

IDIOPATHIC DILATED CARDIOMYOPATHY IN WOMEN

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PURPOSE

- Sex differences exist in normal heart physiology and function.
- Clinical and experimental evidence suggests that the pathogenesis and prognosis of many cardiovascular diseases differ between sexes.
- Dilated cardiomyopathy (DCM) can be considered the most genetically heterogeneous cardiac disease, with mutations in more than 50 single genes encoding cytoskeletal, nucleoskeletal, mitochondrial, and calcium-handling proteins.
- DCM has a slightly greater prevalence in men than in women: recent trials and registries report a female/male ratio between 1:1.3 and 1:1.5. However there are few information about gender differences in DCM.

AIMS OF THE STUDY

The present investigation examine possible clinical, laboratory, echocardiography and prognostic divergencies in women and men with DCM.

METHODS

From January 1st,1988 to December 31st, 2012, **803 consecutive patients with DCM** were recorded in the Heart Muscle Registry of Trieste.

Patients had serial follow-up evaluation at the heart failure outpatient clinic of the Cardiology Department of Trieste at 6, 12, and 24 months, and subsequently every two years, or more frequently if clinically indicated.

We considered and compared some clinical, laboratoristic, electrocardiographic and echocardiographic characteristics between men and women at baseline, then we evaluated the longitudinal changes of the most significant parameter during follow-up.

The primary endpoint of the study was long-term total death/ heart transplantation (D/HT) . The secondary endpoint were cardiovascular death (CVD) and sudden death/ appropriate ICD interventions (SD/AII).

Baseline clinical instrumental characteristics

Variable	All (N=803)	Males (N= 576, 72%)	Females (N=227, 28%)	P value
Age (y)	45	45 (34-55)	48 (37-58)	0,008
Body mass index (kg/m2)	25,3 (22,7-27,9)	25,7 (23,3-28,0)	24,0 (21,6-26,8)	< 0,001
Body surface area (m2)	1,9	1,9 (1,8-2,1)	1,7 (1,6-1,8)	< 0,001
Heart rate at rest (beats/min)	75 (68-87)	75 (68-85)	76 (70-90)	0,110
Systolic blood pressure (mmHg)	120 (110-135)	125 (110-135)	120 (110-140)	0,164
NYHA I	277 (34,6%)	209 (36%)	68 (30%)	
II	327 (41%)	231 (40%)	96 (42%)	0,348
III	152 (19%)	103 (18%)	49 (22%)	
IV	44 (5,5%)	31 (5%)	13 (6%)	
NYHA III-IV	196 (24,5%)	134 (23%)	62 (28%)	0,226
Heart Failure duration (y)	1 (0-7)	1 (0-7)	1 (0-8,5)	0,577
Laboratory findings				
Haemoglobin (mg/dL)	14 (13-15)	14,6 (13,8-15,4)	12,9 (12,1-13,9)	< 0,001
Creatinine (mg/dL)	1,1 (0,9-1,2)	1,1 (1,0-1,2)	0,9 (0,8-1,1)	<0,001

Variable	All (N=803)	Males (N= 576, 72%)	Females (N=227, 28%)	P value
Echocardiographic findings				
LVEF (%)	32 (24-39)	32 (24-39)	31 (24-41)	0,976
Indexed LVEDD (mm/m2)	35 ds5,7	34 (31-38)	36 (33-40)	< 0,001
Indexed LVESD (mm/m2)	29 ds 6,4	29 (24-33)	29 (26-33)	0,05
Restrictive filling pattern	184 (28 %)	140 (29 %)	44 (25,4 %)	0,365
Moderate-severe MR	271 (36 %)	180 (33,5 %)	91 (42,9 %)	0,015
Indexed LVEDV (mL/m2)	91 (72-117)	93 (75-120)	85 (67-111)	0,002
Indexed LVESV (mL/m2)	63 (44-86)	64 (46-89)	57 (40-81)	0,008
DASIN	19 (15-23)	19 (15-23)	20 (13-24)	0,334
Electrocardiographic findings				
Sinus rhythm	697 (89,5 %)	489 (87,5 %)	208 (94,5 %)	0,004
RBBB	136 (17,6 %)	88 (15,9%)	48 (21,7%)	0,055
LBBB	242 (31,2%)	158 (28,5%)	84 (38%)	0,01
QTC (msec)	437 (403-468)	433 (400-466)	440 (411-476)	0,076

