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CLINICAL RESEARCH
Heart failure/cardiomyopathy

The Cardiomyopathy Registry of the EURObservational Research Programme of the European Society of Cardiology: baseline data and contemporary management of adult patients with cardiomyopathies

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Aims The Cardiomyopathy Registry of the EURObservational Research Programme is a prospective, observational, and multinational registry of consecutive patients with four cardiomyopathy subtypes: hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and restrictive cardiomyopathy (RCM). We report the baseline characteristics and management of adults enrolled in the registry.

Methods and results A total of 3208 patients were enrolled by 69 centres in 18 countries [HCM ($n = 1739$); DCM ($n = 1260$); ARVC ($n = 143$); and RCM ($n = 66$)]. Differences between cardiomyopathy subtypes ($P < 0.001$) were observed for age at diagnosis, history of familial disease, history of sustained ventricular arrhythmia, use of magnetic resonance imaging or genetic testing, and implantation of defibrillators. When compared with probands, relatives had a lower age at diagnosis ($P < 0.001$), but a similar rate of symptoms and defibrillators. When compared with the Long-Term phase, patients of the Pilot phase (enrolled in more expert centres) had a more frequent rate of familial disease ($P < 0.001$), were more frequently diagnosed with a rare underlying disease ($P < 0.001$), and more frequently implanted with a defibrillator ($P = 0.023$). Comparing four geographical areas, patients from Southern Europe had a familial disease more frequently ($P < 0.001$), were more frequently diagnosed in the context of a family screening ($P < 0.001$), and more frequently diagnosed with a rare underlying disease ($P < 0.001$).

Conclusion By providing contemporary observational data on characteristics and management of patients with cardiomyopathies, the registry provides a platform for the evaluation of guideline implementation. Potential gaps with existing recommendations are discussed as well as some suggestions for improvement of health care provision in Europe.

Keywords Cardiomyopathy • Registry • Hypertrophic • Dilated • Restrictive • Arrhythmogenic right ventricular

Introduction

Cardiomyopathies are a heterogeneous group of disorders characterized by structural and functional abnormalities of the myocardium that are not explained solely by coronary artery disease or abnormal loading conditions.[1] These disorders represent a significant health burden since they can cause premature death from arrhythmia, progressive heart failure, or stroke.[2–9] To date, most information about the presentation and natural history of cardiomyopathies has derived from cohort studies in a small number of specialized centres, and there is very little data describing the contemporary profile and the practical management of the patients outside highly expert units.

The EURObservational Research Programme (EORP) Cardiomyopathy registry was conceived by the European Society of Cardiology (ESC) Working Group on Myocardial and Pericardial Disease, to collect clinical data on patients with a confirmed diagnosis of a cardiomyopathy (*Figure 1*). The general aim of the registry is to provide a summary of contemporary features and management of patients with cardiomyopathy or myocarditis, across a large range of centres in the Europe in order to improve clinical service provision and therapy.

In this article, we present the data on the adult population with a cardiomyopathy, combining Pilot and Long-Term phases. Enrollment of patients with a myocarditis or paediatric patients with a cardiomyopathy, is still ongoing.

Methods

General design

This is a prospective observational multinational multicentre registry of consecutive patients presenting to cardiology centres in the European countries. Participating centres were selected using pre-specified criteria (see Supplementary material online, *File S1*). Each centre was asked to enter about 40 consecutively-assessed patients (up to 40 in Pilot phase, minimum 40 in Long-Term phase) over a 12-month period. The study was approved by each local Ethical Committee according to the local rules. Written informed consent was obtained from all participants before data collection. All diagnostic or management procedures were left to the discretion of the attending physician, including the clinical investigations made at the time of enrollment, and diagnostic criteria were not centrally verified. Baseline data were collected (including demographic, clinical, cardiac, genetic, and therapeutic parameters) using a web-based electronic case report form. The EORP department of the ESC was responsible for study management, data quality control, and statistical analyses.

The registry was conducted by an Executive Committee and managed by the EORP department of the ESC. A Pilot phase of the registry, restricted to adult patients with a cardiomyopathy, was conducted for validating the structure and quality of the data set.[10] A Long-Term phase was subsequently agreed and extended in three directions: (i) further enrollment of adult patients with a cardiomyopathy, (ii) extended enrollment of paediatric patients with a cardiomyopathy, in collaboration with the Association for European Paediatric and Congenital Cardiology Working Group on Genetics, Basic Science and Inherited Muscle

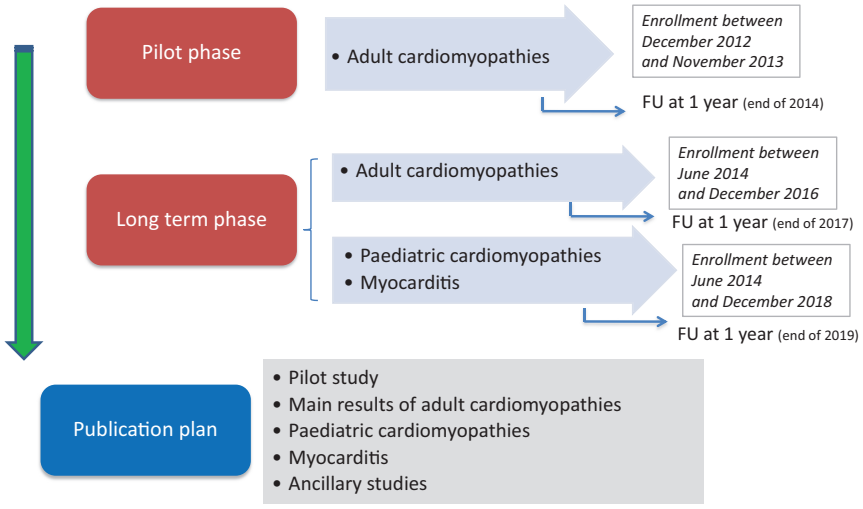


Figure 1 General plan of the Cardiomyopathy Registry. FU, follow-up.

