The diagnostic performance of imaging methods in ARVC using the 2010 Task Force criteria.

Borgquist, Rasmus; Haugaa, Kristina H; Gilljam, Thomas; Bundgaard, Henning; Hansen, Jim; Eschen, Ole; Jensen, Henrik Kjærulf; Holst, Anders G; Edvardsen, Thor; Svendsen, Jesper H; Platonov, Pyotr

Published in:
European Heart Journal-Cardiovascular Imaging

DOI:
10.1093/ehjci/jeu109

2014

The diagnostic performance of imaging methods in ARVC using the 2010 Task Force criteria

Rasmus Borgquist MD, PhD[1], *Kristina H Haugaa MD, PhD*[2], *Thomas Gilljam MD PhD*[3], *Henning Bundgaard MD PhD*[4], *Jim Hansen MD PhD*[5], *Ole Eschen MD PhD*[6], *Henrik Kjærulf Jensen MD PhD*[7], *Anders G. Holst MD PhD*[4], *Thor Edvardsen MD Professor*[2], *Jesper Svendsen MD Professor*[4*] *and Pyotr G Platonov MD Associate Professor*[1*]. [*]Shared senior authorship.

[1] Lund University, Arrhythmia Clinic, Skane University hospital, Lund, Sweden.

[2] Dept of Cardiology and Center for Cardiological Innovation, Oslo University Hospital, Rikshospitalet and University of Oslo, Norway

[3] Institute of Medicine at Sahlgrenska Academy. University of Gothenburg, Sweden.

[4] Department of Cardiology, Rigshospitalet, University of Copenhagen & Department of Clinical Medicine, University of Copenhagen & Danish Arrhythmia Research Centre, University of Copenhagen

[5] Gentofte University Hospital, Copenhagen, Denmark

[6] Aalborg University Hospital, Aalborg, Denmark

[7] Department of Cardiology, Aarhus University Hospital Skejby, Aarhus, Denmark

Address for correspondence:

Dr. Rasmus Borgquist

Arrhythmia Clinic, Skane University Hospital, Getingevagen, 221 85 Lund, Sweden

Email: Rasmus.borgquist@med.lu.se. Phone: +46704057350. Fax. +4646323574

Abstract and keywords:

Aims: This study evaluates the agreement between echocardiographic and cardiac magnetic resonace imaging (CMR) data, and the impact a discrepancy between the two may have on the clinical diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC).

Methods and results: From the Nordic ARVC Registry, 102 patients with definite ARVC who had undergone both echocardiography and CMR were included (median age 42±16 years, 36% female, 78% probands). Patients were divided into two groups according to CMR-positive or -negative criteria, and the echocardiographic data was compared between the two. There were 72 CMR-positive patients. They had significantly larger RV dimensions and lower fractional area change on echocardiography compared to CMR-negative patients; PLAX RVOT 37±7 vs. 32±5 mm, PSAX RVOT 38±7 vs. 32±6 mm, FAC; 31±9% vs. 39±9% ($p<0.003$ for all). Only 36 (50%) of the CMR-positive patients fulfilled ARVC criteria by echocardiography, hence the diagnostic performance was low; sensitivity 50% and specificity 70%, PPV 80% and NPV 37%. Individuals with regional wall abnormalities on CMR were more likely to have ventricular arrhythmias (77% vs. 57%, $p=0.047$).

Conclusion: A significant proportion of patients with imaging-positive ARVC by CMR did not fulfil echocardiographic ARVC 2010 criteria. These findings confirm that echocardiographic evaluation of subtle structural changes in the right ventricle may be unreliable, and the diagnostic performance of CMR compared to echocardiography should be reflected in the guidelines.

Key words: Echocardiography, cardiac magnetic resonance imaging, ARVC, diagnostic performance

Introduction:

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is considered to be an inherited disease with autosomal dominant inheritance and variable penetrance and phenotype expression[1-3]. It is characterized by a fibrous and fatty replacement of primarily right ventricular myocardium, and an increased risk of ventricular arrhythmias and sudden cardiac death. The initial presentation varies, but a significant minority of patients present with sudden cardiac arrest as the first symptom, and ARVC may account for up to 25% of exercise related SCD in young individuals[4]. An early correct diagnosis is important, considering the prognostic implications of the disease.

