tailed significance level of .05 was considered to indicate a statistically significant difference between groups.

**RESULTS**

**MR Imaging Phantom**

The in-plane pixel sizes and spatial resolutions of the various pulse sequences and section thicknesses (3, 5, and 7 mm) are shown in Table 2. A total of 45 MR images were evaluated, each depicting the resolution insert that contained three upper left and lower right array holes. Images that required a consensus opinion were acquired with double R-R fast SE (ETL of 12 and 32) and single R-R fast SE MR sequences. Examples of images obtained with the different protocols from the phantom resolution insert are shown in Figure 1.

**Heart Specimens**

*Comparison with histologic findings.—* The high-spatial-resolution SE MR images of one of the heart specimens showed marked adipose tissue infiltration along the entire RV free wall and outflow tract (Fig 2). This infiltration extended from the epicardium inward toward the endocardium along the perimysial connective tissue network, replacing bundles of myocyte fascicles. This type of replacement created a saw- or fingerlike pattern of irregular myocardial replacement.

The border between epicardial fat and RV myocardium in areas of fat replacement was faintly observed on some of the images as a thin and continuous hypointense line. Histologic findings demonstrated that this line corresponded to a few remaining scattered myocytes. The endocardial border of the thin myocardial wall (average thickness, 2 mm) could not be distinguished easily on SE MR images from the subendocardial muscular trabeculae, since the specimen was collapsed; this can give the impression of an overall thickened free wall (Fig 2).

On the SE MR images of the second necropsy specimen, the RV was mildly enlarged, the RV free wall was thickened, and there was nearly transmural fatty infiltration of the middle third of the anterior and diaphragmatic portions of the RV free wall. Again, the same fingerlike pattern of fatty infiltration was identified; it obscured the epicardial border and extended toward the endocardium (Fig 3). The “original” border between epicardial fat and the epicardium was replaced by fat and was not identified. In addition, there was also diffuse fatty infiltration of the RV free wall along the perforating branches of the coronary arteries; in these regions, the border between myocardium and epicardial fat was preserved.

*Quantitative analysis.—* The CNRs of fat versus myocardial signal intensity for the different pulse sequences are shown in

---

**TABLE 2**

Limiting Spatial Resolution in ECG-gated SE and Fast SE MR Sequences

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR</th>
<th>ETL</th>
<th>Matrix</th>
<th>Pixel Size (mm)</th>
<th>Encoding</th>
<th>3 mm*</th>
<th>5 mm*</th>
<th>7 mm*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gated SE</td>
<td>Single R-R</td>
<td>-</td>
<td>256</td>
<td>1.09</td>
<td>Frequency</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>192</td>
<td>1.43</td>
<td>Phase</td>
<td>&gt;1.1</td>
<td>&gt;1.1</td>
<td>&gt;1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>160</td>
<td>1.6</td>
<td>Phase</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Frequency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIR fast SE</td>
<td>Double R-R</td>
<td>12–32</td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12, 16</td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>DIR fast SE</td>
<td>Single R-R</td>
<td>12–32</td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.0</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12, 16</td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>DIR fast SE</td>
<td>Single R-R</td>
<td>12–32</td>
<td>256</td>
<td>1.09</td>
<td>Phase</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Note.—FOV was 28 cm for all sequences, and three-quarter FOV was used for fast SE sequences. Lower values indicate better spatial resolution. DIR = double inversion recovery. * Section thickness.
The highest CNR was obtained with the ECG-gated SE pulse sequence (3-mm section thickness, 62.4 ± 33.4; 5-mm, 73.3 ± 26.1; 7-mm, 79.8 ± 25.3). There was no statistically significant difference in CNR for the various section thicknesses. When the ETL was varied (12, 16, 24, 32) with the single and double R-R fast SE sequences, there was no statistically significant difference for the CNR obtained for a given section thickness (P = .99).