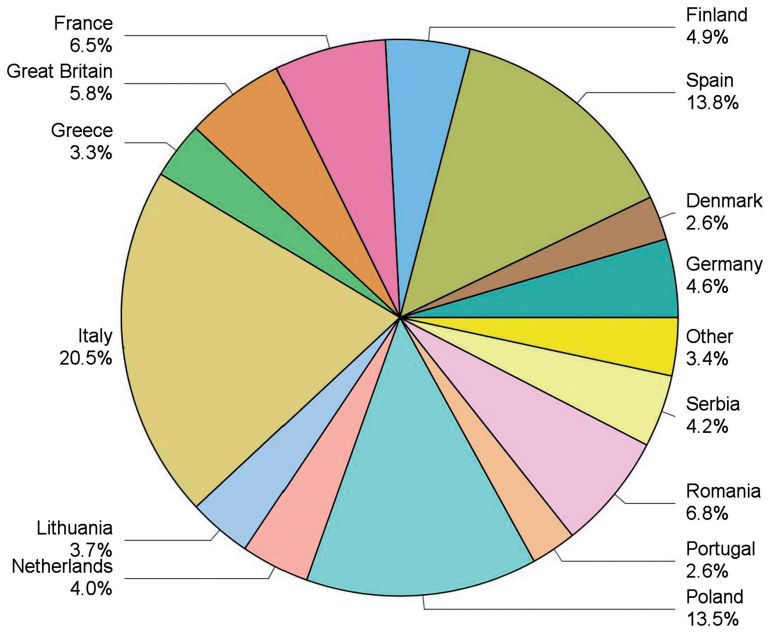


Figure 2 Pie chart showing the proportion of patients recruited in the global registry ($n = 3208$) enrolled in each participating country.

Diseases (AEPC WG), and (iii) extended enrollment of patients with clinically suspected or biopsy-proven myocarditis.

Patients and cardiomyopathies subtypes

Patients with one of four major cardiomyopathy subtypes were eligible for the study: hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and restrictive cardiomyopathy (RCM). Familial/genetic forms and non-familial/non-genetic forms were included. Patients met the following inclusion criteria for the adult cardiomyopathies registry: (i) age at enrollment >18 years, (ii) willing and able to give informed consent, (iii) able to comply with all study requirements, and (iv) documented cardiomyopathy fulfilling standard diagnostic criteria for probands or for relatives (see Supplementary material online, *File S2*). Relevant definitions used for analyses of subgroups (including definition of regions) are included in the Supplementary material online, *File S3*.

Statistical analyses

Univariable analysis was applied to both continuous and categorical variables. Continuous variables were reported as mean ± standard deviation

