European Cardiomyopathy Pilot Registry: EURObservational Research Programme of the European Society of Cardiology

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Aims	Cardiomyopathies are a heterogeneous group of disorders associated with premature death due to ventricular arrhythmia or heart failure. The purpose of this study was to examine the characteristics of patients enrolled in the pilot phase of the EURObservational Research Programme (EORP) cardiomyopathy registry.
Methods and results	Between 1 December 2012 and 30 November 2013, four cardiomyopathy phenotypes were studied: hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and restrictive cardiomyopathy (RCM). Twenty-seven centres in 12 countries participated; 1115 patients were enrolled. The commonest cardiomyopathy was HCM ($n = 681$), followed by DCM ($n = 346$), ARVC ($n = 59$), and RCM ($n = 29$); 423 patients (46.4% of those reported) had familial disease; and 56 (5.0%) had rare disease phenocopies. Median age at enrolment and diagnosis was 54 [interquartile range (IQR), 42−64] and 46 years (IQR, 32−58), respectively; fewer patients with ARVC and more with RCM were diagnosed in the upper age quartile ($P < 0.0001$). There was a male predominance for all cardiomyopathies except RCM ($P = 0.0023$). Most patients were in New York Heart Association functional class I ($n = 813$) at enrolment; 139 (12.5%) reported syncope, most frequently in ARVC ($P = 0.0009$). Five hundred and seven (45.5%) patients underwent cardiac magnetic resonance imaging, 117 (10.6%) endomyocardial biopsy, and 462 (41.4%) genetic testing with a causative mutation reported in 236 individuals (51.1%). 1026 patients (92.0%) were receiving drug therapy; 316 (28.3%) had received an implantable cardioverter defibrillator (highest proportion in ARVC, $P < 0.0001$).
Conclusion	This pilot study shows that services for patients with cardiomyopathy are complex, requiring access to a large range of invasive and non-invasive investigations and involvement of multidisciplinary teams. Treatment regimens are equally multifaceted and show that patients are likely to need long-term follow-up in close liaison with expert centres.
Keywords	Cardiomyopathy • Registry • Hypertrophic • Dilated • Restrictive • Arrhythmogenic right ventricular

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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] Individually, the various subtypes of cardiomyopathies are relatively uncommon, but collectively they represent a major health burden for the European population.[2–9] All cardiomyopathies can cause premature death from arrhythmia and progressive heart failure.[2,4–9]

To date, most information about the presentation and natural history of individual disorders has come from cohort studies in a few centres in Europe and the USA. The European Society of Cardiology (ESC) launched the EURObservational Research Programme (EORP) in 2009 with the aim of improving the understanding of medical practice by collecting observational data using robust methodological procedures.[10] The programme is based on networks of volunteer centres appointed by ESC constituent bodies, and the cardiomyopathy registry is a prospective, multicentre, observational study of patients presenting to referral cardiomyopathy centres in European countries, conducted by the ESC Working Group on Myocardial and Pericardial Disease (http://www.escardio.org/The-ESC/Communities/Working-Groups/Working-Group-on-Myocardial-and-Pericardial-Diseases/Myocardial-and-Pericardial-Disease).

The primary aim of the cardiomyopathy registry is to collect data on the epidemiology and outcomes of patients seen across a range of centres in Europe in order to provide information that can be used to improve clinical management and service provision. This first report summarizes the pilot phase of the survey, conducted in advance of the long-term project (http://www.escardio.org/Guidelines-&-Education/Trials-and-Registries/EURObservational-Research-Programme) to test feasibility of recruitment and to refine data collection procedures.

Methods

Registry design and methodology

Participating centres in each country were selected using pre-specified inclusion and exclusion criteria (Supplementary material online, File S1). Briefly, all participating centres in the pilot phase were required to have dedicated cardiomyopathy clinics staffed by experienced medical and nursing teams and access to facilities for genetic testing of the main genes implicated in cardiomyopathy with demonstrable experience in the interpretation of the results.

The primary aims of the registry were as follows:

(i) to describe the demographic, clinical, and genetic characteristics of patients with cardiomyopathy evaluated in referral centres across Europe;
(ii) to record the current standards for diagnostic workup and clinical follow-up of patients and families with cardiomyopathy;
(iii) to describe the therapeutic approaches currently employed for patients with different forms of cardiomyopathy across Europe;
(iv) to determine the proportion of patients with potentially inheritable disorders that is offered genetic counselling and testing;
(v) to determine the genetic profile of patients with familial forms of cardiomyopathy;
(vi) to report the long-term outcomes including the benefits and complications of treatments.