The double R-R fast SE sequences provided higher CNR (3-mm section thickness, 20.8 ± 1.1; 5-mm, 24.8 ± 1.8; 7-mm, 31.5 ± 1.2) than that of the single R-R fast SE sequence (256 × 256 matrix: 10.6 ± 0.7, 15.4 ± 1.2, and 20.4 ± 0.7 for 3-, 5-, and 7-mm section thickness, respectively; 384 × 256 matrix: 8.5 ± 0.88, 12.4 ± 1.36, and 11.2 ± 0.3 for 3-, 5-, and 7-mm section thickness, respectively). Within each type of modified fast SE sequence, the increase of CNR with thicker sections was statistically significant (P ≤ .008). A single exception to statistical significance was found in the high-spatial-resolution single R-R fast SE sequence for 5- and 7-mm section thickness (P = .37).

There was a statistically significant difference in CNR values of the double R-R fast SE sequence when compared with the single R-R fast SE sequence and the high-spatial-resolution single R-R fast SE sequence together as a group (P < .0001) and for the section thicknesses of 7 mm (double R-R fast SE vs single R-R fast SE, P = .03; double R-R fast SE vs high-spatial-resolution single R-R fast SE, P = .04) and 5 mm (P = .02 and .03, respectively) but not for 3 mm (both P = .1). The differences between the two modified single R-R fast SE sequences were not statistically significant when all section thicknesses were considered either as a group (P = .9) or separately (P = .9, .1, and .9 for 7, 5, and 3 mm, respectively). Figure 5 illustrates the influence of edge blurring due to increasing ETL and different TE's in the depiction of intramyocardial fatty foci within the RV free wall.

The differences in CNR when using fat suppression and double inversion-recovery fast SE MR imaging are shown in Figure 4. The highest CNR for fat suppression was obtained with single R-R fast SE

---

**Figure 4.** The highest CNR was obtained with 3-mm section thickness (1.1 mm). Images obtained with different protocols and a 5-mm section thickness are shown. A, High-spatial-resolution SE MR image (300/14, 14-cm FOV, 512 × 256 matrix) shows good resolution of all three hole diameters in the upper left and lower right arrays. B, ECG-gated SE MR image (one R-R/14, two signals acquired, 28-cm FOV, 256 × 192 matrix) shows well-resolved holes in all sizes along the frequency-encoding (anterior-posterior) direction but not along the phase-encoding (right-left) direction. C-E, Double inversion-recovery fast SE MR images with an ETL of 32, 28-cm FOV, and different TR's of double R-R (C) and single R-R (D and E, matrix sizes of 256 × 256 and 384 × 256, respectively). Along the frequency-encoding direction, the limiting spatial resolution was 1.0 mm for C and D and 0.9 mm for E because of increased resolution. Along the phase-encoding direction, all three fast SE images show limiting spatial resolution of 1.1 mm.
MR imaging (−72.3 ± 0.5, −111.7 ± 3.6, and −158.2 ± 4.2 for 3-, 5-, and 7-mm section thickness, respectively). CNR values were negative because fat had lower signal intensity than that of myocardium. Increasing the number of frequency-encoding steps to 384 for the single R-R sequence did not improve the CNR (−57.7 ± 0.6, −95.2 ± 2.2, and −131.5 ± 3.4 for 3-, 5-, and 7-mm section thickness, respectively). However, this still provided more contrast than did the dou-