Table 1 Baseline characteristics in relation to cardiomyopathy subtypes

	HCM (*n* = 1739)	DCM (*n* = 1260)	RCM (*n* = 66)	ARVC (*n* = 143)	*P*-value
Age at enrollment (years), *n*	1739	1260	66	143	
Median (Q1–Q3)	55.0 (42.0–65.0)	55.0 (45.0–63.0)	60.0 (44.0–69.0)	48.0 (34.0–56.0)	<0.001
Age at diagnosis (years), *n*	1046	900	37	82	
Median (Q1–Q3)	47.0 (33.0–59.0)	49.0 (40.0–58.0)	57.0 (37.0–68.0)	39.0 (30.0–51.0)	<0.001
Males, *n* (%)	1028/1739 (59.1)	935/1260 (74.2)	32/66 (48.5)	94/143 (65.7)	<0.001
Family history of SCD, *n* (%)	350/1662 (21.1)	132/1111 (11.9)	8/60 (13.3)	34/136 (25.0)	<0.001
Familial disease, *n* (%)	661/1362 (48.5)	238/945 (25.2)	15/50 (30.0)	43/106 (40.6)	<0.001
Reason for diagnosis, *n* (%)					
Incidental	364/1616 (22.5)	116/1198 (9.7)	5/66 (7.6)	14/140 (10.0)	<0.001
Symptoms	904/1616 (55.9)	970/1198 (81.0)	58/66 (87.9)	90/140 (64.3)	
Sudden death/cardiac arrest	18/1616 (1.1)	20/1198 (1.7)	0/66 (0.0)	9/140 (6.4)	
Family screening	268/1616 (16.6)	57/1198 (4.8)	1/66 (1.5)	22/140 (15.7)	
Other	62/1616 (3.8)	35/1198 (2.9)	2/66 (3.0)	5/140 (3.6)	
Presence of symptoms, *n* (%)	1470/1734 (84.8)	1128/1257 (89.7)	64/66 (97.0)	120/143 (83.9)	<0.001
Suspected arrhythmic/cardiogenic syncope, *n* (%)	179/1453 (12.3)	90/1103 (8.2)	6/64 (9.4)	41/116 (35.3)	<0.001
Anginal chest pain, *n* (%)	513/1475 (34.8)	235/1131 (20.8)	8/64 (12.5)	17/120 (14.2)	<0.001
NYHA class, *n* (%)					
Class I	463/1417 (32.7)	198/1049 (18.9)	11/63 (17.5)	61/103 (59.2)	<0.001
Class II	707/1417 (49.9)	448/1049 (42.7)	26/63 (41.3)	38/103 (36.9)	
Class III	228/1417 (16.1)	316/1049 (30.1)	25/63 (39.7)	4/103 (3.9)	
Class IV	19/1417 (1.3)	87/1049 (8.3)	1/63 (1.6)	0/103 (0.0)	
Palpitations, *n* (%)	547/1475 (37.1)	407/1131 (36.0)	12/64 (18.8)	74/120 (61.7)	<0.001
Arrhythmia and stroke history, *n* (%)					
History of atrial fibrillation	463/1739 (26.6)	356/1260 (28.3)	32/66 (48.5)	20/143 (14.0)	<0.001
History of sustained ventricular tachycardia	134/1739 (7.7)	171/1260 (13.6)	1/66 (1.5)	56/143 (39.2)	<0.001
History of resuscitated ventricular fibrillation/ cardiac arrest	49/1739 (2.8)	61/1260 (4.8)	3/66 (4.5)	18/143 (12.6)	<0.001
History of stroke	59/1728 (3.4)	57/1254 (4.5)	3/66 (4.5)	3/143 (2.1)	NC
History of AV block	101/1058 (9.5)	83/914 (9.1)	7/37 (18.9)	6/84 (7.1)	0.206
Procedures prior or at the time to enrollment, *n* (%)					
ECG	1684/1739 (96.8)	1241/1260 (98.5)	66/66 (100.0)	142/143 (99.3)	0.008[a]
Echocardiogram	1666/1739 (95.8)	1221/1260 (96.9)	63/66 (95.5)	136/143 (95.1)	0.387
LVEDD (mm), mean (SD)	45.4 (6.9)	64.2 (9.8)	46.6 (8.6)	50.4 (6.3)	<0.001
LV ejection fraction (Simpson's biplane) (%), mean (SD)	62.2 (11.4)	32.5 (11.8)	53.8 (10.4)	55.4 (10.9)	<0.001
Maximum LV thickness (mm), mean (SD)	19.7 (5.0)	10.4 (2.1)	15.1 (4.4)	9.7 (1.7)	<0.001
MRI	588/1739 (33.8)	259/1260 (20.6)	24/66 (36.4)	73/143 (51.0)	<0.001
Holter ECG	1163/1739 (66.9)	469/1260 (37.2)	23/66 (34.8)	97/143 (67.8)	<0.001
Exercise test	687/1739 (39.5)	349/1260 (27.7)	5/66 (7.6)	69/143 (48.3)	<0.001
Endomyocardial biopsy	15/676 (2.2)	73/348 (21.0)	17/29 (58.6)	14/58 (24.1)	<0.001
Genetic testing performed	755/1627 (46.4)	203/1137 (17.9)	27/63 (42.9)	71/130 (54.6)	<0.001

AV, atrioventricular; ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; LVEDD, left ventricular end diastolic diameter; RCM, restrictive cardiomyopathy; MRI, magnetic resonance imaging; NC, not computed; NYHA, New York Heart Association; SCD, sudden cardiac death; SD, standard deviation; Q, quartile.
[a]The Fisher's exact test.

and/or as median and interquartile range (IQR) when appropriate. Among-group comparisons were made using a non-parametric test (Kruskal–Wallis). Categorical variables were reported as percentages. Among-group comparisons were made using a χ^2 test or a Fisher's exact test if any expected cell count was <5. A two-sided *P*-value of <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

Enrollment

Sixty-nine centres from 18 countries participated in the study (*Figure 2*, Supplementary material online, *Table S1*, *Figure S1*). A total of 3208 consecutive adult patients with a cardiomyopathy were enrolled (*Table 1*),