In this article, we report an overview of the first four aims in anticipation of further detailed studies examining specific components of the database.

Patient population

For the purposes of this registry, cardiomyopathies were defined as myocardial disorders in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valve disease, and congenital heart disease sufficient to cause the observed myocardial abnormality.[1] Four major phenotypes of cardiomyopathies were eligible for inclusion in the pilot: hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and restrictive cardiomyopathy (RCM). Left ventricular non-compaction (LVNC) was reported as a clinical feature in each of the four major cardiomyopathy subtypes but not in isolation. Genetic and non-genetic forms of cardiomyopathy were eligible for inclusion. Paediatric patients were also excluded from the pilot phase.

Inclusion criteria

This study was formulated in compliance with the principles of the declaration of Helsinki, October 2000. Each participating centre was asked to enter up to 40 consecutively assessed patients over a 12-month period. Informed consent was obtained from all participants before any interviews or investigations were performed. All drug treatments and diagnostic or therapeutic procedures were left to the discretion of the attending physician. Individual investigators examined medical records to confirm that patients met the following inclusion criteria:

(i) age >18 years;
(ii) willing and able to give informed consent;
(iii) ability (in the investigators' opinion) to comply with all study requirements;
(iv) a documented cardiomyopathy fulfilling standard diagnostic criteria (Supplementary material online, File S2) for probands or for relatives according to modified criteria where applicable. Relatives who fulfilled diagnostic criteria were eligible for recruitment as long as they were seen prospectively as part of a consecutive population with cardiomyopathy.

Patients who were unable to give informed consent were excluded from the study.

Statistical analysis

Univariable analysis was applied to both continuous and categorical variables. Continuous variables were reported as mean $\pm$ SD and/or as median and interquartile range (IQR) when appropriate. Among-group comparisons were made using a non-parametric test (Kruskal–Wallis test). 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 less than five. A two-sided P-value of less than 0.05 was considered as statistically significant. All analyses were performed using SAS statistical software version 9.4 (SAS Institute Inc., Cary, NC, USA).

This registry was conceived by the Working Group on Myocardial and Pericardial Disease of the ESC, conducted by an Executive Committee, and managed by the EORP Department of the ESC.

Results

Data collection

Data collection for the pilot phase of the cardiomyopathy registry began on 1 December 2012. Recruitment was complete by

30 November 2013. One-year follow-up of patients enrolled in the study ended on 1 December 2014.

Geographical distribution and number of patients enrolled

Twenty-seven centres in 12 European countries participated in the pilot survey (*Figure 1*); the total number of patients recruited was 1115. More than 50% of the patients came from one of the four countries (France, Italy, Spain, and the UK). The majority of the patients enrolled were follow-ups rather than new referrals (876 follow-up, 216 new, 23 unknown), although the proportion varied for individual centres (median new-to-follow-up ratio 24.7%, range 5.5–84.0).

Aetiology

The commonest cardiomyopathy recorded was HCM (*n* = 681, 61.1%), followed, in the descending order, by DCM (*n* = 346, 31.0%), ARVC (*n* = 59, 5.3%), and RCM (*n* = 29, 2.6%). Data on LVNC were reported in 1086 of 1115 patients; of these, 35 (3.2%) had LVNC; the associated phenotype most commonly reported in patients with LVNC was DCM (*n* = 20/340, 5.9%) followed by HCM (*n* = 13/659, 2.0%) and ARVC (*n* = 2/58, 3.5%).

A total of 56 (5.0%) patients were reported to have rare disease phenocopies (*Table 1*). The most common was amyloidosis, which was reported only in patients with HCM and RCM. Twenty-four of these patients came from two centres (France and Italy).

A history of familial disease was recorded in 423 patients (46.4% of those reported). This proportion was greatest for HCM and ARVC and least for DCM and RCM (*Table 2*). The range for individual participating countries is shown in *Figure 2*. Four hundred and sixty-two patients (41.4%) underwent genetic testing with a causative mutation reported in 236 individuals (51.1%).

Age and sex

The characteristics of the patient cohort are summarized in *Table 2*. The median age at enrolment for the entire cohort was 54 years (IQR, 42–64). The overall median age at diagnosis was 46 years (IQR 32–58). For the cohort as a whole, there was an age-related trend in the age at diagnosis, but there were significant differences between cardiomyopathies with fewer patients with ARVC and more with RCM diagnosed in the upper age quartile (*P* < 0.0001) (*Figure 3A* and *B*). There was a male predominance for all cardiomyopathy subtypes except RCM in which more women were recorded (*P* = 0.0023) (*Table 2*).