Diagnostic criteria have previously been based on the 1994 task force criteria[5], but in recognition of new improved imaging techniques and genetic tests, updated diagnostic task force criteria and genetic guidelines have more recently been published[1, 3]. As in the previous version, regional right ventricular (RV) wall abnormalities (aneurysm, dyskinesia or akinesia) are a prerequisite in imaging-criteria, and the level of RV dilatation determines whether or not a minor or major ARVC criterion is met. A problem with the task force criteria may be that the sensitivity of echocardiography is low for detection of subtle regional RV wall abnormalities. Cardiac magnetic resonance imaging (CMR) is less available than echocardiography, but in centres with the appropriate CMR scanner and experience, the evaluation of RV regional wall abnormalities is presumably more robust due to better quality images (as compared to echocardiography).

The present study aims to explore the diagnostic performance of echocardiography-based imaging criteria for ARVC diagnosis, and compare these data to CMR-based criteria in a cohort based on the Nordic ARVC Registry. The patients in the Nordic ARVC registry have been handled according to standard clinical practice in their respective countries, (i.e. not

using any core-lab analyses), thus making the results representative of the "real-world" setting.

Methods:

The Nordic ARVC registry (www.arvc.dk) includes patients with diagnosed ARVC and their first-degree relatives, enrolled from eight centres in Denmark, Norway and Sweden[6-8]. The study was cross-sectional by design and was based on the patients who were followed in the participating centres and had been entered into the Registry before May 2013, and fulfilled definite ARVC diagnostic criteria according to the Task Force 2010. The study was approved by the regional ethics committee and all individuals signed a written informed consent prior to enrolment in all countries except in Denmark, where this type of observational registry by law does not involve approval by the ethics committee. The study complies with the Declaration of Helsinki.

In the registry, baseline clinical data (age, gender, previous cardiovascular disease, diabetes) is collected, in addition to ARVC-relevant data for diagnostic criteria as proposed in the guidelines from 1994 and the updated task force criteria from 2010[3, 5]. This includes ARVC-related symptoms, imaging data from echocardiography, CMR and RV angiography, histology data from cardiac biopsies, electrocardiographic data including depolarisation and repolarisation pathology, ventricular arrhythmia data and family history.

For the purpose of this analysis, all patients included in the Registry with a definite ARVC diagnosis according to 2010 criteria were screened for availability of both CMR and echocardiography. The patients were divided into two groups according to CMR-positive or -negative (major or minor) criteria, and the echocardiographic and clinical data was compared between the two. CMR positivity was based on the definitions included in the Task Force

2010 criteria, and did not include results regarding fat-infiltration or fibrosis in the left or right ventricle. Both CMR and echocardiography investigations were performed in accordance with current guidelines and interpreted by experienced physicians at each participating site.

Statistical methods

Continuous data is presented as mean ± standard deviation or median [IQ range] as appropriate. Nominal data is presented as number (% of cases). Chi^2 or Fischer's exact test was used for comparison between categorical variables and t-test was used for comparison of continuous variables. For assessment of diagnostic performance, positive predictive value, negative predictive value, sensitivity and specificity were used. A two-sided p-value < 0.05 was considered statistically significant.

Results:

Patient population

A total of 179 patients with definite ARVC according to 2010 task force criteria were screened for inclusion, and 102 patients with both echocardiography and CMR data were included in the study (Figure 1). On average, the patients had 2.5 major criteria (range 1-5) and 1.0 minor criteria (range 0-3). In 30% of the cases the total score from the other five diagnostic criteria (excluding imaging) would not have been sufficient to reach the definite ARVC diagnosis threshold (i.e. the total ARVC score according to 2010 task force criteria being 1-2 major criteria in combination with 0-2 minor criteria, or 4 minor criteria). The

remaining 70% of patients would have been diagnosed as positive regardless of imaging data. Clinical data is shown in Table 1.

Imaging data

Imaging data is presented in table 2 and table 3. The mean time difference between echocardiography and CMR investigation was 5.2 months (IQ range 3.1months), the echocardiography preceded the CMR in 77 of the cases. For 26 patients the timespan was more than a year, and therefore further test analyses were made without these patients, producing results similar to the tests on the whole group (data not shown). On the basis of this, these patients were also included in the final material.