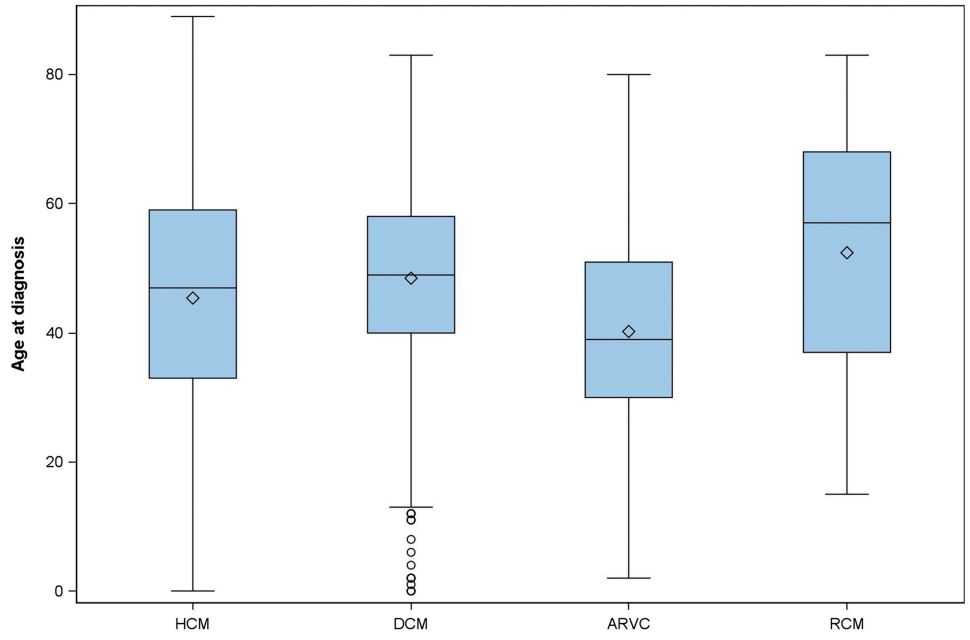


Figure 3 Box-plot with distribution of age at diagnosis for each cardiomyopathy subtype. ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy. Distribution is presented with mean, lower extreme, 1st quartile (25th percentile), median (50th percentile), 3rd quartile (75th percentile), upper extreme and outliers.

including 42.9% incident patients vs. 57.1% prevalent patients, 83.0% proband vs. 17.0% relatives, 34.8% patients from the Pilot phase vs. 65.2% from the Long-Term phase, and 59.7% outpatients vs. 40.3% inpatients. Median age at enrollment was 55.0 years (IQR 43–64) and there was a male predominance for all cardiomyopathy subtypes except RCM ($P < 0.001$). The mean number of patients enrolled per centre was 46.5 (median 40, IQR 22–50).

Diagnosis

The commonest diagnosis was HCM ($n = 1739$, 54.2%), then DCM ($n = 1260$, 39.3%), ARVC ($n = 143$, 4.4%), and RCM ($n = 66$, 2.1%) (*Table 1*). In addition, left ventricular non-compaction was reported in 4.1% of total patients. Median age at diagnosis was 49.0 years (IQR 38–59) (*Figure 3*), differed significantly between cardiomyopathies ($P < 0.001$) and was lower in patients with ARVC (39.0 years IQR 30–51) than in patients with RCM (54.0 years IQR 37–65). A large distribution for age at diagnosis was observed for all subtypes, with a 'lower extreme limit' of box-plot that was 0 years for HCM, 13 years for DCM, 15 years for RCM, and 2 years for ARVC.

Familial disease and aetiology

A history of familial disease was observed in 38.9% of the total population (*Table 1*), with significant differences according to cardiomyopathy subtypes ($P < 0.001$). The proportion was higher in HCM and ARVC (48.5% and 40.6%, respectively) and lower in RCM and DCM (30.0% and 25.2%, respectively). Details concerning rare causes of cardiomyopathy subtypes are reported in Supplementary material online, *Table S2*.

History of arrhythmia, symptoms, and diagnostic tests

Main symptoms, history of arrhythmia or stroke, and use of cardiac investigations are reported in *Table 1*. History of sustained ventricular tachycardia was observed most often in patients with ARVC (39.2%) and the least in RCM (1.5%). History of atrial fibrillation was recorded most frequently in patients with RCM (48.5%) and the least in ARVC (14.0%). Electrocardiogram and echocardiogram were performed in nearly all patients (≥95.1%). Magnetic resonance imaging (MRI) was performed most frequently in patients with ARVC (51.0%) and least frequently in DCM (20.6%) (global comparison $P < 0.001$). Genetic testing was performed in 35.7% of patients. Endomyocardial biospsy was performed in 119 patients (10.7% of the patients for whom this item was completed).

Drugs and therapeutic procedures prior to enrollment

Table 2 describes medications and procedures prior to enrollment. Beta-blockers were the most frequently recorded drugs (80.6% of all patients). Implantable cardioverter defibrillator (ICD) was reported in 25.9% of the whole population (primary prophylaxis 81.4%), most frequently in patients with ARVC (56.6% of patients) followed by DCM (31.7%), HCM (19.9%), and RCM (9.1%). A pacemaker was implanted in 10.2% of the whole cohort, most frequently in patients with DCM (14.3%) and least frequently in ARVC (2.8%).

Subgroups

Subgroup analyses are presented in *Table 3*.