Reason for diagnosis

The commonest reason for diagnosis in the cohort as a whole was symptomatic presentation (56.1%), followed by incidental diagnosis and family screening (17.2 and 15.1%, respectively). Symptomatic presentation was more common in patients with RCM and DCM, compared with HCM and ARVC [HCM 318 (46.7%), DCM 245 (70.8%), RCM 27 (93.1%), and ARVC 35 (59.3%)] (*P* ≤ 0.0001). Diagnosis through family screening was more common in HCM and ARVC than in DCM and RCM (*P* ≤ 0.0001).
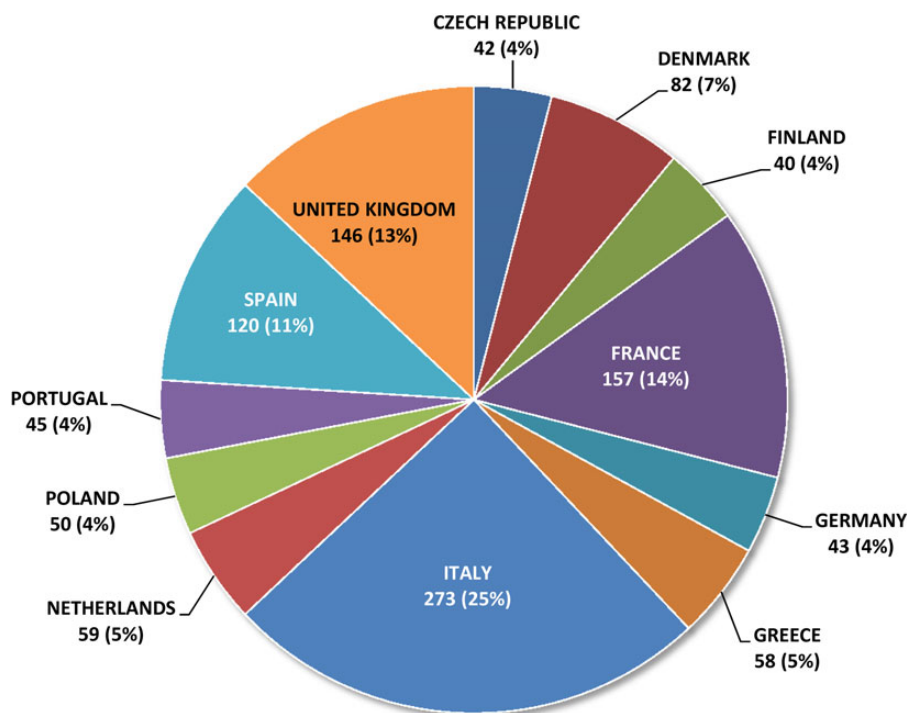
Figure 1 Pie chart showing the proportion of patients recruited in the pilot registry (*n* = 1115) enrolled in each participating country.
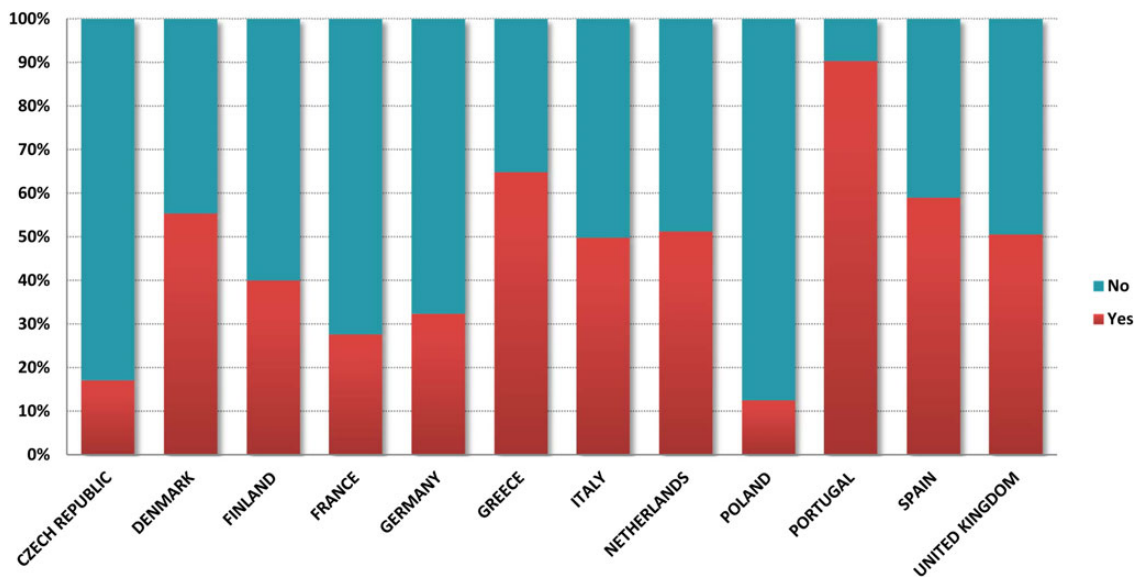
Figure 2 Proportion of patients in each cardiomyopathy subtype with a family history of cardiomyopathy in each participating country.