Figure 3. Two RV sections from an 18-year-old woman who died suddenly while at rest. A, Gross pathologic specimen shows diffuse fatty infiltration (arrows) along RV myocardium. B, MR image obtained with a view equivalent to in vivo transverse plane with same SE sequence as that used in Figure 1 shows ill-defined hyperintensity that corresponds to fatty infiltration within RV myocardium (arrows) and preserved epicardial border (arrowheads). C, Higher-magnification MR image and, D, histologic specimen demonstrate predominantly fatty infiltration (arrows) along perforating branches of coronary arteries. This pattern is not specific for ARVD. In another slice obtained from same specimen (E–H), however, there is characteristic fatty infiltration pattern of ARVD. E, Transillumination of gross specimen shows paucity of myocardium deficiency in RV free wall secondary to fatty infiltration (arrows on E–H) with vanishing border of epicardial fat-myocardium interface (arrowheads on E–H). This correlates well with SE MR images (F, G) and histologic findings (H). (Masson trichrome stain; original magnification, ×5.5.)
Figure 5. Effect of ETL and section thickness on edge blurring for same specimen as in Figure 3. All images have 5-mm section thickness and were obtained with a view equivalent to the in vivo transverse plane. A, High-spatial-resolution SE MR image (14-cm FOV, 512 × 256 matrix). B, ECG-gated SE MR image with spatial resolution used clinically (28-cm FOV, 256 × 192 matrix). Note substantial loss in fat depiction on gated SE image. C–F, Double inversion-recovery fast SE (DIR-FSE) MR images (double R-R/30; increasing ETL of 12, 16, 24, and 32 for C, D, E, and F, respectively) show increasing edge blurring with loss in resolution of fatty changes. G–N, Fast SE (one R-R/5) MR images with identical ETL and matrix of 256 × 256 (G–J) and increased matrix of 384 × 256 along the frequency-encoding direction (K–N). Increased blurring is caused by shorter TE and slightly increased resolution of fatty changes with increased matrix size (arrowheads).
ble R-R fast SE MR sequence (−19.6 ± 1.1, −37.2 ± 0.6, and −45.5 ± 0.8 for 3-, 5-, and 7-mm section thickness, respectively). Figure 6 demonstrates the effect of fat suppression in the depiction of intramyocardial fatty infiltration.

Patients and Control Subjects

Demographic differences according to sex were not significant (P > .05) between groups of patients and control subjects considered either together or separately. Diagnostic criteria and MR findings regarding the presence of fat for the 11 patients are summarized in Table 3. High signal intensity within the RV myocardium that corresponded to fatty change was observed in eight of the 11 patients (73%) and in none of the age-matched healthy control subjects (P < .001). This difference was also present in the female (six of six, 100%) and male (two of five, 40%) groups when considered separately (P < .0001 and P = .007, respectively).

Among patients who underwent septal biopsy, fibrofatty changes were present, but isolated fatty deposits without fibrosis were not. Examples of intramural fatty infiltration as seen in vivo are shown in Figure 7. The presence of fat signal intensity on MR images was classified as indeterminate in three of 11 patients (27%). The two readers also disagreed on the location of fat in these three patients.

One patient had poor blood signal suppression in the region of subendocardial trabeculation. This caused multiple small areas of high signal intensity that could mimic fatty changes within the thinned RV free wall. Images from a second patient were degraded because of motion artifacts. A fat-suppressed fast SE MR sequence did not improve RV free wall visualization further. Readers disagreed as to the presence of fat in a third patient with an enlarged RV and scattered high signal intensity in the RV free wall and outflow tract. Fat-suppressed fast SE MR images showed decreased signal intensity in these areas when compared with non-fat-suppressed MR images (Fig 8). The relationship between image quality and arrhythmia status yielded no statistically significant difference (P = .6 in all cases) overall and separately for female and male patients.

DISCUSSION

The results of our study can be summarized as follows: (a) High-spatial-resolution MR images and histopathologic findings demonstrated a similar pattern of RV infiltration by fatty tissue in ARVD, primarily occurring at the epicardial border and extending inward toward the endocardium; (b) double R-R fast SE MR images with a TE of 30 msec, ETL of 24–32 or less if possible, section thickness of 5 mm, and FOV of 24–28 cm were superior to those obtained with other sequences that could be used clinically; and (c) even state-of-the-art clinical MR protocols involving the use of double inversion-recovery fast SE sequences may be limited in both spatial and contrast resolution.
for the detection of fine structural detail of fatty infiltration in ARVD.

The ECG-gated SE MR pulse sequence achieved the highest absolute CNR values but also the largest SD, which suggests considerable heterogeneity in the RV free wall among the cadaveric specimens. Although modified fast SE MR sequences achieved lower CNR values than those of gated SE sequences, they overcame some of the limitations of long imaging times and insufficient blood suppression of the gated SE sequence. A double inversion-recovery magnetization preparation pulse ensures that signal from the blood pool is adequately suppressed (16). Breath-hold fast SE sequences consistently provide end-diastolic images with minimal motion artifacts and improve resolution of small cardiac structures, such as valve leaflets and the coronary vessel wall (17–19).