Table 2 Therapeutics at baseline in relation to cardiomyopathy subtypes

	HCM ($n = 1739$)	DCM ($n = 1260$)	RCM ($n = 66$)	ARVC ($n = 143$)	P-value
Procedures prior to enrollment, *n* (%)					
Cardioverter defibrillator implanted	346/1739 (19.9)	399/1260 (31.7)	6/66 (9.1)	81/143 (56.6)	<0.001
Reason for cardioverter defibrillator					
Primary prophylaxis	297/346 (85.8)	331/399 (83.0)	3/6 (50.0)	46/81 (56.8)	<0.001[b]
Secondary prophylaxis	49/346 (14.2)	68/399 (17.0)	3/6 (50.0)	35/81 (43.2)	
Pacemaker implanted	135/1723 (7.8)	177/1240 (14.3)	8/65 (12.3)	4/141 (2.8)	<0.001
Septal myectomy	85/1739 (4.9)	—	—	—	
Alcohol septal ablation	70/1739 (4.0)	—	—	—	
Cardiac ablation[a]	62/1739 (3.6)	44/1260 (3.5)	2/66 (3.0)	16/143 (11.2)	<0.001
Medications, *n* (%)					
Beta-blockers	1294/1739 (74.4)	1130/1260 (89.7)	42/66 (63.6)	119/143 (83.2)	<0.001
Diuretics, oral	491/1563 (31.4)	895/1247 (71.8)	53/62 (85.5)	24/131 (18.3)	<0.001
ACE-inhibitors	342/1739 (19.7)	917/1260 (72.8)	15/66 (22.7)	33/143 (23.1)	<0.001
Angiotensin II receptor blockers	265/1739 (15.2)	210/1260 (16.7)	7/66 (10.6)	11/143 (7.7)	0.026
Mineralocorticoid receptor antagonists	233/1739 (13.4)	795/1260 (63.1)	30/66 (45.5)	17/143 (11.9)	<0.001
Antiplatelets	420/1739 (24.2)	299/1260 (23.7)	15/66 (22.7)	26/143 (18.2)	0.451
Oral anticoagulants	424/1561 (27.2)	443/1246 (35.6)	36/62 (58.1)	19/131 (14.5)	<0.001
Vitamin K antagonists	296/1561 (19.0)	345/1246 (27.7)	24/62 (38.7)	15/131 (11.5)	<0.001
All other (rivaroxaban, apixaban, dabigatran, other)	128/1561 (8.2)	98/1246 (7.9)	12/62 (19.4)	4/131 (3.1)	
Antiarrhythmic drugs	264/1739 (15.2)	361/1260 (28.7)	12/66 (18.2)	34/143 (23.8)	<0.001

ACE, angiotensin-converting enzyme; ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy.
[a]Whatever reason (atrial or ventricular arrhythmia).
[b]The Fisher's exact test.

Relatives when compared with probands were characterized by a lower median age at diagnosis (39.0 years, IQR 24–50, vs. 50.0 years, IQR 38–59, $P < 0.001$), they underwent cardiac investigations [electrocardiogram (ECG), echocardiogram, Holter-ECG, and MRI] in a similar or greater proportion and a defibrillator was implanted as frequently (25.6% vs. 25.0%).

Incident patients when compared with prevalent patients were characterized by a greater median age at diagnosis (51.0 years, IQR 40–60, vs. 47.0 years, IQR 35–57, $P < 0.001$), were more frequently probands (89.0% vs. 77.5%, $P < 0.001$), had a familial disease less frequently (28.7% vs. 45.7%, $P < 0.001$) and had a defibrillator implanted less frequently (16.7% vs. 33.6%, $P < 0.001$).

Patients of the Pilot phase, when compared with the Long-Term phase, were more frequently relatives (52.9% vs. 9.7%, $P < 0.001$), had a familial disease more frequently (46.4% vs. 34.4%, $P < 0.001$), were more frequently diagnosed in the context of a family screening (16.1% vs. 9.1%, $P < 0.001$), more frequently diagnosed with a rare underlying disease (6.2% vs. 3.1%, $P < 0.001$) and were more frequently implanted with a defibrillator (28.3% vs. 24.7%, $P = 0.023$).

Considering the four main regions, patients from South area were most frequently relatives (25.0%, global comparison, $P < 0.001$), had a familial disease most frequently (49.4%, $P < 0.001$), were most frequently diagnosed in the context of a family screening (17.1%, $P < 0.001$) and more frequently diagnosed with a rare underlying disease (5.7%, $P < 0.001$). Patients from East area were less likely to undergo MRI and genetic testing but more had Holter-ECG. Patients from West area were more frequently implanted with a defibrillator (32.7%, $P < 0.001$).

Discussion

This is the first multinational European registry on cardiomyopathies. The analysis shows that the mode of presentation varies substantially between cardiomyopathy subtypes, and that all patients, whether probands or relatives, undergo multiple cardiac investigations and require substantial medical and device therapy. By providing real-world contemporary data on clinical characteristics and management, the registry provides a platform for the evaluation of guideline implementation across a range of different health care providers and organizations in the Europe and elsewhere.

