Cardiomiopatia dilatativa senza dilatazione. Esiste?"

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OSPEDALI RIUNITI DI TRIESTE

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Classification of the cardiomyopathies: a position statement from the european society of cardiology working group on myocardial and pericardial diseases

Perry Elliott, Bert Andersson, Eloisa Arbustini, Zofia Bilinska, Franco Cecchi, Philippe Charron, Olivier Dubourg, Uwe Kühl, Bernhard Maisch, William J. McKenna, Lorenzo Monserrat, Sabine Pankuweit, Claudio Rapezzi, Petar Seferovic, Luigi Tavazzi, and Andre Keren*

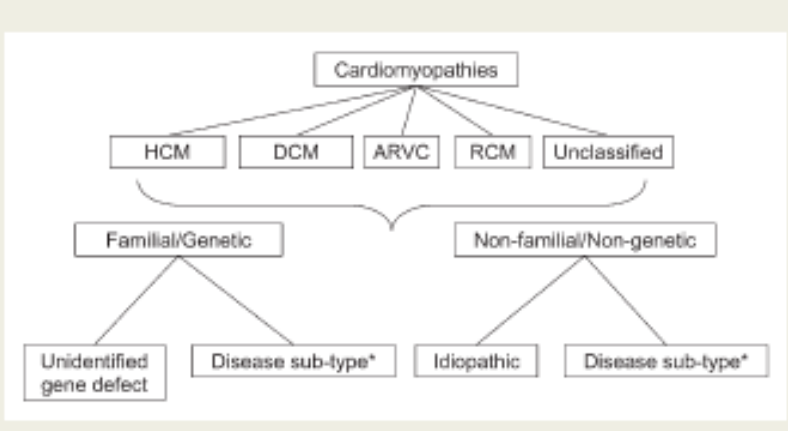
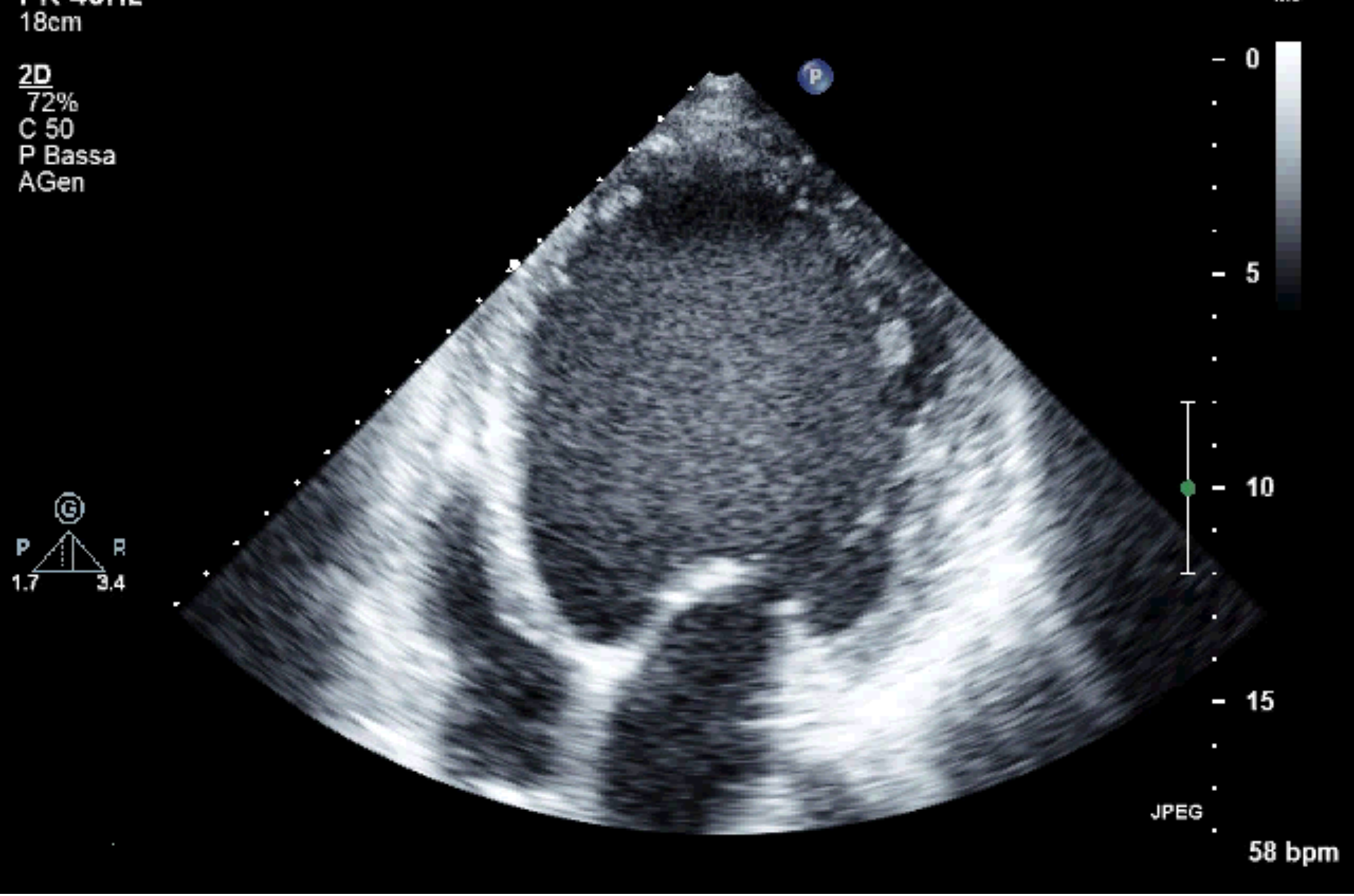