Table 1 Reported rare disease phenocopies in relation to cardiomyopathy subtype[a]

Diagnosis	Total cohort	HCM (n = 681)	DCM (n = 346)	RCM (n = 29)
Mitochondrial disease, n (%)	5/1115 (0.4)	3/681 (0.4)	2/346 (0.6)	0 (0)
Danon disease, n (%)	4/1115 (0.4)	3/681 (0.4)	0 (0)	1/29 (3.5)
Friedreich's ataxia, n (%)	2/1115 (0.2)	1/681 (0.1)	1/346 (0.3)	0 (0)
LEOPARD syndrome, n (%)	1/1115 (0.1)	1/681 (0.1)	0 (0)	0 (0)
Noonan syndrome, n (%)	1/1115 (0.1)	1/681 (0.1)	0 (0)	0 (0)
Anderson−Fabry disease, n (%)	12/1115 (1.1)	12/681 (1.8)	0 (0)	0 (0)
Amyloidosis, n (%)	31/1115 (2.8)	15/681 (2.2)	0 (0)	16/29 (55.2)
Total, n (%)[b]	56/1115 (5.0)	36/681 (5.3)	3/346 (0.9)	17/29 (58.6)

ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LEOPARD, lentigines, electrocardiographic abnormalities, ocular hypertelorism, pulmonary stenosis, abnormalities of the genitalia, retardation of growth, deafness.
[a]No phenocopies were reported in ARVC.
[b]No patient presented with more than one phenocopy.

Symptoms at enrolment

Most patients were in New York Heart Association (NYHA) functional classes I and II (n = 813, 72.9%) at enrolment (*Table 2*). Patients with ARVC were youngest and those with RCM oldest with respect to age at first symptoms [HCM 42.7 ± 18.7 years, 44 (30−56); DCM 45.8 ± 16.6 years, 47 (38−57); ARVC 36.4 ± 16.5 years, 39 (22−51); and RCM 54.2 ± 21.2 years, 59 (36−72), P < 0.0001].

Suspected arrhythmic/cardiogenic syncope was reported in 139 (12.5%) patients (greatest proportion in patients with ARVC, *Table 2*) (P = 0.0009). Patients with DCM were the oldest at last syncope [50.2 ± 18.6 years, 52 (47−63)] and those with ARVC the youngest [35.2 ± 15.6 years, 32 (21−43)] (P = 0.0158).

Family history of sudden cardiac death

Two hundred and forty-six (22.1%) of all patients had a family history of sudden cardiac death (*Table 2*). This was most prevalent in patients with ARVC followed by HCM, DCM, and RCM (P = 0.0003). The percentage of reported deaths among relatives aged <45 years was greatest in value, although not statistically significant in patients with ARVC (n = 13, 65.0%) compared with other groups.

Use of specialized diagnostic tests

The utilization of cardiac investigations is summarized in *Table 3*. The majority of patients had an ECG or echocardiogram performed. Ambulatory ECG monitoring and exercise testing were performed

Table 2 Baseline characteristics for each cardiomyopathy subtype enrolled into the cardiomyopathy registry