Men were more likely than women to have CMR-positive imaging (79% positive versus 57% females positive, p=0.02). Individuals with CMR positive findings were more likely to have ventricular arrhythmias (77% vs. 57%, p=0.047), but in contrast those with positive findings on echocardiography did not have more arrhythmias (70% vs. 73%, p=0.73). Other baseline ARVC-related clinical data did not differ between CMR groups, except for the expected finding that CMR positive patients were more likely to be "probands" than relatives (88% vs. 57%, p=0.001) and less likely to have a family history of ARVC. Analyzing baseline data by positive/negative echocardiography criteria revealed a trend for echocardiography-positive patients to be probands (86% vs. 71%, p=0.09), but showed no association to arrhythmias (p=0.9). 43% of the "non-probands" had positive findings on CMR, as compared to 31% who had positive findings on echocardiography.

Notably, in 10 CMR-negative patients there were positive echocardiographic criteria (5 major, 4 minor and 1 with regional abnormalities but no volume measurements available). LVEF and body surface area did not differ between CMR positive and negative patients, but

all measures of RV volume were larger in CMR positives (see tables 2 and 3). In identifying patients with regional RV dysfunction and dilatation, the diagnostic performance of echocardiography compared to CMR was poor (Table 4a). Furthermore, RVOT dilatation on echocardiography showed poor correlation with overall RV dilatation on CMR (p=0.8).

In order to investigate if the sensitivity for echocardiography could be improved (with acceptable specificity) by omitting the requirement for regional wall abnormalities, a similar analysis was done, using Task Force criterion for RV volume measurements only (i.e. the prerequisite for regional wall motion pathology was omitted). This simplification increased the sensitivity to 78% whereas the specificity decreased to only 20% (Table 4b). Echocardiography was more sensitive but less specific in probands compared with family members to probands, (Table 5a and 5b). Patients with regional RV wall abnormalities on CMR were more likely to have an arrhythmia fulfilling ARVC major or minor criteria (77% vs. 57%, p=0.047). In contrast, echocardiographic regional RV wall abnormalities did not discriminate between patients with and without arrhythmia criteria (70% vs. 73%, p=0.73).

Discussion

Our study shows that agreement between echocardiography and CMR for evaluation of the 2010 ARVC criteria is low in patients fulfilling definite ARVC diagnosis. Even though echocardiography evaluations of right ventricular volumes point in the same direction as CMR based evaluations (as shown in table 2), the discrepancy in fulfilment of diagnostic criteria may have clinical implications since imaging data becomes a pivotal diagnostic criterion in a significant amount of the cases. It seems that in particular the detection of regional RV structural abnormalities was difficult, but echocardiography based measures of RVOT dilatation also showed a poor correlation with CMR based measures of RV dilatation. This indicates that ARVC may present with segmental RV dilatation, excluding the outflow

tract, and thereby not fulfilling echocardiography based task force criteria. The present cohort is larger than previously published ARVC cohorts evaluated using CMR, and is based on all known ARVC cases in the uptake areas of the participating sites in Scandinavia. Compared to the cohort on which the current 2010 task force recommendations are based, the present cohort included more cases, and in particular more cases with both CMR and echocardiography evaluation[3].

The data in this study was collected retrospectively, and there was a time-lapse between the CMR and echocardiography investigations in some patients. Presuming that ARVC in some patients is a progressive disease, this time-difference may have had an impact on the difference in positive findings - favouring CMR data, which was collected 5 months later on average.

Assessment of right ventricular size and volume

The 2010 Task Force criteria are based on a cohort of data from 108 probands with newly diagnosed ARVC, including 44 individuals with a CMR performed. Data was compared to different cohorts with appropriate normal subjects, and cut-off values for imaging were determined as the value that yielded 95% specificity (major criterion), and sensitivity ranged from 79%-89% (major) and 68%-78% (minor)[3].

