

Current use of cardiac magnetic resonance in tertiary referral centres for the diagnosis of cardiomyopathy: the ESC EORP Cardiomyopathy/Myocarditis Registry

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Aims

Cardiac magnetic resonance (CMR) is recommended in the diagnosis of cardiomyopathies, but it is time-consuming, expensive, and limited in availability in some European regions. The aim of this study was to determine the use of CMR in cardiomyopathy patients enrolled into the European Society of Cardiology (ESC) cardiomyopathy registry [part of the EURObservational Research Programme (EORP)].

Methods and results

Three thousand, two hundred, and eight consecutive adult patients (34.6% female; median age: 53.0 ± 15 years) with cardiomyopathy were studied: 1260 with dilated (DCM), 1739 with hypertrophic (HCM), 66 with restrictive (RCM), and 143 with arrhythmogenic right ventricular cardiomyopathy (ARVC). CMR scans were performed at baseline in only 29.4% of patients. CMR utilization was variable according to cardiomyopathy subtypes: from 51.1% in ARVC to 36.4% in RCM, 33.8% in HCM, and 20.6% in DCM ($P < 0.001$). CMR use in tertiary referral centres located in different European countries varied from 1% to 63.2%. Patients undergoing CMR were younger, less symptomatic, less frequently had implantable cardioverter-defibrillator (ICD)/pacemaker implanted, had fewer cardiovascular risk factors and comorbidities ($P < 0.001$). In 28.6% of patients, CMR was used along with transthoracic echocardiography (TTE); 67.6% patients underwent TTE alone, and 0.9% only CMR.

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studied: 1260 had dilated cardiomyopathy (DCM); 1739 hypertrophic cardiomyopathy (HCM); 66 restrictive cardiomyopathy (RCM); and 143 arrhythmogenic right ventricular cardiomyopathy (ARVC). Patients were recruited in 68 centres located in 18 countries. Participating centres should have the expertise in management of cardiomyopathies and were selected using pre-specified criteria, that is, Cardiac Magnetic Resonance Imaging Lab with experience in diagnosis of typical and atypical cardiomyopathies.¹³ The number of enrolled patients was diverse from 27 up to 659 per country. The inclusion criteria comprised: age >18 years, consent to study participation and unequivocal diagnosis of cardiomyopathy consistent with diagnostic criteria for either probands or relatives. All the definitions applied for the study population were formerly specified in the core manuscript.¹³ For the purpose of the study, the whole cardiomyopathy population was divided into subjects with CMR (CMR population) and without CMR used in the diagnostic process (non-CMR population).

Diagnostic tests

Data on the following tests regarding cardiomyopathy diagnosis were noted in the CRF: electrocardiogram, transthoracic echocardiography (TTE) with Doppler assessment, CMR, 24 h ECG Holter monitoring, exercise test, and genetics. Data on all tests were recorded at two time points: at baseline and at 1-year follow-up. The analysis presented here was focused on CMR application in the cardiomyopathy diagnostic process; TTE was used as a comparator for CMR applicability.

Among detailed TTE and CMR parameters registered in the CRF protocol, the study presented information on whether CMR and TTE were performed and on conclusion of the CMR scanning (normal, abnormal, and inconclusive). According to the EORP Registry CRF, the following reasons for diagnosis were taken into account: incidental, symptoms, history of cardiac arrest, family screening, and so on.

Statistical analysis

Univariate analysis was applied to both continuous and categorical variables. Continuous variables were reported as mean \pm standard deviation (SD) and/or as median and interquartile range (IQR) when appropriate. Among-group comparisons were made using the non-parametric test (Kruskal–Wallis test). Categorical variables were reported as percentages. Among-group comparisons were made using the χ^2 test or a Fisher's exact test if any expected cell count was <5. A univariate logistic regression analysis was performed to identify variables associated with CMR use in study population. Odds ratio (OR) and 95% confidence interval (95% CI) were obtained. A two-sided *P*-value <0.05 was considered as statistically significant. All analyses were performed using SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Prevalence of CMR use in cardiomyopathy patients

Baseline CMR scans were performed in 944 (29.4%) patients. The prevalence of CMR use in different cardiomyopathies was as follows: 20.6% in DCM, 33.8% in HCM, 36.4% in RCM, and 51.1% in ARVC (*P* < 0.001) (Table 1 and Figure 1). Abnormal CMR results were present in 93.4% of patients, with the highest percentage in RCM (95.8%) and HCM (94.9%) followed by DCM (91.5%) and ARVC (87.7%) (*P* = 0.030); normal CMR results were registered in 5.6% of

patients, and only 1.0% the CMR results were inconclusive for diagnosis (Table 1).

In 83 subjects without a baseline CMR imaging, the CMR evaluation was completed during 1-year follow-up. Finally, the total prevalence of CMR use at baseline and at 1-year follow-up raised to 32.0% with the highest prevalence in ARVC (53.9%) (Table 1).