	HCM (*n* = 681)	DCM (*n* = 346)	RCM (*n* = 29)	ARVC (*n* = 59)	*P*-value
Age at enrolment, mean ± SD; median (IQR)	53.4 ± 15.88 54 (42−65)	52.6 ± 14.65 54 (44−64)	60.5 ± 17.14 65 (52−74)	46.4 ± 13.57 49 (33−56)	0.0003
Age at diagnosis, mean ± SD; median (IQR)	43.7 ± 19.0 45 (30−58)	46.1 ± 15.7 46 (37−57)	56.9 ± 20.56 64 (37−75)	37.7 ± 15.39 39 (29−49)	<0.0001
Males, *n* (%)	404/681 (59.3)	243/346 (70.2)	14/29 (48.3)	35/59 (59.3)	0.0023
Family history of SCD, *n* (%)	171/655 (26.1)	52/318 (16.4)	3/27 (11.1)	20/56 (35.7)	0.0003
Familial disease, *n* (%)	303/569 (53.3)	90/275 (32.7)	7/23 (30.4)	23/45 (51.1)	<0.0001
NYHA					<0.0001
Class I	282/681 (41.4)	99/346 (28.6)	6/29 (20.7)	31/59 (52.5)	
Class II	262/681 (38.5)	103/346 (29.8)	13/29 (44.8)	17/59 (28.8)	
Class III	96/681 (14.1)	75/346 (21.7)	9/29 (31.0)	1/59 (1.7)	
Class IV	9/681 (1.3)	38/346 (11)	0 (0)	0 (0)	
Chest pain	206/681 (30.3)	51/346 (14.7)	4/29 (13.7)	11/59 (18.6)	<0.0001
Extreme lethargy	62/681 (9.1)	63/346 (18.2)	2/29 (6.9)	2/59 (3.4)	<0.0001
Palpitations	175/681 (25.7)	73/346 (21.1)	3/29 (10.3)	31/59 (52.5)	<0.0001
Vasovagal or non-cardiac syncope, *n* (%)	31/681 (4.6)	8 (2.3)	0 (0)	0 (0)	0.0039
Suspected arrhythmic/cardiogenic syncope, *n* (%)	82/681 (12.0)	38/346 (11.0)	2/29 (6.9)	17/59 (28.8)	
Syncope of uncertain mechanism, *n* (%)	28/681 (4.1)	7/346 (2.0)	3/29 (10.3)	2/59 (3.4)	
Procedures prior to enrolment					
Septal myectomy, *n* (%)	31/681 (4.6)	–	–	–	
Alcohol septal ablation, *n* (%)	49/681 (7.2)	–	–	–	
AF ablation procedure, *n* (%)	17/24 (70.8)	8/19 (42.1)	0 (0)	2/6 (33.3)	0.0079
ICD primary prophylaxis	132/681 (19.4)	97/346 (28.0)	1/29 (3.5)	26/59 (44.1)	<0.0001
ICD secondary prophylaxis	21/681 (3.1)	30/346 (8.7)	1/29 (3.5)	8/59 (13.6)	
Medications					
Beta-blockers, *n* (%)	470/603 (77.9)	301/341 (88.3)	15/27 (55.6)	49/55 (89.1)	<0.0001
ACE-inhibitors, *n* (%)	100/603 (16.6)	249/341 (73.0)	6/27 (22.2)	14/55 (25.5)	<0.0001
Angiotensin II receptor blockers, *n* (%)	92/603 (15.3)	65/341 (19.1)	3/27 (11.1)	4/55 (7.3)	0.1010
Mineralocorticoid receptor antagonists, *n* (%)	78/603 (12.9)	173/341 (50.7)	11/27 (40.7)	6/55 (10.9)	<0.0001
Diuretics, *n* (%)	181/603 (30.0)	218/341 (63.6)	23/27 (85.2)	10/55 (18.2)	<0.0001
Antiplatelets, *n* (%)	148/601 (24.5)	71/340 (20.8)	7/27 (25.9)	12/55 (21.8)	0.5985
Oral anticoagulants, *n* (%)	160/601 (26.5)	100/340 (29.3)	16/27 (59.3)	7/55 (12.7)	0.0001

ACE, angiotensin converting enzyme; AF, atrial fibrillation; ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; ICD, Implantable cardioverter defibrillator; NYHA, New York Heart Association; RCM, restrictive cardiomyopathy; SCD, sudden cardiac death.

in 847 (76.0%) of the total cohort, with the highest proportion seen in patients with HCM and ARVC. Patients with ARVC had the greatest use of cardiac magnetic resonance imaging (*n* = 37, 62.7%). Invasive electrophysiology study was reported in 77 (7%) patients in the entire cohort (23 of whom had DCM). Endomyocardial biopsies were performed in 117 (10.5%) patients, of which 70 were reported to be diagnostic. Seventy one (60.1%) patients were entered by centres from Italy (*n* = 40, 34.2%) and a single centre in the Czech Republic (*n* = 31, 26.5%). Endomyocardial biopsy was performed most frequently in patients with RCM.

