



Impact of the Revision of Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia Task Force Criteria on Its Prevalence by CMR Criteria

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OBJECTIVES The purpose of our study was to assess the impact of revised versus original criteria on the prevalence of arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) criteria in cardiac magnetic resonance (CMR) studies.

BACKGROUND Recently, the ARVC/D task force criteria have been revised, aiming for a better diagnostic sensitivity. The implications of this revision on clinical decision making are unknown.

METHODS We retrospectively evaluated the CMR scans of 294 patients referred for ARVC/D between 2005 and 2010, and determined the presence or absence of major and minor CMR criteria using the original and the revised task force criteria. Previously, major and minor abnormalities were identified by the presence of right ventricle dilation (global or segmental), right ventricle microaneurysm, or regional hypokinesis. The revised criteria require the combination of severe regional wall motion abnormalities (akinesis or dyskinesis or dyssynchrony) with global right ventricle dilation or dysfunction (quantitative assessment).

RESULTS Applying the original criteria, 69 patients (23.5%) had major original criteria, versus 19 patients (6.5%) with the revised criteria. Forty-three patients (62.3%) with major original criteria did not meet any of the revised criteria. Using the original criteria, 172 patients (58.5%) had at least 1 minor criterion versus 12 patients (4%) with the revised task force criteria; 167 patients (97%) with minor original criteria did not meet any of the revised criteria. In the subgroup of 134 patients with complete diagnostic work-up of ARVC, 10 patients met the diagnosis of proven ARVC/D without counting imaging criteria. Only 4 of 10 met major criteria according to the revised CMR criteria; none met minor criteria. However, 112 of 124 patients without ARVC/D were correctly classified as negative by major and minor criteria (specificity 94% and 96%, respectively).

CONCLUSIONS In our experience, the revision of the ARVC/D task force imaging criteria significantly reduced the overall prevalence of major and minor criteria. The revision, although maintaining a high specificity, may not have improved the sensitivity for identifying patients with ARVC/D. Larger studies including follow-up are required. (J Am Coll Cardiol Img 2011;4:282–7) © 2011 by the American College of Cardiology Foundation

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Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is an inherited cardiomyopathy characterized by structural and functional abnormalities due to a progressive replacement of predominantly right ventricular myocardium by fibrofatty tissue (1–4). ARVC/D predisposes patients to complex ventricular arrhythmias and sudden cardiac death, typically among young subjects.

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Establishing the clinical diagnosis of ARVC/D remains challenging because of the lack of a single test to establish a definite diagnosis. Even endomyocardial biopsy, sometimes considered to be the gold standard for ARVC/D, is limited because the interventricular septum as a typical sampling site is less commonly involved (5). In 1994, the Task Force of the European Society of Cardiology and the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology proposed a set of criteria (6). These criteria were based on medical history, as well as on morphological, functional, and structural abnormalities, including right ventricular dilation, regional dysfunction, (fibro)fatty replacement of the right ventricle (RV), electrocardiographic (ECG) changes, arrhythmias, and a family history of sudden cardiac death. These original task force criteria (TFC) were universally used to identify patients with ARVC/D. They were considered highly specific, but some authors have suggested that they may lack sensitivity, especially for early and familial disease (7,8). Moreover, most of these criteria (global and structural abnormalities) were based on qualitative rather than quantitative information and were defined based on the experience before the wide availability of cardiac magnetic resonance (CMR).

Over the past 15 years, CMR has emerged as the noninvasive diagnostic tool of choice for assessing RV anatomy, structure, and function (9,10). High-resolution cine imaging with state-of-the-art steady-state free-precession techniques is widely considered the gold standard for the assessment of ventricular volumes, myocardial mass, and systolic function; and CMR demonstrates high intraobserver and interobserver agreement and accuracy (11,12). The high spatial and temporal resolution enables a detailed assessment of the RV for regions of severely reduced wall thickness and wall motion abnormalities.

The CMR evidence of intramyocardial fat and fibrosis in the RV has been used as supportive diagnostic information; however, because of the limited specificity of these findings and technical limitations of CMR in visualizing the thin RV myocardium, the diagnostic utility of intramyocardial fat and fibrosis as diagnostic targets in ARVC/D remains controversial (13).

Recently, a revision of the TFC has been proposed, incorporating quantitative assessment of RV size and RV function (14). On the basis of as yet unpublished pilot data from a partially genetically defined cohort of patients, the authors propose imaging criteria using a combination of RV dilation and severe regional wall motion abnormalities to establish evidence for ARVC/D. The main differences to the previous set of criteria include the removal of RV microaneurysms (focal akinesis with early diastolic bulging) (Fig. 1) and segmental RV dilation, and the use of a different and more detailed quantitative definition of RV dilation.