Measurements of RV volume measurements differ between CMR and echocardiography, and it is important to recognize that these data are based on different methods. The shape of the RV is complex and makes it inherently difficult to assess both the size and systolic function in a reproducible fashion, especially when using 2D images[9]. Even though quantitative measurements have been shown to significantly increase sensitivity and specificity in echocardiographic evaluation of the RV, angulation of the probe is still crucial. Depending on

which angulation is used, the size of the RV varies considerably, which is reflected by a significant variability of results even in experienced hands. The method is particularly vulnerable, since RV size is calculated quantitatively by one 2D projection only (the standard 4 chamber view). The new 3D based technique is promising and has shown lower inter-individual variability than 2D measurements[10], but many patients do not offer acoustic windows that allow for the entire RV to be evaluated by 3D. In addition, the current ARVC guidelines do not include 3D volume measurements by echocardiography, thus 3D based echocardiography measurements were not performed in our cohort.

Assessment of right ventricular regional wall motion abnormalities

We used CMR based task force 2010 criteria as "gold-standard" for comparison with the echocardiography results. Interpretation of CMR may be more reliable due to more precise definition of the endocardial and myocardial layers and freedom of projection of the images in any preferred direction, once a proper collection of raw data has been made. A theoretical risk of applying CMR data as "gold-standard" is that it may lead to over-diagnosing of small regional abnormalities in the RV, which may in fact not be related to the disease (and which would not have caught any attention in an echocardiographic examination). Previous studies have pointed to some inter-individual variation in interpretation of CMR in patients with suspected ARVC, and optimally one would need pathology specimen for comparison[11, 12]. However, in lack of this, we believe that CMR in experienced hands (such as the tertiary referral centres of this study) should be regarded as gold standard when it comes to evaluation of early structural changes in ARVC.

Segmental evaluation of the right ventricle is challenging due to the complex shape of the chamber and the position of the RVOT immediately under the sternum, narrowing down the acoustic window for some parts of the myocardium. In recognition of this, newer techniques

such as tissue-doppler and speckle tracking strain analysis have been used in order to improve the sensitivity for diagnosing RV structural disease[13-16]. However, some of these studies are hampered by the low feasibility of speckle tracking evaluation of the free wall (58% in the study by Aneq et al.[13]) and the time-consuming and operator dependent results generated from tissue-doppler imaging. The most promising results were reported by Teske et al. on a cohort of mutation-positive but asymptomatic individuals, compared with a control group[15]. They could show a high feasibility (>90%), and diagnostic sensitivity and specificity of echocardiography could be improved to 71% sensitivity and 81% (speckle tracking) - 100% (TDI) specificity. Vermont et al. studied 69 patients who fulfilled major imaging criteria according to the 1994 guidelines, but only 38% of these patients met minor or major imaging criteria of 2010 - the main reason for this, according to the authors, being a lack of the distinct regional RV wall pathology required in the 2010 criteria[17].

Diagnosing ARVC

The importance of a high sensitivity for diagnosing early disease is emphasized by the findings that sudden cardiac death occurs also in individuals with no or subtle evidence of structural heart disease[18, 19]. It is also important to distinguish between individuals with advanced disease, where gross RV pathology is present, and the diagnosis is easy by any given imaging modality, and individuals with pre-symptomatic disease where no structural changes can be seen. On the other hand, in subjects with non-specific symptoms and / or subtle abnormalities, there is of course also a risk of over-diagnosing disease, especially by inexperienced interpreters. This was highlighted by the two studies of Sen-Chowdhry and Bomma, and the importance of looking at all different aspects of the task force criteria was emphasized[20, 21]. This conclusion is firmly supported by our results, and we believe it is important that all diagnostic imaging possibilities are used in order to maximize sensitivity

and specificity for correctly diagnosing ARVC. CMR more often has the potential to "catch" family members with early subclinical disease, compared to echocardiography, but in some cases echocardiography is positive when CMR is negative. In some of the cases, the CMR preceded the echocardiography in time; this may explain why some structural alterations were detected by echocardiography and not by CMR. In other instances it may be that the changes were overlooked in the CMR setting, or that normal trabeculation has been interpreted as regional wall abnormality if the image quality was suboptimal. Therefore, in particular for cases where the diagnosis depends on the presence or absence of imaging criteria, both CMR and echocardiography should be performed. Unless excellent image quality is provided by echocardiography, serial evaluation by CMR should be considered if the findings are ambiguous or non-diagnostic. This is also supported by the finding that regional RV pathology on CMR was associated with ventricular arrhythmias - as opposed to regional RV pathology on echocardiography, which was not associated with arrhythmias.