RESULTS

BASELINE CLINICAL INSTRUMENTALE CHARACTERISTICS

576 (72 %) were male and 227 (28 %) were female.

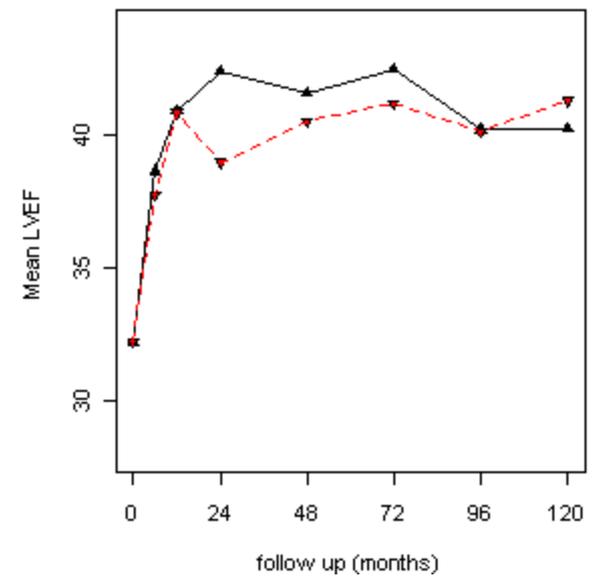
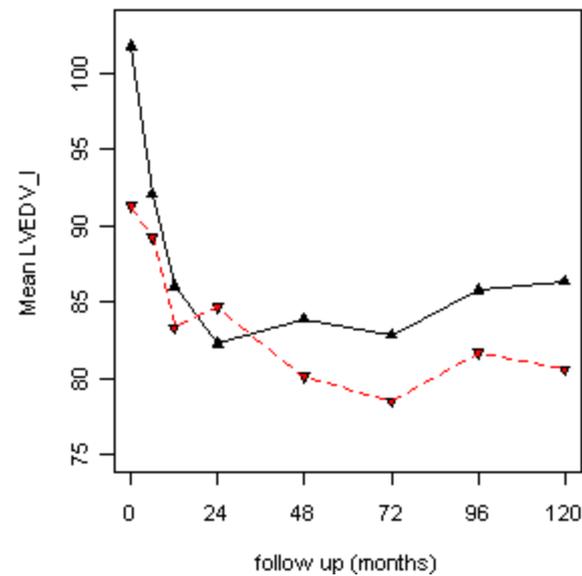
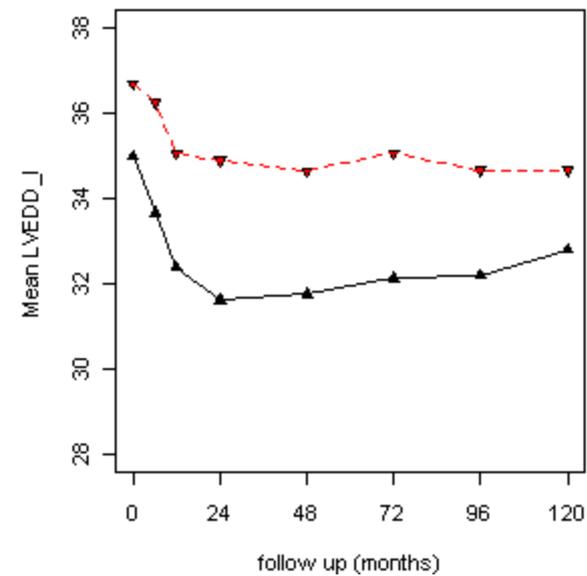
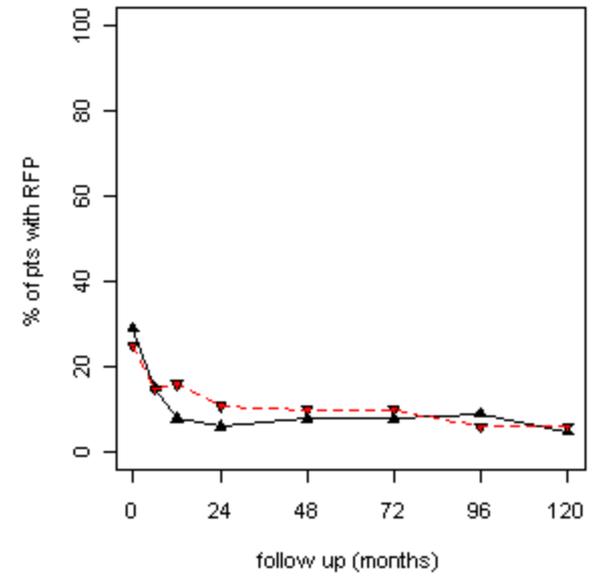
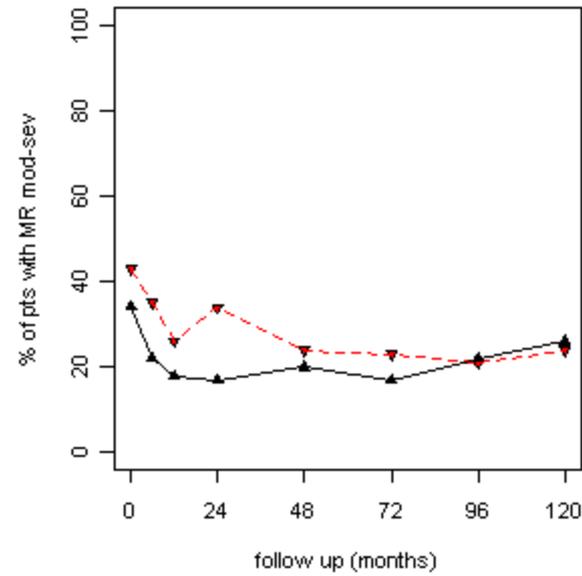
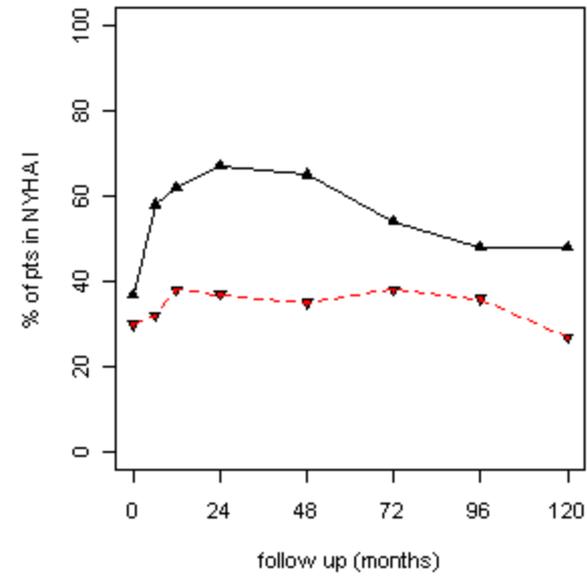
The mean age was 45 years and at the first evaluation women resulted older (48 vs 45 years old, $p=0,008$); At baseline 62 (27%) of women and 134 (23%) of men were in NYHA functional class III-IV ($p=0,226$). The median duration of heart failure was about 1 year in both sexes ($p=0,577$).

Laboratory findings showed in women lower hemoglobin (12,9 vs 14,6 g/dL, $p<0,001$) and lower glomerular filtration rate (66 vs 115 mL/min, $p<0,001$).