Figure 1 Summary of proposed classification system. ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy (*see table)

CARDIOMIOPATIA DILATATIVA DEFINIZIONE

- Malattia del miocardio caratterizzata da dilatazione e ridotta funzione di pompa del ventricolo sinistro o di entrambi i ventricoli.
- Criteri diagnostici (eco, angio, scintigrafia):
- Ridotta FE del ventricolo sinistro (<45%)
- Dilatazione della camera ventricolare (DTD >2.7 cm/mq o >117% valore corretto x età e sc)* non assoluto: "mildly-dilated CMP
- Esclusione di malattie "specifiche" (ischemica, ipertensiva, valvolare)


18cm
2D
72%
C 50
P Bassa
AGen
P
0
5
10
15
P
R
1.7
3.4
JPEG
58 bpm

“MILDLY-DILATED” CMP
CRITERI DIAGNOSTICI

- Significativa riduzione della funzione di pompa VSn (FE < 45%)
- Assenza di importante dilatazione VSn (DTD non sup. al 15% oltre i valori normali)
- Rientrano nello spettro delle CMPD
- Clinica e prognosi simile

(Gavazzi et al. AHJ 1993;125:410)

Mildly dilated cardiomyopathy (MDCM) is a subgroup of idiopathic dilated cardiomyopathy characterized by slightly dilated left ventricle and presenting systolic dysfunction

PATHOPHYSIOLOGY AND NATURAL HISTORY

CARDIOMYOPATHY

Mildly dilated congestive cardiomyopathy

ANDRE KEREN, M.D., MARGARET E. BILLINGHAM, M.D., DOMINIQUE WEINTRAUB, M.D., EDWARD B. STINSON, M.D., AND RICHARD L. POPP, M.D.

MDCM was firstly reported in 1985. It was described as a disease with the characteristic features of DCM but without significant ventricular enlargement [1]

1) Keren A et al. Mildly dilated congestive cardiomyopathy. Circulation. 1985;72(2):302-9.

Long-Term Prognosis of Patients With Mildly Dilated Cardiomyopathy

Hiroaki Kitaoka, MD; Yoshihisa Matsumura, MD; Naohito Yamasaki, MD;
Fumiaki Kondo, MD; Takashi Furuno, MD; Yoshinori Doi, MD

A careful history was obtained from all patients, who also underwent physical examination, routine blood tests, chest radiography, standard ECG, exercise stress testing, echocardiography, and right- and left-heart cardiac catheterization with coronary angiography and left ventriculography. DCM was diagnosed based on exclusion of other causes of LV dysfunction, such as acute myocarditis, significant coronary artery stenosis, valvular disease and/or other secondary myocardial diseases. MDCM was defined by (1) a LV ejection fraction (LVEF) ≤40% with a LV end-diastolic volume ≤120 ml/m^2 on left ventriculography and (2) the absence of a dip-and-plateau right ventricular pressure caused by a restrictive cardiomyopathy? Therefore, of 144 consecutive patients with DCM, 21 (15%) were diagnosed with MDCM.

MDCM was arbitrarily defined in patients with 1) idiopathic cardiomyopathy, exhibiting severe heart failure, 2) in the presence of decreased left ventricular contraction (left ventricular ejection fraction less than 30%), but 3) without early diastolic dip and plateau pressure patterns or equalization of right and left ventricular diastolic pressures typical of restrictive myopathy,[5,6] and 4) which occurred with no or only mild ventricular dilation (less than 15% above normal range corrected for body surface area).

Keren A et al. Mildly dilated congestive cardiomyopathy. Use of prospective diagnostic criteria and description of the clinical course without heart transplantation. Circulation 1990;81:506-17.

ular end-diastolic diameter index [7,8]. Accordingly, all cases with an end-diastolic ventricular diameter not exceeding 15% of this value, i.e. 37 mm/m^2, were arbitrarily defined as MDCM. Patients with DCM, showing end-diastolic left ventricular diameter at enrollment ≥40 mm/m^2, were chosen as controls. Patients with left ventricular end-diastolic diameter >37 and <40 mm/m^2 were not considered in this analysis, to avoid inclusion of a possibly confusing intermediate population.

Porcu M et al.Mildly dilated cardiomyopathy. In “Advances in Cardiomyopathies”. Springer1988;194-202.