There is a difference in the diagnostic performance of echocardiography in *probands* as compared to *family members*, detected by screening programmes (as presented in tables 5a and 5b), which probably reflects the fact that probands with mostly symptomatic disease are more likely to have structural manifestations of the disease as well. When the structural abnormalites are more pronounced they are also more likely to be detected by echocardiography, even if the image quality is not optimal. This makes it even more important to include CMR in the screening of asymptomatic relatives at risk of disease, where the sensitivity of echocardiography is clearly unacceptably low. A revision of the current guidelines may be considered, and one option could be to add CMR as a compulsory modality for evaluation of regional abnormalities, unless already visualised positively by echocardiography. New cut-off limits might need to be considered, and should be based on data from multiple large cohorts.

Limitations:

The major limitation is the retrospective data collection, resulting in a time difference between when echocardiography and CMR investigations were performed, and in some instances the interpreting physician may have been aware of the previous results from other imaging modalities, possibly introducing a bias. Nevertheless, the population is large, and the majority of patients had only a small timespan between the two investigations, thus making the results reliable even with the limitation of retrospective data collection. The cohort did not include any matched controls, and the diagnostic performance of different echocardiography cut-off values could therefore not be evaluated in a "general population". The investigations were not performed by a core lab, but at eight different tertiary referral University Hospitals. This will likely have resulted in a greater variability in the evaluations, but conversely the results are more likely to reflect the "real-world" diagnostic performance of echocardiography and CMR, since imaging results for most patients with suspected ARVC would not routinely be subject to secondary evaluation from a certified core lab. The present study therefore does not intend to suggest specific cutoff-values for the diagnostic criteria in ARVC, but rather to offer an insight into the ambiguity and level of difficulty for image-interpretation in patients with suspected or confirmed ARVC.

Conclusion

Evaluation of regional structural changes of the right ventricle using echocardiography is difficult, and the sensitivity for detection of ARVC criteria is lower than for CMR-based images. A significant number of patients with imaging-positive ARVC by CMR showed normal echocardiographic study at baseline, and the correct diagnosis could have been missed. These findings indicate that both echocardiography and CMR should be performed

when there is a clinical suspicion of ARVC, and the difference in diagnostic performance should be reflected in the guidelines.

Conflict of interest:

Anders G. Holst is an employee of Novo Nordisk A/S, Denmark

Figure legends:

Figure 1

Patient inclusion scheme – From 171 patients in the registry with definite ARVC, the final cohort of 102 patients with both CMR and echocardiography were selected for this study.


171
Definite ARVC
163
Echo performed
8
No echo data available
102
CMR performed
61
CMR data not available
72
CMR imaging criteria positive
27
RV dilatation
Major criteria fulfilled
9
RV dilatation
Minor criteria fulfilled
26%
Regional abnormalities
RV dilatation unknown
32 No echo criteria fulfilled

References

1. Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, Berul C*, et al.* Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. Europace 2013;**15**(10):1389-406.

2. Ackerman MJ, Priori SG, Willems S, Berul C, Brugada R, Calkins H*, et al.* HRS/EHRA expert consensus statement on the state of genetic testing for the channelopathies and cardiomyopathies: this document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA). Europace 2011;**13**(8):1077-109.

3. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA*, et al.* Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. Circulation 2010;**121**(13):1533-41.

4. Kies P, Bootsma M, Bax J, Schalij MJ, van der Wall EE. Arrhythmogenic right ventricular dysplasia/cardiomyopathy: screening, diagnosis, and treatment. Heart Rhythm 2006;**3**(2):225-34.

5. McKenna WJ, Thiene G, Nava A, Fontaliran F, Blomstrom-Lundqvist C, Fontaine G*, et al.* Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. Task Force of the Working Group Myocardial and Pericardial Disease of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology. Br Heart J 1994;**71**(3):215-8.

6. Borgquist R, Gilljam T, Haugaa K, Edvardsen T, Bundgaard H, Holst A*, et al.* Echocardiographic Evaluation Has A Low Sensitivity For Detection Of Patients With Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC),

Using The Guidelines Criteria Of 2010. J Am Coll Cardiol 2013; **61(10_S)**.