Medication

One thousand and twenty-six patients (92.0%) were receiving one or more drugs for their cardiomyopathy. The breakdown of individual classes of drug by cardiomyopathy subtype is shown in *Table 2*. The majority of patients with all types of cardiomyopathies were

receiving a beta-blocker. Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and mineralocorticoid receptor antagonists were used in all four types of cardiomyopathies, with the highest use of all three classes of drug in patients with DCM. Oral anticoagulants were used in 283 (27.6% of those recorded) and in >50% of the patients with RCM. Two hundred and thirteen patients (20.8%) with a history of atrial fibrillation (AF) were receiving oral anticoagulants [133 (22.1%) with HCM; 66 (19.4%) with DCM; 3 (5.5%) with ARVC; and 11 (40.74%) with RCM].

Pacemakers and internal cardioverter defibrillators

Three hundred and sixteen patients (28.3%) received an implantable cardioverter defibrillator (ICD). The proportion was highest in

Table 3 Cardiac investigations performed in individual cardiomyopathy subtypes

	HCM (n = 681)	DCM (n = 346)	RCM (n = 29)	ARVC (n = 59)
ECG, n (%)	650/681 (95.5)	345/346 (99.7)	29/29 (100)	59/59 (100)
Transthoracic echocardiography, n (%)	675/681 (99.1)	342/346 (98.8)	29/29 (100)	58/59 (98.3)
Cardiac MRI, n (%)	334/681 (49.0)	124/346 (35.8)	12/29 (41.4)	37/59 (62.7)
Ambulatory ECG monitoring, n (%)	541/681 (79.4)	153/346 (44.2)	10/29 (34.5)	49/59 (83.1)
Exercise test, n (%)	416/681 (61.1)	108/346 (31.2)	2/29 (6.90)	38/59 (64.4)
Endomyocardial biopsy, n (%)	15/676 (2.5)	71/346 (20.5)	17/29 (58.6)	14/58 (24.1)

ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy; MRI, magnetic resonance imaging.

patients with ARVC (n = 34, 57.6%) and lowest in those with RCM (n = 2, 6.9%). The majority of devices were for primary prophylaxis. The highest proportion for secondary prophylaxis was observed in patients with ARVC (n = 8). The number of patients with a pacemaker alone was 86 (8.0%). The commonest indication was for bradyarrhythmia/conduction disease, followed by treatment for left ventricular outflow tract gradient in patients with HCM. A total of 58 (5.2%) patients had a cardiac resynchronization therapy device at enrolment.

Discussion

This is the first European registry for cardiomyopathy. As the centres selected for the pilot phase were, by definition, specialized referral units with a high volume of cases, the data reported are not necessarily representative of the usual standard in different European nations, but the registry does show that patients in such centres require intensive investigation and access to specialized diagnostic tests. The data also show that the utilization of drug and device therapy is considerable for this selected group of patients.

General characteristics of the cohort

In accordance with published data, HCM was the most frequently recorded cardiomyopathy, followed by DCM, ARVC, and RCM.[2–9] Although rare, features consistent with LVNC were most commonly reported in patients with DCM, consistent with previous studies reporting a relatively high prevalence of LVNC in patients with systolic LV failure and may represent the low specificity of current diagnostic criteria.[11]

In the three most common cardiomyopathy subtypes, the majority of patients were diagnosed before the age of 50 years, a trend that was most striking for ARVC. Although the commonest reason for diagnosis in the cohort as a whole was symptomatic presentation, diagnosis through screening accounted a relatively large proportion (particularly for HCM and ARVC), illustrating the growing importance of family evaluation—and by implication genetic counselling and testing—in contemporary cardiomyopathy services.[12–14] The age trend was reversed in patients with RCM, reflecting the high proportion of patients in this group with transthyretin and light chain amyloidosis, diseases that present in the later decades of life.[15,16]

In all cardiomyopathy subtypes, there was an unequal sex distribution, with a skew towards men for HCM, DCM, and ARVC and towards women for RCM. The bias towards men has been observed previously in HCM, DCM, and ARVC and is usually attributed to an earlier onset of cardiac expression (or penetrance) in males when compared with women, but the mechanism remains largely unexplained.[17] It is possible that the modifier effects of sex hormones are responsible, but other factors ranging from genetics to behavioural patterns and social influences are likely to be equally if not more important.