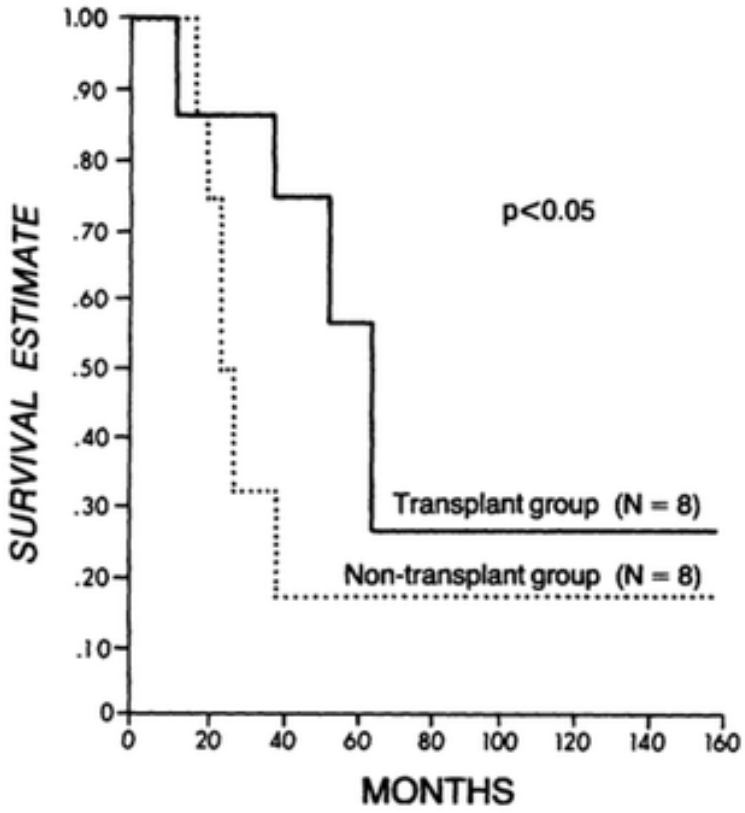


FIGURE 2. *Plot of survival estimate versus time for two groups with persistent mildly dilated congestive cardiomyopathy, using Kaplan-Meier analysis (Reference 24). Survival of transplant group is significantly different by Cox-Mantel test (p<0.05).*

Keren A et al.Circulation 1990;81:506-17.

Table 1 Baseline Characteristics of the 21 Patients With MDCM

	Event (+) (n=9)	*Event (–) (n=12)*	*p value*
Clinical characteristics			
Male	*7 (78%)*	*9 (75%)*	*0.66*
Age at diagnosis (years)	*55±9*	*62±9*	*0.13*
NYHA class at diagnosis	*2.6±1.1*	*2.1±0.7*	*0.18*
Atrial fibrillation (%)	*4 (44%)*	*4 (33%)*	*0.68*
Cardiothoracic ratio (%)	*53±4*	*52±3*	*0.27*
Hemodynamic findings			
LV ejection fraction (%)	*34.1±3.5*	*33.5±5.2*	*0.76*
LV end-diastolic volume (ml/m^2)	*106.0±93.0*	*95.6±18.2*	*0.14*
LV end-systolic volume (ml/m^2)	*69.7±6.3*	*63.3±12.8*	*0.2*
LV end-diastolic pressure (mmHg)	*12.2±6.7*	*8.8±2.3*	*0.12*
Pulmonary wedge pressure (mmHg)	*10.9±7.1*	*7.6±2.0*	*0.16*
Mean pulmonary artery pressure (mmHg)	*19.7±7.2*	*15.0±3.1*	*0.06*
RV end-diastolic pressure (mmHg)	*7.0±2.2*	*7.4±1.8*	*0.64*
Mean right atrial pressure (mmHg)	*5.8±2.6*	*6.0±1.9*	*0.82*
Cardiac index (L·min^{-1}·m^{-2})	*2.1±0.6*	*2.1±0.5*	*0.83*
Mitral regurgitation			
Absent-mild	*9*	*12*	*0.99*
Moderate-severe	*0*	*0*	
Echocardiographic findings			
LV end-diastolic dimension (mm)	*58.7±3.7*	*59.3±6.5*	*0.81*
LV end-systolic dimension (mm)	*49.0±5.5*	*49.1±7.0*	*0.91*
Fractional shortening (%)	*16.6±6.7*	*17.0±4.5*	*0.86*
Left atrial dimension (mm)	*39.2±5.3*	*37.7±5.0*	*0.5*
Medication			
Digitalis (%)	*100*	*58*	*0.04*
Diuretics (%)	*100*	*92*	*0.99*
ACE inhibitor (%)	*67*	*83*	*0.61*
β-blocker (%)	*0*	*42*	*0.04*

Kitaoka et al. Circ J 2002 Jun;66(6):557-60.