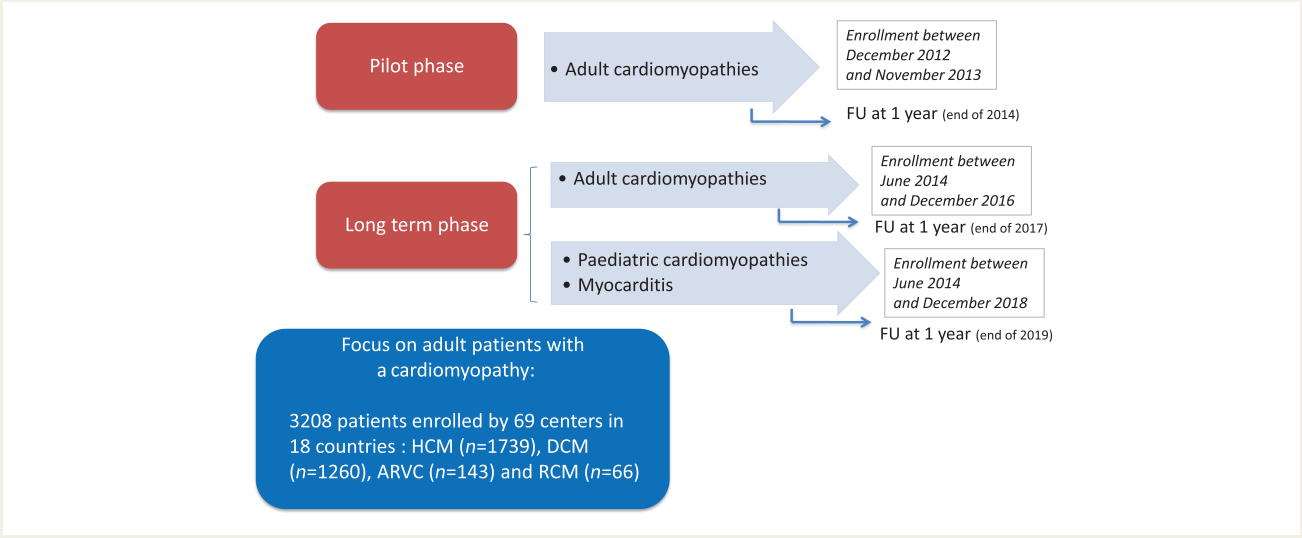
Cardiomyopathy subtypes

As anticipated from previous studies,[3–6,11] HCM was the most frequent cardiomyopathy in the registry, followed by DCM, and then ARVC and RCM. The design of the registry did not allow us to estimate population prevalence of specific phenotypes, but it is notable that the ratio for DCM/HCM patients in this consecutive series was unexpectedly high, suggesting that the true prevalence of DCM could be higher than previously estimated and closer to the estimated prevalence of HCM. The study also shows the diversity and frequency of diagnostic tests that were performed, either for assessment of the cardiomyopathy, management of symptoms, or stratification of risk. This is illustrated by MRI, performed in nearly one-third of all patients, or by genetic testing, performed in more than one-third of patients. All these results emphasize the multidisciplinary approach and

Table 3 Summary of basic features in adult patients with a cardiomyopathy according to predefined sub-groups

	Probands (*n* = 1929)	Relatives (*n* = 395)	*P*-value	Incident (*n* = 1335)	Prevalent (*n* = 1774)	*P*-value	Pilot patient (*n* = 1115)	Long-Term patient (*n* = 2093)	*P*-value	North (*n* = 543)	East (*n* = 713)	West (*n* = 481)	South (*n* = 1427)	*P*-value
Age at diagnosis (years), median (Q1–Q3), *n*	50.0 (38.0–59.0) 1728	39.0 (24.0–50.0) 180	<0.001	51.0 (40.0–60.0) 1004	47.0 (35.0–57.0) 969	<0.001	46.0 (32.0–58.0) 1092	49.0 (38.0–59.0) 2065		49.0 (38.0–60.0) 272	48.0 (37.0–58.0) 620	50.0 (40.0–57.0) 201	49.5 (37.0–60.0) 928	0.384
Males, *n* (%)	1282/1929 (66.5)	216/395 (54.7)	<0.001	915/1335 (68.5)	1117/1774 (63.0)	0.001	696/1115 (62.4)	1393/2093 (66.6)	0.019	349/543 (64.3)	472/713 (66.2)	333/481 (69.2)	908/1427 (63.6)	0.138
Proband (vs. relative), *n* (%)				883/992 (89.0)	963/1242 (77.5)	<0.001	184/391 (47.1)	1745/1933 (90.3)	<0.001	262/320 (81.9)	601/630 (95.4)	212/250 (84.8)	810/1080 (75.0)	<0.001
Familial disease, *n* (%)	524/1510 (34.7)	389/389 (100.0)	<0.001	285/993 (28.7)	655/1434 (45.7)	<0.001	423/912 (46.4)	534/1551 (34.4)	<0.001	141/358 (39.4)	132/500 (26.4)	108/396 (27.3)	576/1165 (49.4)	<0.001
Incident patient (vs. prevalent), *n* (%)	883/1846 (47.8)	109/388 (28.1)	<0.001				326/1111 (29.3)	1009/1998 (50.5)	<0.001	143/534 (26.8)	499/641 (77.8)	184/476 (38.7)	465/1414 (32.9)	<0.001
Family screening as a reason for diagnosis, *n* (%)	68/1808 (3.8)	264/387 (68.2)	<0.001	95/1269 (7.5)	246/1676 (14.7)	0.001	168/1042 (16.1)	180/1978 (9.1)	<0.001	46/520 (8.8)	36/669 (5.4)	31/416 (7.5)	235/1371 (17.1)	<0.001
Rare disease, *n* (%)[a]	62/1929 (3.2)	16/395 (4.1)	0.400	54/1335 (4.0)	75/1774 (4.2)	0.800	69/1115 (6.2)	65/2093 (3.1)	<0.001	12/543 (2.2)	21/713 (2.9)	19/481 (4.0)	82/1427 (5.7)	<0.001
Presence of symptoms, *n* (%)	1613/1928 (83.7)	313/395 (79.2)	0.033	1165/1332 (87.5)	1538/1769 (86.9)	0.668	1107/1107 (100.0)	1675/2093 (80.0)	<0.001	512/543 (94.3)	627/712 (88.1)	456/475 (96.0)	1143/1426 (80.2)	<0.001
MRI, *n* (%)	468/1929 (24.3)	140/395 (35.4)	<0.001	427/1335 (32.0)	506/1774 (28.5)	0.037	507/1115 (45.5)	437/2093 (20.9)	<0.001	176/543 (32.4)	139/713 (19.5)	153/481 (31.8)	474/1427 (33.2)	<0.001
Holter ECG, *n* (%)	1005/1929 (52.1)	254/395 (64.3)	<0.001	716/1335 (53.6)	976/1774 (55.0)	0.443	753/1115 (67.5)	999/2093 (47.7)	<0.001	246/543 (45.3)	464/713 (65.1)	176/481 (36.6)	857/1427 (60.1)	<0.001
Exercise test, *n* (%)	582/1929 (30.2)	169/395 (42.8)	<0.001	377/1335 (28.2)	722/1774 (40.7)	<0.001	564/1115 (50.6)	546/2093 (26.1)	<0.001	206/543 (37.9)	146/713 (20.5)	254/481 (52.8)	492/1427 (34.5)	<0.001
Genetic testing performed, *n* (%)	596/1763 (33.8)	227/373 (60.9)	<0.001	228/1222 (18.7)	782/1644 (47.6)	<0.001	462/1044 (44.3)	594/1913 (31.1)	<0.001	175/524 (33.4)	70/672 (10.4)	169/408 (41.4)	642/1315 (48.8)	<0.001
Cardioverter defibrillator implanted, *n* (%)	482/1929 (25.0)	101/395 (25.6)	0.808	223/1335 (16.7)	596/1774 (33.6)	<0.001	316/1115 (28.3)	516/2093 (24.7)	0.023	148/543 (27.3)	122/713 (17.1)	179/481 (37.2)	381/1427 (26.7)	<0.001
Pacemaker implanted, *n* (%)	213/1919 (11.1)	27/387 (7.0)	0.015	104/1327 (7.8)	208/1743 (11.9)	<0.001	86/1077 (8.0)	238/2092 (11.4)	0.003	61/536 (11.4)	56/704 (8.0)	65/477 (13.6)	136/1408 (9.7)	0.010