A potential disadvantage of fast SE MR sequences is increased edge blurring with longer ETLs. Clinical imaging protocols with double inversion-recovery fast SE imaging involve the use of an ETL of at least 20–32 to obtain single-section images within a breath hold (16). In the case of nontransmural fatty infiltration, an ETL of 24 or more compromised fat detection in the cadaveric study. In vivo, edge blurring is likely to be compounded further by small amounts of motion that occur during breath holding. We explored the potential to reduce the ETL to 12–16 by using a TR of one R-R interval. This resulted in an intermediate-weighted MR image (depending on the heart rate) and reduced fat signal intensity that was otherwise relatively increased on T2-weighted fast SE MR images obtained with double R-R sequences (22).

Edge blurring increases not only with the number of echoes in the echo train but also with increased echo spacing. Echo spacing may be reduced with higher bandwidth, reduced matrix, or increased FOV. A high receiver bandwidth (62.5 kHz) was used for all measurements performed in the study. We used a single R-R sequence with the minimum TE available (5 msec). This resulted in a slight increase in edge blurring compared with the TE of 30 msec. We also examined the effect of increasing the frequency matrix to achieve higher spatial resolution. Investigators in previous studies with gated SE sequences have used frequency-encoding values of 256–320 and phase-encoding values of 128–256 (5–11,14) with FOVs similar to those in the current study. An increase in the frequency encoding of the single R-R fast SE sequence to 384 slightly increased the spatial resolution by 0.1 mm at the expense of further decreased CNR compared with the single and double R-R fast

---

**Figure 7.** Clinical application of optimized MR pulse sequence. (a) MR image in a 45-year-old woman with histologically proved ARVD. Transverse double inversion-recovery fast SE image (double R-R/30, ETL of 32) shows hyperintensity within RV free wall (subtricuspid and midwall regions, arrows) beyond original epicardial border (arrowheads), which corresponds to fatty infiltration. (b) Similar findings are observed for a 35-year-old woman with a diagnosis of ARVD based on standard criteria. Again, on the transverse image there is extensive fatty infiltration of the RV myocardium along the free wall (arrows) beyond the original epicardial border (arrowheads).

<table>
<thead>
<tr>
<th>Patient No./ Age (y)/Sex</th>
<th>RV Biopsy Finding</th>
<th>Diagnostic Criteria Fulfilled</th>
<th>Fat Conspicuity Major</th>
<th>Fat Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/58/M /58/M Fibrofatty 2 2 Present RV outflow tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/40/M /40/M Fibrofatty 2 0 Indeterminate Subtricuspid and middle free wall, RV outflow tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/45/F /45/F Fibrofatty 1 3 Present Subtricuspid and middle free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/25/F /25/F Fibrofatty 1 2 Present Subtricuspid and middle free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/45/F /45/F Fibrofatty 1 2 Present RV outflow tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/23/M /23/M Fibrofatty 1 2 Present Subtricuspid and middle free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7/16/M /16/M Normal 1 2 Indeterminate Apical free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/40/M /40/M Normal 1 2 Present Subtricuspid and middle free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/46/F /46/F NP 1 2 Present Subtricuspid and middle free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/33/F /33/F NP 1 2 Present Subtricuspid and middle free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11/35/F /35/F NP 1 2 Present Subtricuspid and middle free wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note.** NP = not performed.
SE sequences. Thus, the small gain achieved in limiting spatial resolution did not outweigh the CNR loss.

The section thickness used most commonly in previous studies of ARVD ranged between 7 and 10 mm (6–10), although two groups used 5 mm (11,14). In our study, the highest CNR for all sequences was obtained with 7-mm section thickness, with exception of the high-spatial-resolution single R-R fast SE sequence, mainly because of a decrease in the SD of background noise. However, the limiting spatial resolution did not vary for the different section thicknesses we examined. Thus, we consider a section thickness of 5 mm to be optimal for clinical studies as a good compromise in the complex relationship between thinner sections for higher spatial resolution and thicker sections to increase CNR and for avoidance of blurring that occurs with thicker sections. Potential improvements to increase the spatial resolution may come from newer coil designs, parallel imaging techniques (ie, simultaneous acquisition of spatial harmonics, or SMASH, and sensitivity encoding, or SENSE), and navigator-based free-breathing techniques (23–24).