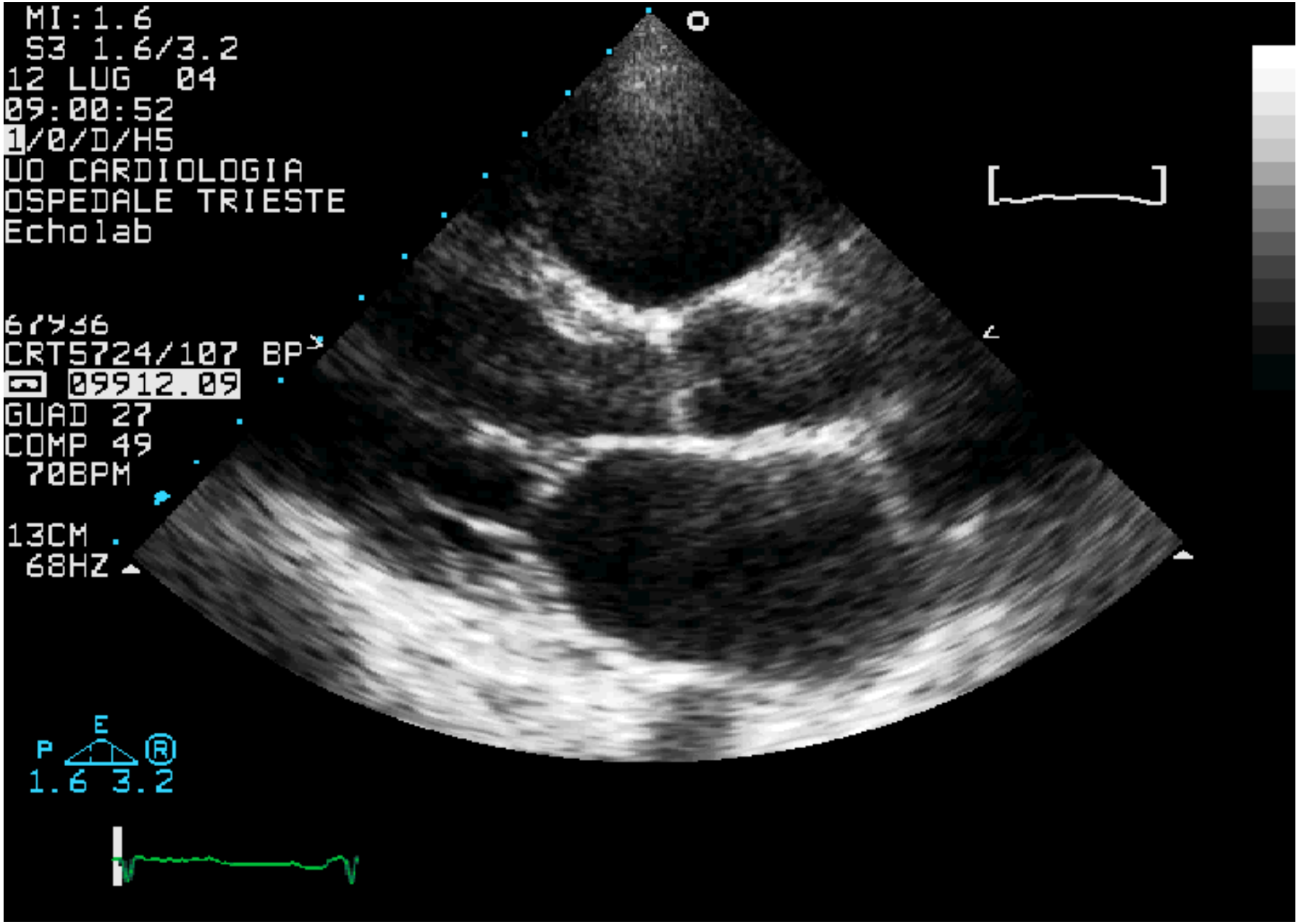
Table 5 Reference limits and partition values of left ventricular size

	Women				Men			
	Reference range	Mildly abnormal	Moderately abnormal	Severely abnormal	Reference range	Mildly abnormal	Moderately abnormal	Severely abnormal
LV dimension								
LV diastolic diameter	3.9–5.3	5.4–5.7	5.8–6.1	≥6.2	4.2–5.9	6.0–6.3	6.4–6.8	≥6.9
LV diastolic diameter/BSA, cm/m^2	2.4–3.2	3.3–3.4	3.5–3.7	≥3.8	2.2–3.1	3.2–3.4	3.5–3.6	≥3.7
LV diastolic diameter/height, cm/m	2.5–3.2	3.3–3.4	3.5–3.6	≥3.7	2.4–3.3	3.4–3.5	3.6–3.7	≥3.8
LV volume								
LV diastolic volume, mL	56–104	105–117	118–130	≥131	67–155	156–178	179–201	≥201
LV diastolic volume/BSA, mL/m^2	***35–75***	***76–86***	***87–96***	***≥97***	***35–75***	***76–86***	***87–96***	***≥97***
LV systolic volume, mL	19–49	50–59	60–69	≥70	22–58	59–70	71–82	≥83
LV systolic volume/BSA, mL/m^2	***12–30***	***31–36***	***37–42***	***≥43***	***12–30***	***31–36***	***37–42***	***≥43***