ECG, electrocardiogram; MRI, magnetic resonance imaging; Q, quartile.
[a]Rare disease: figures on pooled Pilot + LT phase populations.



Take home figure Overview of the EORP Cardiomyopathy Registry.

expertise that is required for the management of patients with a cardiomyopathy.[6,12–17]

Arrhythmia burden

All cardiomyopathies increase the odds for life-threatening arrhythmias, but the degree to which they do so continues to raise controversy.[3–9] While recognizing that the patients enrolled in this series are necessarily selected, the frequency of malignant ventricular arrhythmia and atrial fibrillation was impressively high. This was paralleled by a high prevalence of prophylactic ICD implantation,[3–8,18,19] ablation procedures, and pacemaker implantation. Importantly, the arrhythmic risk varied substantially between cardiomyopathy subtypes with ventricular arrhythmia or ICD implantation most frequently reported in ARVC and atrial fibrillation being the dominant rhythm issue in RCM. The fact that Holter-ECG and exercise test were performed in two-third or less of patients, even in incident patients where investigations are expected to be optimal, suggest a gap in cardiac investigations.

Familial forms and age at diagnosis

The registry emphasizes the high prevalence of inherited disease, with nearly 40% of the entire cohort reporting a familial disease, and the importance of referring relatives for evaluation since two-thirds of relatives were diagnosed through family screening. In addition, the burden of the disease in relatives was important since prevalence of symptoms and ICD implantation were as frequent as in probands. The fact that the number of relatives in the registry was relatively low (less than one-fifth) suggests there is still a gap in family screening.[7,8,15,16] In the total cohort of probands and relatives, the median age at diagnosis was relatively low, below, or equal to 50 years of age for all cardiomyopathies except RCM.[3–6] Age at diagnosis was variable, in agreement with the known age-related penetrance of these diseases. Distribution of age at diagnosis was, however, unexpectedly wide with the 'extreme upper limit' beyond 70 years of age for all cardiomyopathy subtypes and the 'extreme lower limit' well below 10 years of age for HCM and ARVC. These results may suggest a modification of the recommendations about family screening in relatives,[7,8,15,16] starting family screening earlier than the current threshold of ~10 years of age and extending family screening or follow-up beyond the currently recommended age of 50–60 years.

From gaps to improvement of health care

The identification of potential gaps with existing recommendations is also supported by the heterogeneous management we observed between centres and between geographical areas. Important differences were especially observed between the Pilot phase, where centres were preselected because of a high level of expertise, and the Long-Term phase, were centres had a more variable level of expertise. This is illustrated by the high percentage of relatives in the Pilot phase, which probably reflects more developed family screening programs. The careful analysis of the Registry findings therefore suggests that some characteristics may be considered as potential markers of excellence in the context of quality evaluation of health services, particularly in the perspective of dedicated multidisciplinary heart teams that might be useful as shown in other areas.[20,21] These indicators of expertise for a given centre may include the percentage of cardiac and extracardiac investigations performed in patients, the ratio of relatives vs. probands, the rate of patients with a rare cause, the median age at diagnosis of patients.