Familial disease

A major finding in this study was the large proportion of patients in whom familial disease was reported. This is particularly striking given that only 15% of the patients were diagnosed as the result of family screening, illustrating the delay in referring individuals with a family history for further evaluation. A more detailed analysis of the genetic workup of patients in the registry will follow this report, but the large proportion of patients undergoing genetic testing and the high diagnostic yield show that, at least within specialist cardiomyopathy centres, genetic evaluation is firmly established as part of routine practice and is very efficient in experienced hands.

Diagnostic workup

This pilot shows that in specialist centres, patients with cardiomyopathy are subjected to many non-invasive tests. This reflects the complexity of diagnosis in some subtypes and the need for risk assessment for disease-related complications such as atrial and ventricular arrhythmia. The number of patients undergoing cardiac magnetic resonance imaging was relatively high, particularly in ARVC in which detection of subtle structural abnormalities in the right and left ventricles is challenging with ultrasound imaging alone.

As there are no randomized, controlled data on the utility of endomyocardial biopsy, current ESC guidelines rely on consensus recommendations built around a set of clinical scenarios in which endomyocardial biopsy has some potential to aid diagnosis.[18] Of these, only two relating to new-onset heart failure of <2 weeks duration are given class 1 status; all recommendations relating to chronic presentations of cardiomyopathy are graded at intermediate levels. It is, therefore, of note that more than 1 in 10 of the pilot registry population underwent a cardiac biopsy. The greatest use
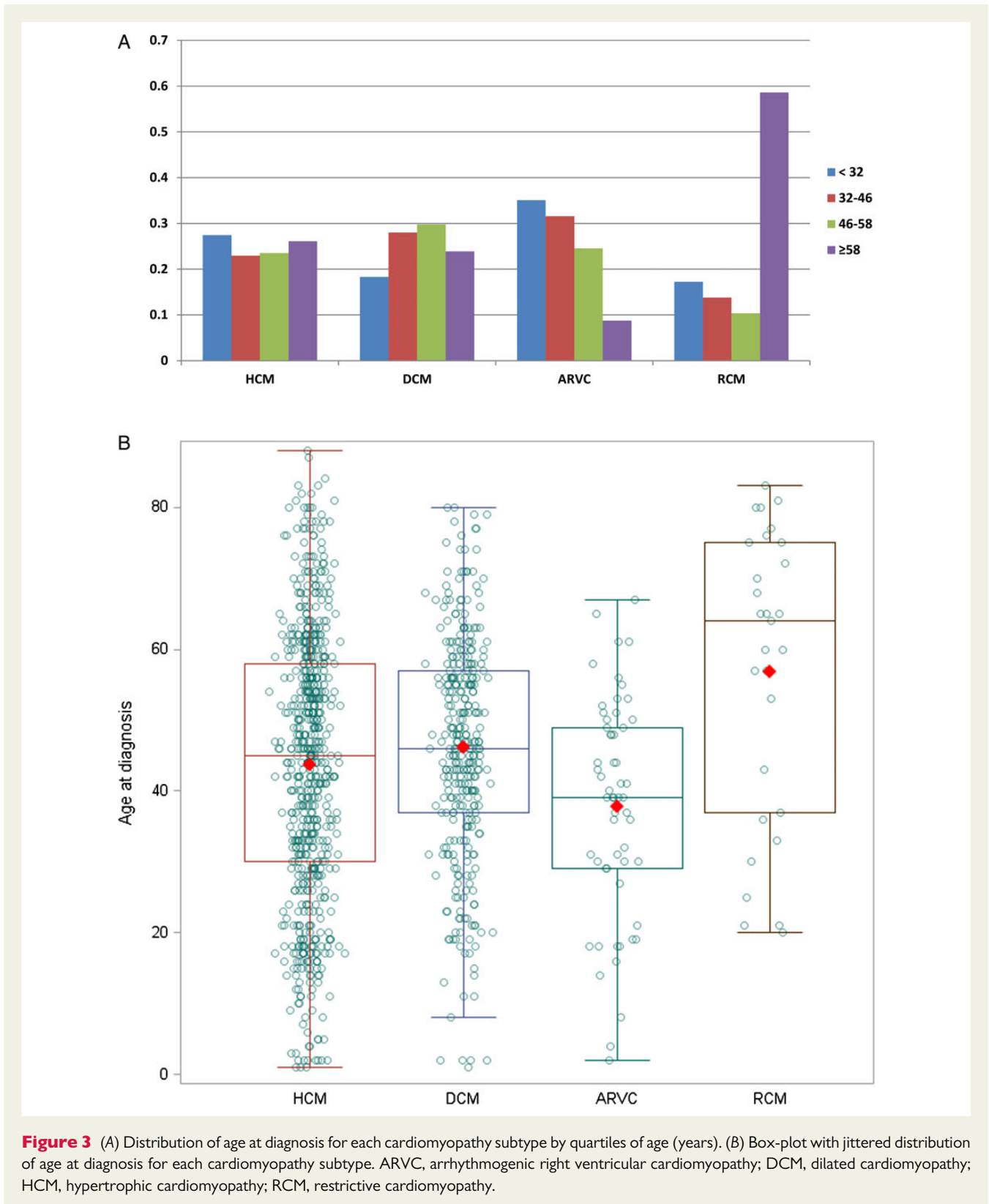
Figure 3 (*A*) Distribution of age at diagnosis for each cardiomyopathy subtype by quartiles of age (years). (*B*) Box-plot with jittered distribution of age at diagnosis for each cardiomyopathy subtype. ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy.