7. Platonov P, Gilljam T, Holst A, Haugaa K, Edvardsen T, Borgquist R*, et al.* Heart transplantations in the Nordic Arrhythmogenic Right Ventricular Cardiomyopathy Registry. J Am Coll Cardiol 2013;**61(10_S)**.

8. Platonov P, Holst A, Haugaa K, Edvardsen T, Gilljam T, Lundin C*, et al.* Performance of Task Force diagnostic criteria for identification of symptomatic patients with Arrhythmogenic Right Ventricular Cardiomyopathy in the Nordic ARVC Registry. Circulation 2012;**126:A13457**.

9. Ling LF, Obuchowski NA, Rodriguez L, Popovic Z, Kwon D, Marwick TH. Accuracy and interobserver concordance of echocardiographic assessment of right ventricular size and systolic function: a quality control exercise. J Am Soc Echocardiogr 2012;**25**(7):709-13.

10. van der Zwaan HB, Geleijnse ML, Soliman OI, McGhie JS, Wiegers-Groeneweg EJ, Helbing WA*, et al.* Test-retest variability of volumetric right ventricular measurements using real-time three-dimensional echocardiography. J Am Soc Echocardiogr 2011;**24**(6):671-9.

11. Tandri H, Calkins H, Nasir K, Bomma C, Castillo E, Rutberg J*, et al.* Magnetic resonance imaging findings in patients meeting task force criteria for arrhythmogenic right ventricular dysplasia. J Cardiovasc Electrophysiol 2003;**14**(5):476-82.

12. Bluemke DA, Krupinski EA, Ovitt T, Gear K, Unger E, Axel L*, et al.* MR Imaging of arrhythmogenic right ventricular cardiomyopathy: morphologic findings and interobserver reliability. Cardiology 2003;**99**(3):153-62.

13. Aneq MA, Engvall J, Brudin L, Nylander E. Evaluation of right and left ventricular function using speckle tracking echocardiography in patients with

arrhythmogenic right ventricular cardiomyopathy and their first degree relatives. Cardiovasc Ultrasound 2012;**10**:37.

14. Teske AJ, Cox MG, De Boeck BW, Doevendans PA, Hauer RN, Cramer MJ. Echocardiographic tissue deformation imaging quantifies abnormal regional right ventricular function in arrhythmogenic right ventricular dysplasia/cardiomyopathy. J Am Soc Echocardiogr 2009;**22**(8):920-7.

15. Teske AJ, Cox MG, Te Riele AS, De Boeck BW, Doevendans PA, Hauer RN*, et al.* Early detection of regional functional abnormalities in asymptomatic ARVD/C gene carriers. J Am Soc Echocardiogr 2012;**25**(9):997-1006.

16. Sarvari SI, Haugaa KH, Anfinsen OG, Leren TP, Smiseth OA, Kongsgaard E*, et al.* Right ventricular mechanical dispersion is related to malignant arrhythmias: a study of patients with arrhythmogenic right ventricular cardiomyopathy and subclinical right ventricular dysfunction. Eur Heart J 2011;**32**(9):1089-96.

17. Vermes E, Strohm O, Otmani A, Childs H, Duff H, Friedrich MG. Impact of the revision of arrhythmogenic right ventricular cardiomyopathy/dysplasia task force criteria on its prevalence by CMR criteria. JACC Cardiovasc Imaging 2011;**4**(3):282-7.

18. Corrado D, Basso C, Thiene G. Sudden cardiac death in young people with apparently normal heart. Cardiovasc Res 2001;**50**(2):399-408.

19. Corrado D, Basso C, Thiene G, McKenna WJ, Davies MJ, Fontaliran F*, et al.* Spectrum of clinicopathologic manifestations of arrhythmogenic right ventricular cardiomyopathy/dysplasia: a multicenter study. J Am Coll Cardiol 1997;**30**(6):1512-20.

20. Bomma C, Rutberg J, Tandri H, Nasir K, Roguin A, Tichnell C*, et al.* Misdiagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy. J Cardiovasc Electrophysiol 2004;**15**(3):300-6.

21. Sen-Chowdhry S, Prasad SK, Syrris P, Wage R, Ward D, Merrifield R*, et al.* Cardiovascular magnetic resonance in arrhythmogenic right ventricular cardiomyopathy revisited: comparison with task force criteria and genotype. J Am Coll Cardiol 2006;**48**(10):2132-40.