Finally, differences we observed among the various geographic areas suggest that comparing the organization of health care systems for cardiomyopathies in the various countries may provide valuable insights that can be used for improvement of health care services in the Europe. Since recommendations or expert consensus for the management of the patients and families are available,[7,8,14–16] including about global management of arrhythmia and prevention of sudden cardiac death[22], it can be hypothesized that variations in service provision are mostly related to economical or structural reasons.

Limitations

Similar to registries in other fields, the voluntary nature of the enrolling centres, associated with their predefined characteristics, inevitably implies an uncertain representativeness of the enrolling network with respect to the Europe as a whole.

Conclusions

This is the first European registry focused on adult patients with the various cardiomyopathy subtypes (see *Take home figure*). It provides a unique picture of contemporary features and management of these patients. The results emphasize the complexity of services and multidisciplinary expertise required for the management of patients with a cardiomyopathy. The analysis of the results also identified potential gaps with existing recommendations. Work is warranted to understand the large variation in services provision as well as renewed efforts to provide evidence-based diagnostic processes and therapies.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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Corrigendum

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Corrigendum to: Clinical implication of an impaired fasting glucose and prehypertension related to new onset atrial fibrillation in a healthy Asian population without underlying disease: a nationwide cohort study in Korea [*Eur Heart J* (2017); 38 (34): 2599–2607].

The authors of the above article wish to inform readers that the following correction has been made post-publication: *Figure 2* was corrected to replace $20 < \text{BMI} \geq 25$ with $20 \leq \text{BMI} < 25$.

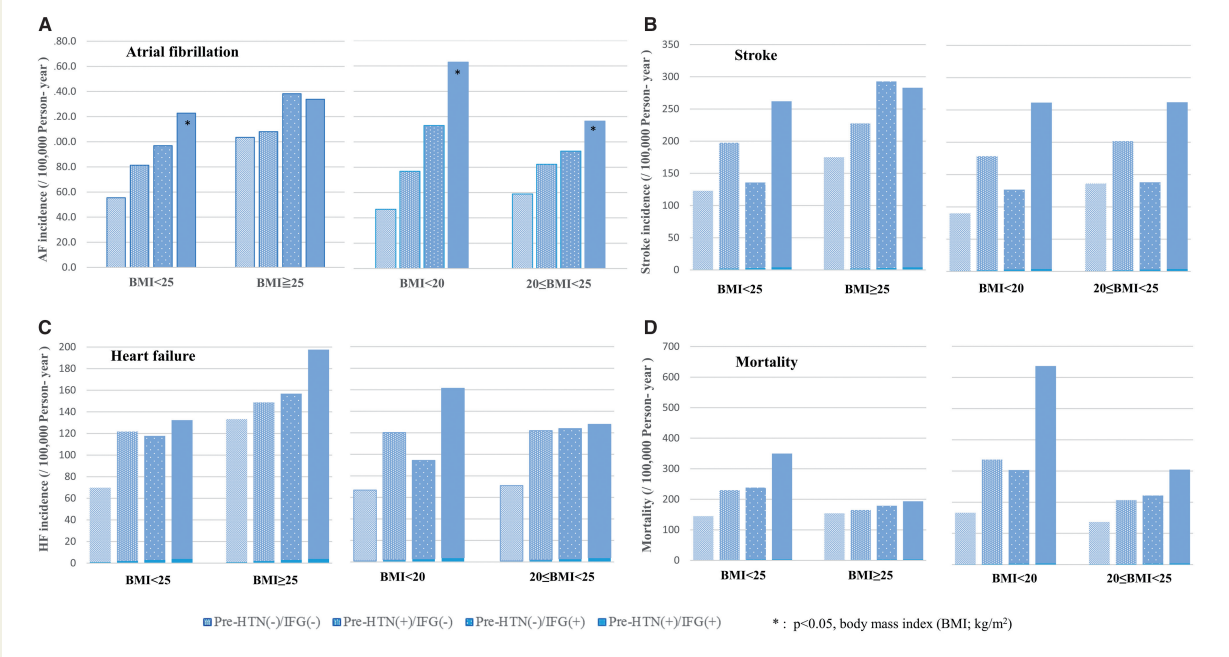

Figure 2 The incidence of new onset AF, strokes, heart failure, and mortality according to the BMI (/100 000 person-years). (Left: BMI <25 kg/m^2 vs. BMI $\geqq 25$ kg/m^2, right: BMI <20 kg/m^2 vs. $20 \leq$BMI <25 kg/m^2). (*A*) The incidence of AF according to the BMI (left, right), (*B*) The incidence of stroke according to the BMI (left, right), (*C*) The incidence of HF according to the BMI (left, right), (D) Mortality according to the BMI (left, right). AF, atrial fibrillation; HF, heart failure; HTN, hypertension; IFG, impaired fasting glucose; BMI, bodymass index.