The purpose of our study was to assess the impact of revised versus original criteria on the prevalence of ARVC/D criteria in CMR studies.

METHODS

Study population. We performed a retrospective analysis of patients referred to our CMR center for ARVC/D between 2005 and 2010. To minimize inappropriate indications, we included only patients re-

ABBREVIATIONS AND ACRONYMS

ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia

CMR = cardiac magnetic resonance

ECG = electrocardiographic

EF = ejection fraction

LV = left ventricle

RV = right ventricle

TFC = task force criteria

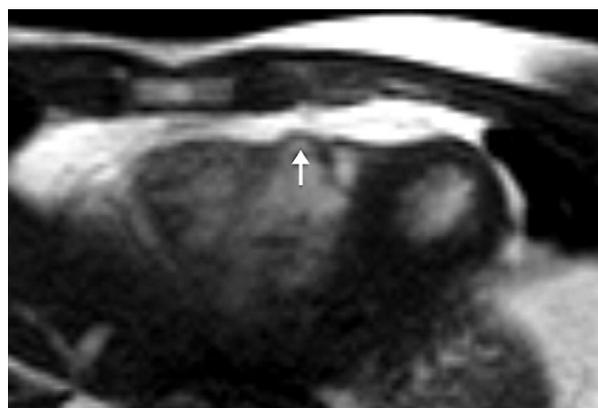


Figure 1. Microaneurysm in a Patient With Suspected ARVC

There is a focal outpouching of the free RV wall in early diastole ("early diastolic bulging," arrow). According to the original criteria, this finding itself was considered a major criterion while the revised criteria require a combination of regional akinesis, dyskinesia, or dyssynchronous contraction with global RV dysfunction or dilation. See [Online Video 1](#). ARVC = arrhythmogenic right ventricular cardiomyopathy; RV = right ventricle.

Table 1. Definition of Major and Minor Imaging Criteria According to Original and Revised Task Force Criteria

Original Criteria	Revised Criteria
Major criteria	
Severe RV dilation and reduced RVEF (normal LV) or Localized RV aneurysms or Severe segmental RV dilation	Regional RV akinesia or Regional dyskinesia or Dyssynchronous RV contraction and RVEDVI/BSA ≥ 110 ml/m ² (male) or RVEDVI/BSA ≥ 100 ml/m ² (female) or RVEF $\leq 40\%$
Minor criteria	
Mild global RV dilation and/or reduced RVEF (normal LV) or Regional RV hypokinesia or Mild segmental RV dilation	Regional RV akinesia or Regional dyskinesia or Dyssynchronous RV contraction and RVEDVI/BSA ≥ 100 to < 110 ml/m ² (male) or RVEDVI/BSA ≥ 90 to < 100 ml/m ² (female) or RVEF $> 40\%$ to $\leq 45\%$
LV = left ventricle; RV = right ventricle; RVEDVI/BSA = right ventricular end-diastolic volume indexed to body surface area; RVEF = right ventricular ejection fraction.	

ferred from cardiologists specialized in electrophysiology. All reports included a quantitative assessment of the RV and, therefore, allowed the post-hoc application of both sets of criteria.

We examined the CMR studies for the presence or absence of major and minor criteria for CMR using both the original TFC and the revised TFC (Table 1). When analyzing the data using the revised TFC, RV volumetric criteria and RV function were assigned strictly quantitatively, using the quantitative cutoff value from the revised TFC (Table 1).

CMR protocol. CMR was performed using a 1.5-T scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany). The left ventricle (LV) and RV function were assessed using standard ECG-gated cine steady-state free-precession sequences (typical repetition time [TR] = 67, echo delay time [TE] = 1.15, field of view = 340 × 276). The RV function was assessed in a contiguous stack of short-axis slices of the RV perpendicular to the anatomic RV long axis (slice thickness 6-mm, no gap) to cover the entire RV, and in sagittal

orientation (slice thickness 8-mm, no gap). LV function was assessed using multiple long-axis views.

Image analysis. All CMR studies were interpreted by at least 2 experienced readers (case review discussions), blinded to the results of other diagnostic tests. For viewing and for the quantitative analysis of RV volumes and function, certified CMR image evaluation software was used (cmr⁴², Circle Cardiovascular Imaging, Calgary, Alberta, Canada). The endocardial and epicardial LV contours and endocardial RV contours were drawn for each diastolic and systolic frame.