On electrocardiographic evaluation, women presented more frequently with left bundle branch block (38% vs 28%, $p=0,01$), but they were more frequently in sinus rhythm (94% vs 87%, $p=0,004$). No significant difference in corrected QT interval duration (QTc) between women and men emerged (440 vs 433 msec, $p=0,076$).

Considering echocardiographic measurements women presented with a significantly greater left ventricular end-diastolic indexed diameter (36 vs 34 mm/m², $p<0,001$) and more frequently with significant mitral regurgitation (43% vs 33%, $p=0,015$).

No significant difference resulted in pharmacological treatment and device implantation: 88% of women and 92% of men received angiotensin-converting enzyme inhibitors or angiotensin receptor blockers ($p=0,054$) and 80% of women and 81% of men received beta-blockers ($p=0,784$); 13,2% of women and 17,7% of men received ICD ($p=0,122$), and 8,4% of women and 5,2% of men received resynchronization therapy ($p=0,092$).



LONG TERM RESULTS

During a 120 months follow-up men presented a better clinical and echocardiographic improvement than women.

In the first 12 months of follow-up more women resulted in NYHA classes III-IV while a higher percentage of men improved clinically and resulted in NYHA class I.

Considering echocardiographic parameters: more women showed a significant mitral regurgitation and a restrictive pattern during the first 24 months and larger index diastolic diameter during the whole follow-up. We found no difference between genders in ventricular ejection fraction during follow-up (table 2).

Considering the longitudinal “evolution” of some clinical and echocardiographic parameters we evaluated significant changes of these characteristics between different follow-up.

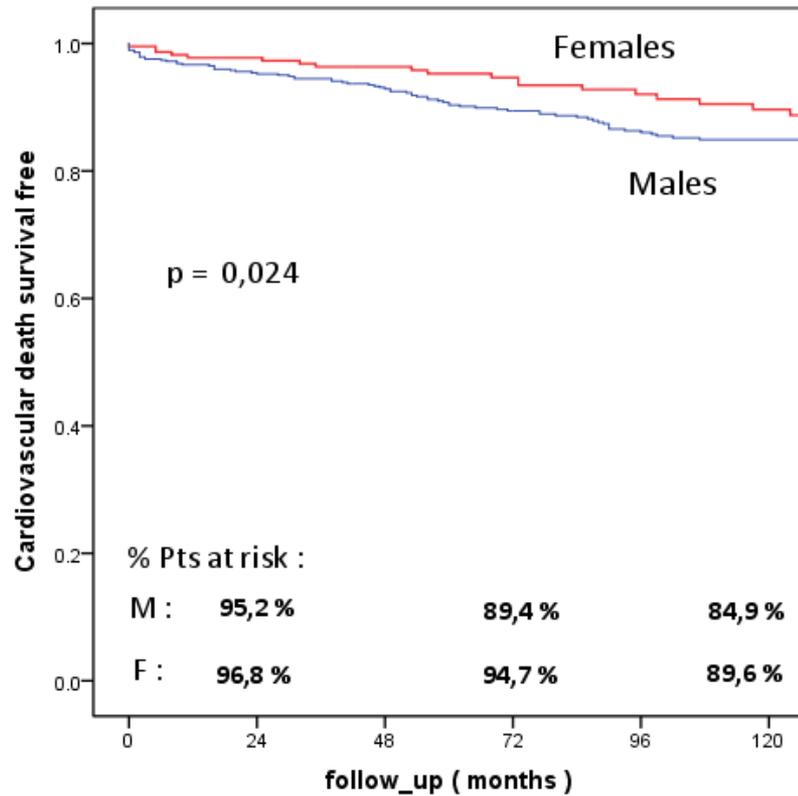
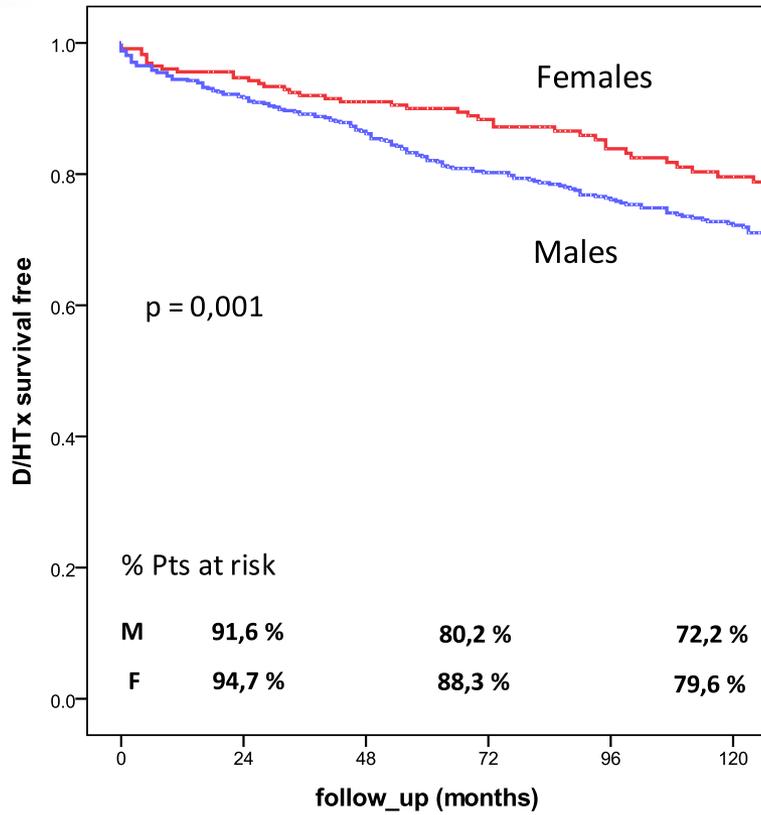
From baseline to 6 months there was a significant increase of the percentage of men in class NYHA I ($p < 0.001$), then the number remained stable until 72 months when there was a statistical significant decrease. Women showed no significant variation.