Lang et al. Recommendations for Chamber quantification, J Am Soc Echocardiogr 2005, 18(12): 1440-63

	Male				Female			
	Normal range	Mildly abnormal	Moderately abnormal	Severely abnormal	Normal range	Mildly abnormal	Moderately abnormal	Severely abnormal
LV volume								
LV diastolic volume (mL)	62–150	151–174	175–200	>200	46–106	107–120	121–130	>130
LV diastolic volume/BSA (mL/m^2)	34–74	75–89	90–100	>100	29–61	62–70	71–80	>80
LV systolic volume (mL)	21–61	62–73	74–85	>85	14–42	43–55	56–67	>67
LV systolic volume/BSA (mL/m^2)	11–31	32–38	39–45	>45	8–24	25–32	33–40	>40

Lang et al. Recommendations for Cardiac Chamber Quantification, J Am Soc Echocardiogr 2015, 28: 1-39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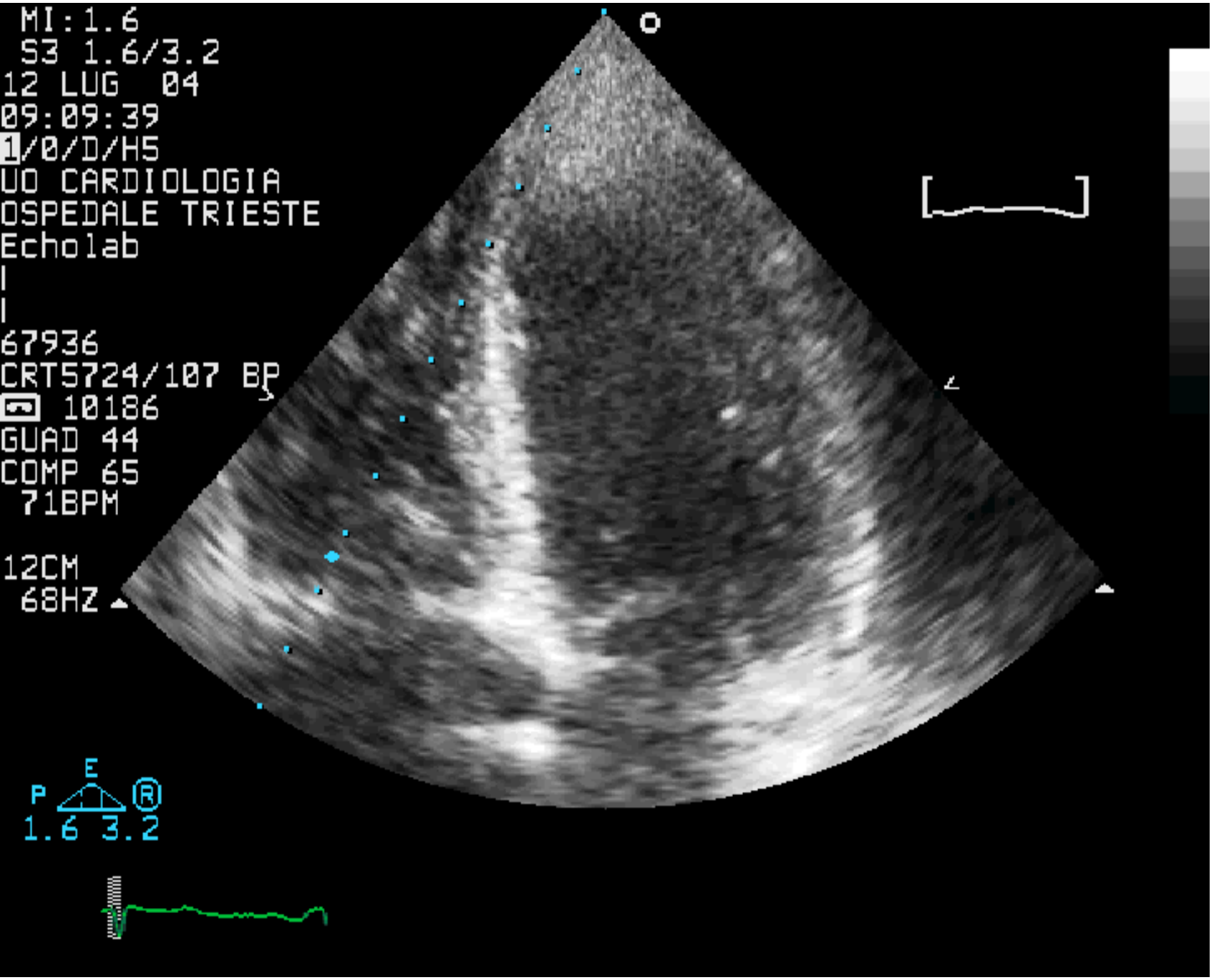
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Echolab
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CRT5724/107 BP
10186
GUAD 44
COMP 65
71BPM
12CM
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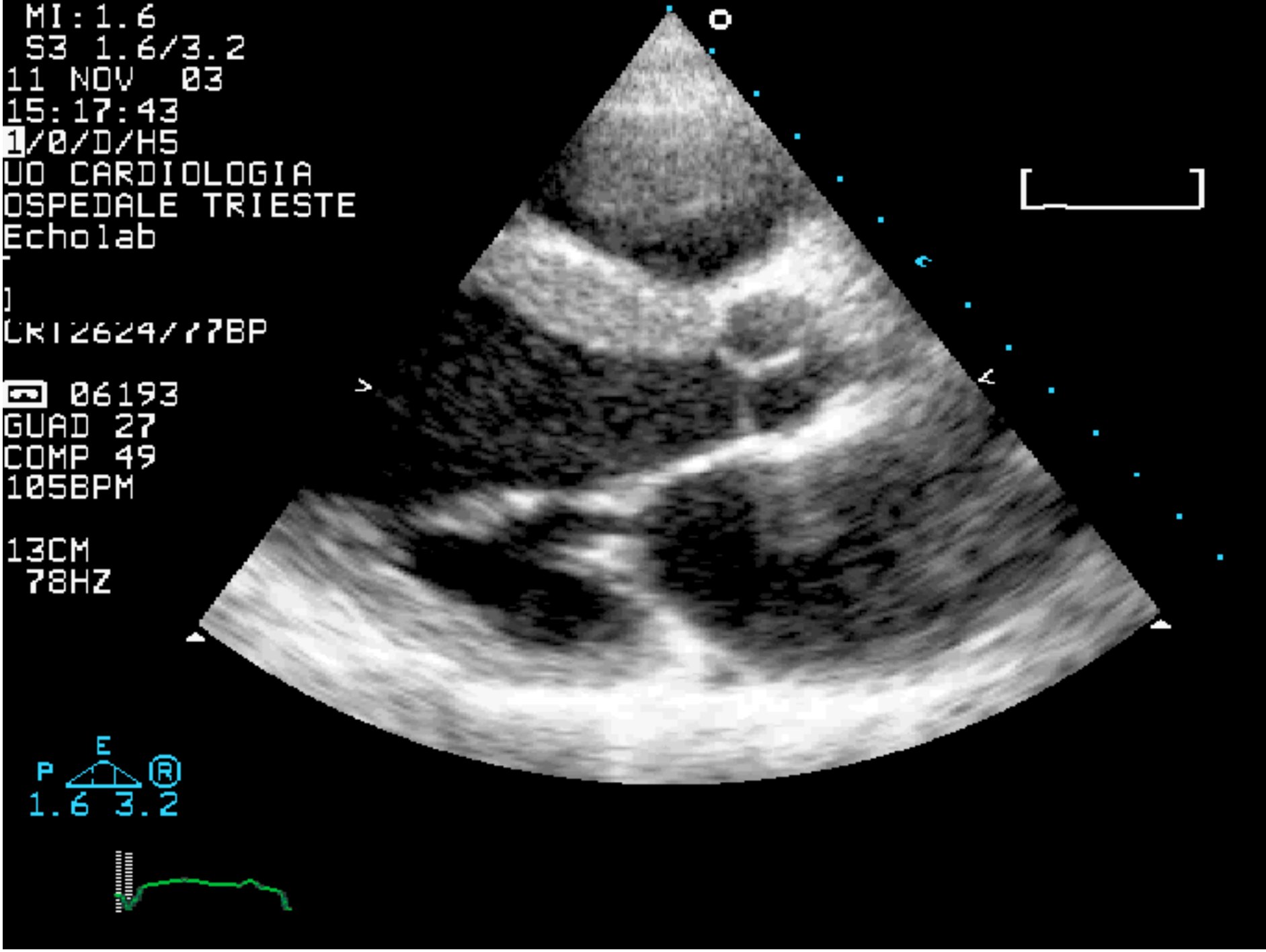
1.6 3.2

Differential Diagnosis

- ✓ Coronary artery disease
- ✓ Sistemic hypertension
- ✓ Hypertrophic CMP (end-stage)
- ✓ Tachy induced cardiomiopathy
- ✓ Myocarditis
- ✓ Peripartum disease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M E T H O D S