Major criteria. Table 1 summarizes the differences for major and minor criteria between original and revised TFC. Important to our sample, localized RV microaneurysm and severe segmental RV dilation, originally classified as a major criterion, are not considered a criteria in the revised TFC, but may, however, qualify as supportive (RV akinesia).

Minor criteria. Mild segmental RV dilation and regional RV hypokinesia, originally classified as minor criteria, are not considered criteria in the revised TFC.

Statistical analysis. Continuous parameters are expressed as mean \pm SD. Criteria were expressed as dichotomous data. Differences between groups were assessed by the McNemar test. A p value < 0.05 was considered significant. Sensitivity and specificity of CMR criteria were calculated for the subgroup of 134 patients with complete information regarding family history, ECG changes, tissue characteristics, and arrhythmias.

RESULTS

During the observed period, 308 patients were referred. The RV volumes and ejection fraction (EF) were not assessable for 14 patients owing to image quality, mostly related to complex arrhythmia patterns. The study population thus consisted of 294 patients (see Table 2 for patient characteristics). The most frequent reason for the referral was a positive family history (ARVC/D and/or sudden cardiac death) in first-degree relatives and/or documented arrhythmias.

The prevalence of major and minor criteria according to the original and revised TFC is shown in Figure 2.

Major criteria. Applying the original TFC, 69 patients (23.5%) had major criteria versus 19 patients (6.5%) with the revised TFC (Fig. 2). The difference was mainly due to findings of regional wall

Table 2. Patient Characteristics

Variables	Patients (n = 294)
Age, years	43 \pm 16
Female sex, n (%)	146 (49.6)
Indications, n (%)	
Family history of ARVC/D in a first-degree relative and/or documented arrhythmia	169 (57.4)
Rule out ARVC/D	125 (42.6)
LVEF (%)	57.6 \pm 6.1
RVEF (%)	54.6 \pm 7.6
RVEDVI/BSA, ml/m ²	88.2 \pm 20.3
ARVC/D = arrhythmogenic right ventricular cardiomyopathy/dysplasia; LVEF = left ventricular ejection fraction; other abbreviations as in Table 1.	

motion abnormalities or microaneurysms in the absence of RV dilation, qualifying as a criterion according to the original but not the revised criteria.

Using the original criteria, localized RV microaneurysm was the most frequent major abnormality (64 of 69 patients), 2 patients showed severe segmental RV dilation, and 3 patients had severe RV dilation and reduced RVEF. With the revised TFC, the most frequent major abnormality was the combination of regional akinesia with moderate to severe RV dilation or RV dysfunction. One patient showed regional dyskinesia, and none had dyssynchronous RV contraction.

Of the 69 patients with major criteria according to the original TFC, only 16 patients (23.1%) had major criteria according to the revised TFC ($p < 0.001$). Forty-three patients (62.3%) did not meet any criteria at all (Fig. 3).

Minor criteria. With the original TFC, 172 patients (58.5%) had minor criteria with the majority of patients having 1 minor criterion ($n = 133$), 38 patients with 2, and 1 patient with 3 minor criteria. Regional hypokinesia was the most frequent minor abnormality among patients with 1 minor criterion ($n = 132$). Using the revised TFC left only 12 patients (4%) with minor criteria (Fig. 2). The most frequent minor abnormality was the conjunction of regional akinesia with mild RV dilation or RV dysfunction; only 1 patient had regional dyskinesia, and none had dyssynchronous RV contraction.

Of the 172 patients initially classified as having minor criteria, only 2 patients (1.1%) still have minor criteria using the revised TFC ($p < 0.001$), and 167 patients (97%) were reclassified to normal according to the revised TFC (Fig. 4).

Correlation of original and revised criteria for CMR in clinically proven ARVC/D patients. Detailed information about family history, ECG changes, tissue characteristics, and arrhythmias were obtained for 134 patients. Ten patients met the definite diagnosis of proven ARVC without counting imaging criteria. Applying the original TFC for imaging, 10 patients had abnormalities (9 patients with major criteria, 1 patient with 1 minor criterion), whereas using the revised TFC, 4 patients had major criteria, yet 6 patients had no criteria at all. If we add microaneurysms as a criterion to the modified TF criteria, the sensitivity increases to 50% (5 of 10 patients).