Considering LVEF there were in both sexes an improvement of left ventricular function in the first 12 months, then men continued to improve until 24 months and then declined after 72 months, while women remained stable.

A similar trend was observed for significant mitral regurgitation and restrictive diastolic pattern.

Index left ventricular end diastolic diameter reduced in both sexes until 24 months and then remained stable (tabella 3, figure andamenti).

	All (N = 803)	Males (N= 576, 72 %)	Females (N=227, 28%)	P value
All cause mortality/heart transplant n(%)	233 (29%)	187 (32,5%)	46 (20,3%)	0,001
Heart transplant n (%)	69 (8,6%)	54 (9,4%)	15 (6,6%)	0,188
Cardiovascular death n (%)	109 (13,6%)	88 (15,3%)	21 (9,3%)	0,024
Pump failure death n (%)	38 (4,7%)	31 (5,4%)	7 (3,1%)	0,244
Unexpected sudden death n (%)	60 (7,5%)	47 (8,2%)	13 (5,7%)	0,22
Unknown cause death n (%)	55 (6,8%)	45 (7,8%)	10 (4,4%)	0,059
Appropriate intervention of ICD N=40 N (% of implanted patients: 132, 102 M e 30 F)	40/132, 30%	29/102 (28%)	11/30 (37%)	0,830
M_II o scarica appropriate	100 (12,5%)	76 (13,2%)	24 (10,6%)	0,244



LONG TERM RESULTS

Total mortality/heart transplantation and cardiovascular mortality at 20 years resulted lower in women (20% vs 32% $p=0,001$, and 9% vs 15% $p=0,024$, respectively). Considering pump failure mortality, unexpected sudden cardiac death and unexpected sudden cardiac death/appropriate ICD intervention there was a trend of lower events in woman but they did not reach statistical significance.