Despite the importance of fat detection in ARVD, fat-suppressed MR techniques have not been evaluated thoroughly for this diagnosis. Recently, Schick et al (25) proposed a spectrally selective fat-suppressed sequence for breath-hold cine gradient-echo MR imaging, although cine sequences are commonly used only for functional assessment and not for tissue characterization. Our results showed higher absolute CNR values for the fat-suppressed double inversion-recovery fast SE sequence for the 5- and 7-mm section thickness than those for the T1-weighted gated SE sequence. In addition, the absolute CNR values were also higher than those obtained without fat suppression by using the fast SE sequences. Fat suppression may therefore be considered as an additional option to increase the confidence of fat detection in clinical studies. However, a detailed examination of the clinical benefit of fat suppression techniques was beyond the scope of our study.

The implication of the proportion of myocardial replacement with fat and fibrous tissue in ARVD is controversial (26,27). Initial reports based on extensive experience in northern Italy outlined two pathologic patterns, the fatty and fibrofatty variants (27). However, fat has been demonstrated to be present in the normal RV, especially in the anterior wall. Fat signal may be present in more than 50% of normal hearts in the elderly population and those with morbid obesity (27–29). Therefore, fat replacement of the RV without fibrosis has been proposed as a distinct clinical-pathologic entity, termed fat dissociation syndrome, with low arrhythmogenicity (27,30).

Contrary to some pathology reports, grossly visible fat replacement is not a sine qua non for the diagnosis of ARVD, and only minimal or microscopic fat replacement, fibrosis, and degenerating myocytes trapped within the fibrosis are thought to be more typical and diagnostic (31). On the basis of our results, considering the usually thin RV free wall (mean thickness of 2.7 mm ± 0.4 to 4.2 mm ± 1.2 [26,27]), fat can be detected with clinical double inversion-recovery fast SE protocols when there is more than 30%–40% myocardial wall replacement. The thinned myocardial RV free wall that can be present in ARVD compounds this further. Thinning of the RV myocardium and functional wall abnormalities assessed with bright-blood cine MR sequences are as important or even more important clinically than the demonstration of fatty tissue itself (6–8,11–14). However, we did not include these imaging features in our study, since we were not able to evaluate them ex vivo.

One limitation of the present study is that only two cadaveric specimens were available. To date, only two studies have shown a correlation between pathologic findings and MR imaging findings (8,26).
To our knowledge, this is the first study in which quantitative CNR measurements were obtained on the basis of MR images of cadaveric ARVD specimens. Although these individuals died from arrhythmias associated with ARVD, we cannot speculate if these specimens are representative of this disease. Unfortunately, we did not have in vivo MR images of these individuals, since sudden death was the first manifestation of ARVD for both.

Another methodologic limitation comes from the endomyocardial biopsy results of the patients with ARVD. In two patients that received a clinical diagnosis of ARVD, the biopsy results were negative, and in another three patients, biopsy was not performed. Endomyocardial biopsy for diagnosis of ARVD is characterized by a low sensitivity (67%) and high specificity (92%) (32). The main reason for this phenomenon is the usually limited tissue sampling from the interventricular septum, which is involved in only 20% of positive cases, rather than from the RV free wall (32). Therefore, endomyocardial biopsy is not routinely recommended to confirm diagnosis of ARVD (1–2).

Another limitation of the study is the small number of patients with ARVD, which reflects the rarity of this disease. The lack of histologic proof for part of our patient population is an additional limitation of the study.

Our results show the challenge of demonstrating fine intramyocardial detail in patients with ARVD, even when state-of-the-art cardiovascular MR imaging is used. Optimized MR images were obtained by using a double R–R fast SE sequence with a short TE of 30 msec, a section thickness of 5 mm, and an ETL of 24–32 or less according to the breath-holding capability of the patient. The additional use of fat suppression improves the CNR of this sequence. Further prospective multicenter clinical studies based on these initial data are currently in progress.

References