Correlation of original and revised criteria for CMR in patients without ARVC/D. One hundred and twenty-four patients did not meet the criteria for ARVC/D. Applying the old imaging criteria, 4

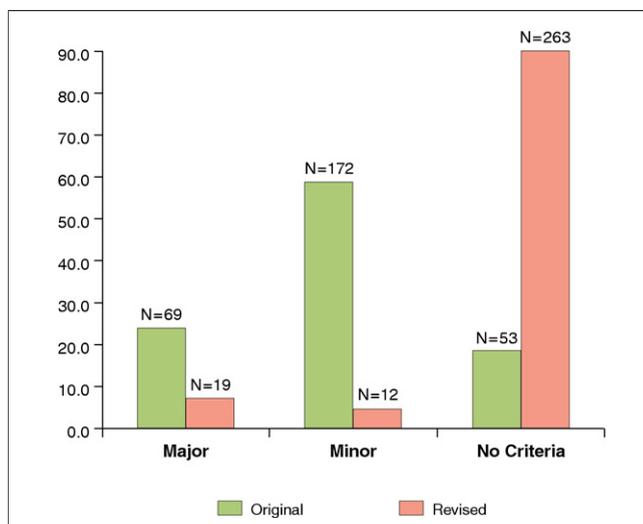


Figure 2. Proportional Incidence of Original and Revised ARVC Criteria

The graph shows the different incidence of patients with major criteria, minor criteria, or without criteria according to the original cardiac magnetic resonance criteria (green bars) and the revised criteria (orange bars). Abbreviation as in Figure 1.

patients were classified as ARVC only because of the imaging findings. Three of them had at least 1 minor criterion, and 1 patient had a major criterion. The complete chart of each patient (including family history, symptoms, ECG, late potentials, Holter monitoring, and follow-up) has been reviewed by a cardiologist specialized in electrophysiology. These 4 patients have been considered without ARVC, and they have been included in the group of 124 patients without ARVC/D. Using the revised TFC, the majority of patients had no criteria ($n = 112$; 90.5%), 7 patients had major

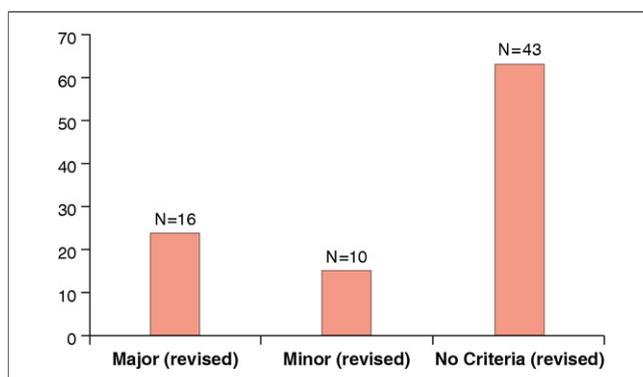
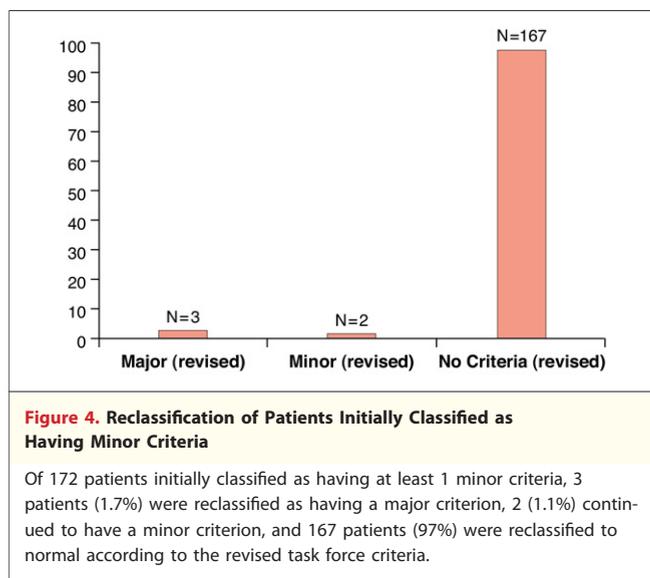


Figure 3. Reclassification of Patients Initially Classified as Having Major Criteria

Of the total of 69 patients with a major criterion according to the original classification, 16 (23.2%) also had a major criterion according to the revised recommendations, 10 patients (14.5%) were reclassified as having a minor criterion, and 43 patients (62.3%) did not have any criteria at all.



criteria (5.5%), and 5 patients had minor criteria (4%). Specificity of major and minor CMR criteria for ARVC/D in our sample was higher for the revised criteria (94% and 96%, respectively) than for the original criteria (78% and 39%, respectively).

Follow-up. With a mean follow-up of 2.2 ± 1.2 years, 293 patients were still alive; 1 patient died of cancer. Of 134 patients with complete diagnostic work-up of ARVC, with a mean follow-up of 2.25 ± 1.25 years, 7 patients underwent insertion of implantable cardioverter-defibrillator, all of them with proven ARVC. Using the original TFC for imaging, 5 patients had major criteria and 2 had a minor criterion; applying the revised TFC, 4 patients had major criteria and 3 had no criteria.