The prevalence of CMR use (baseline+1-year follow-up data) in patients with cardiomyopathies varied from 1% to 63.2% in centres located in different European countries (Figure 2).

Demographic and clinical characteristics of CMR and non-CMR populations

Some demographic features differed in patients diagnosed using CMR compared to the non-CMR population. Age at enrolment (50.0 \pm 15.7 vs. 54.8 \pm 14.6 years, *P* < 0.001) and age at the first evaluation in the centre (46.8 \pm 16.4 vs. 50.5 \pm 15.5 years, *P* < 0.001) were lower in the CMR population. The CMR group had lower BMI (26.5 \pm 4.6 vs. 27.3 \pm 5.0 kg/m², *P* < 0.001). Inherited metabolic disorders were more frequently observed in CMR subjects (2.0 vs. 0.7%, *P* = 0.012). NYHA class was less advanced in the CMR population (NYHA I/II/III/IV: 37.0/43.0/16.5/3.4%) than in non-CMR subjects (NYHA I/II/III/IV: 23.5/47.9/24.3/4.4%, *P* < 0.001). History of arrhythmias, atrial fibrillation (20.3% vs. 36.2%, *P* < 0.001), sustained VT (8.2% vs. 12.8%, *P* < 0.001), and AV block (6.1% vs. 10.5%, *P* = 0.003) were less frequent in CMR than in non-CMR population.

The percentage of the patients with implanted ICD was lower in the CMR as compared with the non-CMR population (18.01% vs. 29.67%, *P* < 0.001). The ICDs were implanted in approximately 80% patients for primary and in 20% for secondary prophylaxis of sudden cardiac death (SCD) both in CMR and non-CMR subjects. Among patients implanted for the primary prophylaxis of SCD (*n* = 677): 148 (21.86%) subjects were examined by CMR. Among patients implanted for the secondary prophylaxis of SCD (*n* = 155): 37 (23.87%) underwent CMR.

The following comorbidities were less prevalent in CMR population: arterial hypertension (29.8% vs. 39.3%, *P* < 0.001), diabetes mellitus (9.8% vs. 13.9%, *P* = 0.001), hyperlipidaemia (28.8% vs. 39.3%, *P* < 0.001), and renal impairment (6.5% vs. 12.8%, *P* < 0.001).

Univariate logistic regression analysis of different demographic, clinical, and imaging variables associated with the CMR use in the whole population confirmed the above-mentioned results and quantified the magnitude of effects through odds ratio (Table 2).

CMR use and reason for cardiomyopathy diagnosis

In patients in whom the CMR imaging was performed at baseline and/or follow-up, incidental, history of cardiac arrest, family screening, and other reasons for diagnosis, were registered more frequently than in non-CMR population. On the other hand, in non-CMR subjects, the presence of symptoms dominated as a reason for diagnosis (71.7% vs. 57.3% in CMR population, *P* < 0.001) (Table 3). Similar observations were obtained in patients with DCM (*P* < 0.001) and HCM (*P* = 0.001) (Table 4).

Table 1 Prevalence of CMR use in a whole cardiomyopathy population and in different types of cardiomyopathies

Variables	Type of cardiomyopathy					P value
	All (N = 3208)	DCM (N = 1260)	HCM (N = 1739)	RCM (N = 66)	ARVC (N = 143)	
Baseline evaluation						
CMR scan performed	944/3208 (29.43%)	259/1260 (20.56%)	588/1739 (33.81%)	24/66 (36.36%)	73/143 (51.05%)	<0.001
CMR scan	53/944 (5.61%)	19/259 (7.34%)	27/588 (4.59%)	0/24 (0.00%)	7/73 (9.59%)	
	882/944 (93.43%)	237/259 (91.51%)	558/588 (94.90%)	23/24 (95.83%)	64/73 (87.67%)	0.030
	9/944 (0.95%)	3/259 (1.16%)	3/588 (0.51%)	1/24 (4.17%)	2/73 (2.74%)	
TTE	3086/3208 (96.20%)	1221/1260 (96.90%)	1666/1739 (95.80%)	63/66 (95.45%)	136/143 (95.10%)	0.387
Baseline+12-month follow-up						
CMR scan performed ^a	1027/3208 (32.01%)	280/1260 (22.22%)	644/1739 (37.03%)	26/66 (39.39%)	77/143 (53.85%)	<0.001
CMR scan ^a	69/1027 (6.72%)	21/280 (7.50%)	39/644 (6.06%)	2/26 (7.69%)	7/77 (9.09%)	0.046
	948/1027 (92.31%)	256/280 (91.43%)	602/644 (93.48%)	23/26 (88.46%)	67/77 (87.01%)	
	10/1027 (0.97%)	3/280 (1.07%)	3/644 (0.47%)	1/26 (3.85%)	3/77 (3.90%)	

^aData were collected from baseline evaluation if CMR was performed at baseline, and from 12-month follow-up evaluation if CMR was not performed at baseline. ARVC, arrhythmic right ventricular CM; CM, cardiomyopathy; CMR, cardiac magnetic resonance; DCM, dilated CM; HCM, hypertrophic CM; RCM, restrictive CM; TTE, transthoracic echocardiography.