was in patients with RCM, reflecting the importance of infiltrative disease in this cohort, and the least in individuals with HCM in whom the current consensus is that it is of only limited use.[9] A cautionary note is that almost two-thirds of the biopsies were reported from Italian centres and a single centre in the Czech Republic. Future work in the long-term registry will explore the

variance between referral centres and examine the clinical utility of endomyocardial biopsy in patients with clinically suspected myocarditis.

Medical therapy

Patients with cardiomyopathy often require drug therapy to improve symptoms and prognosis. It is particularly striking in this pilot that—irrespective of the underlying diagnosis—more than 90% of the patients were receiving one or more long-term medications. The most frequently used drugs across all cardiomyopathy types were beta-blockers, reflecting current guidelines for the management of cardiomyopathy.[19] With respect to other drugs, ACE inhibitors and ARBs were almost universal in patients with DCM, but used much less frequently in other cardiomyopathy types. The use of oral anticoagulants was high, with the greatest use in RCM, probably reflecting the higher incidence of AF in this group.

Implantable devices

More than a quarter of all patients had an ICD at enrolment into the study. The proportions for HCM and DCM are broadly in line with that reported in contemporary studies,[20,21] except for ARVC in which 60% had a device (predominantly for primary prophylaxis).[22] This high rate of ICD implantation might reflect a bias towards patients with more severe disease in the registry, but the explanation may be more complex and reflect the lack of clear guidelines on ICD implantation in this disease. We hope this will be explored in future substudies.

Value of registries

Compared with prospective cohort studies, registries have some limitations with respect to detailed analyses of specific scientific questions, but they are of great value in providing real-world data on the course of disease and variations in treatment and outcomes. One of the goals of the long-term cardiomyopathy registry is to gather data on disparities in the delivery of care and so provide the basis for a better understanding of the effectiveness of care in referral and non-referral settings.

Limitations

The data collected in this pilot are confined to adult patients. Paediatric registries in North America and Australia suggest that there are important differences in the aetiology and natural history of cardiomyopathy in children,[23,24] and the long-term cardiomyopathy registry will prospectively collect data in the paediatric population.

For the purposes of this registry, DCM was defined by dilatation and impairment of systolic function of the left ventricle or both ventricles, in the absence of coronary artery disease, valvular abnormalities, or pericardial disease. Endomyocardial biopsy was not a prerequisite for inclusion into the pilot, and so we are unable to comment on the prevalence of inflammatory cardiomyopathy in this cohort. Data on patients with biopsy-proven myocarditis will be prospectively collected in the long-term registry.

The proportion of individuals with rare phenocopies is relatively low in this pilot survey. This may reflect the true prevalence of these disorders, but might also be explained by variation in the extent of screening (clinical and genetic) for rarer diseases.

Conclusions

Acknowledging that this is only a snap shot of practice in specialized centres, the characteristics of the patient population are in most respects very similar to those reported in the literature from a variety of clinical settings. It is clear from this pilot that services for patients with cardiomyopathy are complex, requiring access to a large range of invasive and non-invasive investigations and involvement of multidisciplinary teams with expertise in genetics, imaging, electrophysiology, and heart failure management. Treatment regimens are equally multifaceted and mean that patients are likely to need long-term follow-up in close liaison with expert centres. Many findings—for example, the very high use of ICDs in ARVC and the high yield from genetic testing—will be examined in substudies from the pilot and in the long-term registry that will also examine inflammatory myocardial disease and younger cohorts.

Supplementary material

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

Authors' contributions

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Appendix

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