DISCUSSION

To our knowledge, this is the first study to compare the original and the revised task force imaging criteria for ARVC/D. In our sample, we observed a significant decrease in the prevalence of minor and major CMR criteria for ARVC/D with the revised TFC, with a potential increase of specificity and decrease of sensitivity.

In a large cohort of 294 patients referred for CMR for suspected ARVC/D, only 31 patients (10.5%) had criteria according to the revised TFC, compared with 241 patients (82%) according to the original TFC. Only 37.7% of our patients initially classified as having major criteria and 2.7% of patients initially classified as having at least 1 minor criterion still met imaging criteria for ARVC/D.

The revision of the classification for major and minor structural abnormalities represents a major

change. Previously, major and minor structural abnormalities were established with the presence of RV dilation (visual assessment of global or segmental dilation), localized microaneurysm, and regional hypokinesis. Dilation of the RV was initially defined by echocardiography or angiography with no quantitative limits to differentiate mild from moderate to severe RV dilation. The newly suggested major and minor criteria are based on data from 108 subjects with newly diagnosed ARVC/D (14). The CMR data from 44 volunteers were compared with results obtained from 462 normal subjects. The combination of regional wall motion abnormalities (akinesis, dyskinesis, or dyssynchrony) with RV dilation or RV dysfunction (with quantitative assessment) had a sensitivity of 89% for major criteria and 78% for minor criteria. In our study, to exclude the bias due to using different cutoff values to assess RV dilation and RV dysfunction, we used the same quantitative cutoff value for both original and revised criteria. However, only 31 patients (10.5%) had a positive criterion as defined by RV dilation (19 with moderate to severe RV dilation and 12 with mild RV dilation) in combination with regional or global RV dysfunction. Of 64 patients with localized microaneurysms according to the original TFC, only 24 still had a criterion in the combination with RV dilation or RV dysfunction. Recently, Cox et al. (15) analyzed 105 patients with proven ARVC/D (using the 1994 TFC), including a subgroup of 64 patients with CMR data. Fifteen of their patients (24%) revealed major or minor criteria using the new imaging TFC. In a less strictly defined population (89 family members), 26 subjects had CMR with only 1 patient (3.8%) showing a structural abnormality using the revised imaging TFC.

Although our sample size of verified ARVC is small, our data indicate that the new criteria may have a limited sensitivity, with only 4 of 10 patients with a definite diagnosis of ARVC/D having major criteria. The reason for that may be that the required combination of regional wall motion criteria with global RV dilation/dysfunction may miss patients with purely or mainly regional RV abnormalities. Therefore, the revision of the criteria may have missed the goal of increasing the sensitivity of such criteria, yet have led to an increase of specificity. If confirmed for a larger population of patients with verified ARVC, this observation may have important clinical implications.

A significant limitation of our study is the lack of a true "gold standard" for the definite diagnosis of

ARVC/D and limited follow-up data. However, the chart of each patient has been reviewed, and the diagnosis of ARVC/D has been confirmed by cardiologists specialized in electrophysiology regarding the family history, symptoms, ECG abnormalities, arrhythmias, tissue characteristics, and follow-up. Prospective studies will have to be performed using the revised TFC and hard end points such as appropriate implantable cardioverter-defibrillator shocks or cardiovascular death.

Our single-site experience may not reflect that of others. The high incidence of microaneurysms as major criteria according to the original criteria may reflect a local tendency to “overcall” this and, therefore, overestimate the negative impact of the revision on the sensitivity. We did not utilize late gadolinium enhancement imaging to assess the myocardium for areas of fibrous or fibrofatty degeneration. Although this was not part of the original or revised criteria and is challenging in the thin wall of the RV, the detection of such areas in the LV may prove useful.

Finally, we have investigated the value of imaging criteria using them as independent markers. Thus,

the diagnostic accuracy would also have to be assessed in the context of combined criteria.

CONCLUSIONS

In CMR studies performed for assessing patients for ARVC/D, the introduction of the revised TFC for ARVC/D may lead to a decrease of the prevalence of major and minor imaging criteria. The revision may, therefore, not have improved their sensitivity but, instead, have improved their specificity for identifying patients with ARVC/D. Prospective studies should be performed to study the prognostic value of the new imaging criteria.

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Key Words: arrhythmogenic right ventricular cardiomyopathy/dysplasia ■ cardiac magnetic resonance ■ Task Force Criteria.

APPENDIX

For a supplementary video, please see the online version of this article.