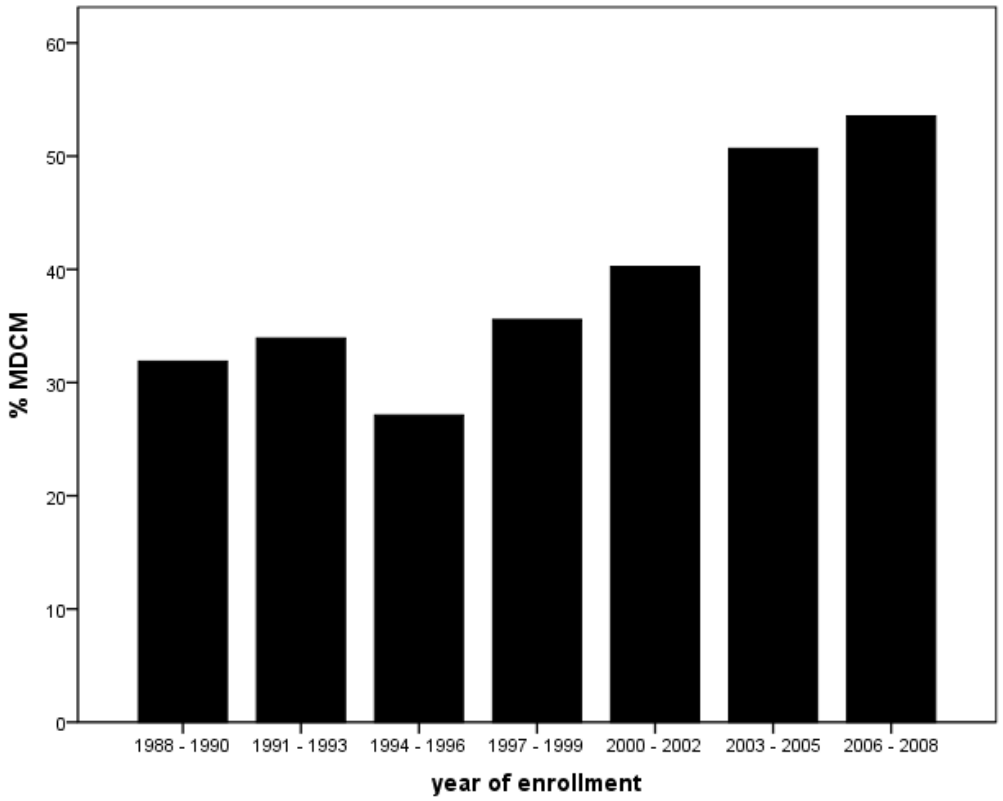
- ✓ LVD was defined as **LVEF≤50%** and **index LV end-diastolic volume≤86 ml/m²**
- ✓ From **1/1/1988** to **31/12/2008** we enrolled **659 DCM** patients
  Mean follow-up was **123** (66-193) **months**

HTx

HTx

1) **SD or malignant ventricular arrhythmia** and/or appropriate **ICD interventions;**
2) **SD or malignant ventricular arrhythmia** and/or appropriate **ICD interventions;**