Application of TTE/CMR for cardiomyopathy diagnosis

At baseline, CMR was used as a single diagnostic method in only 0.9% of patients. In 28.6% of patients, the CMR was used along with transthoracic echocardiography. TTE was the only diagnostic imaging method at baseline in 67.6% of patients (Table 5).

Comparison of the TTE and CMR application among different cardiomyopathies shows that CMR constitutes a single diagnostic method in a limited number of patients: 0.5% in DCM, 1.2% in HCM, 0.0% in RCM, and 1.4% in ARVC. On the other hand, TTE was used without CMR imaging in 76.8% of patients with DCM, in 63.1% of patients with HCM, in 59.1% of patients with RCM, and in 45.6% of patients with ARVC (Table 5).

Discussion

This study shows that less than one-third of adult patients enrolled in the ESC EORP Cardiomyopathy Registry underwent CMR and that the CMR use varied greatly between cardiomyopathy subtypes, clinical profiles of patients, and European centres.

Expert consensus statements and ESC guidelines recommend that CMR scanning should be performed both for diagnosis, prognosis as well as for further therapeutic options in patients with a suspected cardiomyopathy.^{5,14-17} In the ESC Cardiomyopathy Registry, most cardiomyopathy diagnoses were made on the basis of TTE imaging alone, although there were difference between cardiomyopathies and different regions. Indeed, TTE is a non-invasive, cost-effective, and widely available method; however, it has limited application in myocardial tissue evaluation.⁸⁻¹⁰ In contemporary cardiology practice, TTE followed by CMR as complementary modality should be implemented.

The Registry provided data also on the conclusions of the CMR imaging (normal, abnormal, and inconclusive). Most patients presented an abnormal CMR scanning and only 1.0% of the results were inconclusive. However, as many as 5.6% of CMR results were assessed as normal and the final cardiomyopathy diagnosis was based on other diagnostic methods (i.e. TTE, genetic tests). We should be aware that every diagnostic method has some false negative results as well as we cannot exclude some biases in the evaluation process.

CMR in different cardiomyopathy subtypes

CMR has an important clinical role in all cardiomyopathies in terms of diagnosis,^{6,8,10,11,18,19} treatment strategy, and the prediction of prognosis.²⁰⁻²² However, the Registry revealed unsatisfactory availability of CMR in every cardiomyopathy sub-type.

In our study, CMR was used most frequently (51.1%) in patients with ARVC, probably reflecting the limitations of TTE in assessing the right ventricle as well as the importance of tissue characterisation in this disease. In contrast, the use of CMR was low in all other subtypes, in spite of clear guidance on the importance of CMR in characterising phenotypes and in assessing sudden death risk. For example, CMR characterization of myocardial tissue is fundamental in cases of suspected amyloidosis, sarcoidosis, Fabry disease, and

Study limitations

There are limitations intrinsic to all registries including selection bias and lack of adjudication. As most patients were enrolled in tertiary referral centres, our results may not be generally applicable, and CMR use could be even lower in less expert centres. In relation to the considerable disparities among centres located in different countries on prevalence of CMR use, it should be emphasised that our results pertain primarily to centres with high CMR utilization. Participating centres should have the expertise in management of cardiomyopathies, that is, CMR Imaging Lab with experience in diagnosis of typical and atypical cardiomyopathies. Therefore, the presented data may even overestimate the actual CMR use. The considerable disparities among the number of enrolled patients should also be noted. Especially low-number centres may mismatch analysis of the percentage of CMR use. Additionally <50% of the ESC affiliated counties have been enrolled into the Registry and it constitutes the next limitation of the study. It should be noted that some patients had ICD at baseline or underwent ICD implantation during the follow-up, thus limiting CMR use. Generally, a lot of therapeutic decisions, that is, ICD implantation for primary prevention of SCD, have been made without 'gold-standard' like CMR imaging.

The follow-up was as short as 12 months and a waiting time for CMR might have been longer in some countries due to reimbursement issues. The study presents only information on whether CMR was performed and on conclusion of the CMR, without details of the CMR imaging. The registry was not dedicated to study a temporal sequence of the use of CMR and TTE in cardiomyopathy diagnostic process and an impact of the CMR result on the management. This is an inherent limitation of all registries.

Conclusion

The EORP Cardiomyopathy/Myocarditis Registry provides real-life data on the use of CMR in patients with cardiomyopathies. Regardless of the potential value of CMR in this setting, the overall use of CMR in Europe is limited. Less than one-third of patients enrolled in the registry underwent CMR and the use varied greatly between cardiomyopathy subtypes, clinical profiles of patients, and European tertiary referral centres. This gap between society recommendations and clinical practice needs to be better understood and should be considered more deliberately in the drafting of practice guidelines. An improvement regarding access, training, and reimbursement is necessary to provide wider application of CMR in diagnosis of cardiomyopathies.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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