R E S U L T S

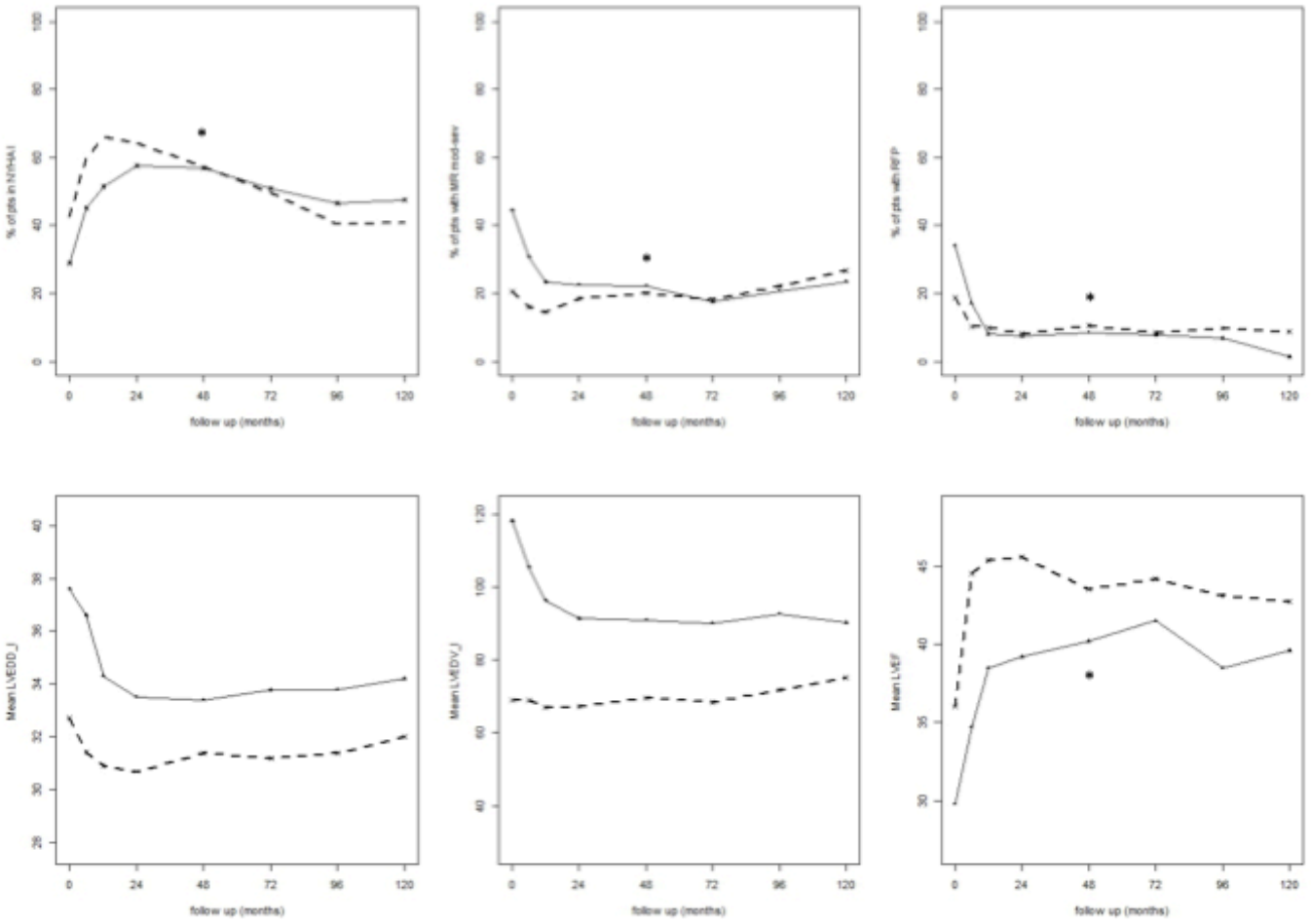


✓ **252** patients (38%) fulfill the pre-specified criteria for **MDCM**

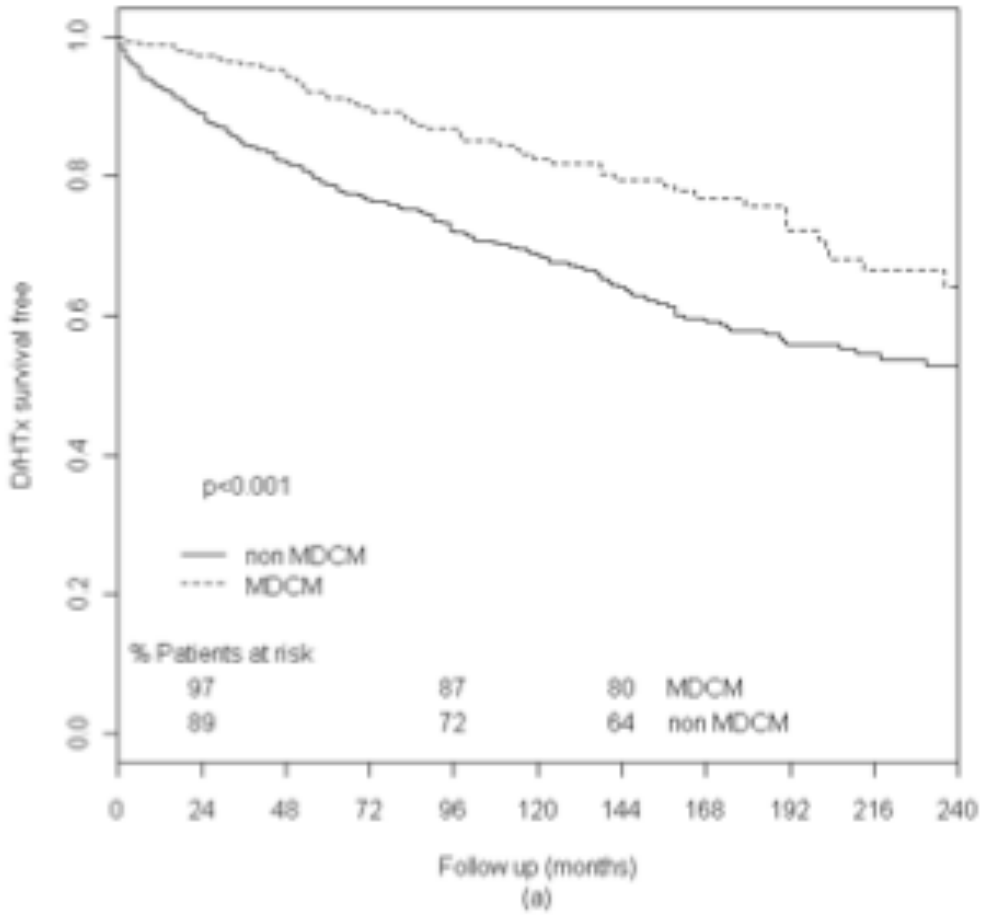
	MDCM	IDCM	p
Age (years)	45 (36-54)	45 (34-55)	0.941
Male sex (%)	66	78	0.002
Median Duration of HF (months)	1 (0-6)	2 (0-10)	<0.001
NYHA III-IV (%)	16	30	<0.001
Diabetes (%)	5	7	0.315
Familiarity (%)	23	19	0.257
LBBB (%)	23	36	<0.001
LVEF (%)	36±9	30±12	<0.001
LVEDDI (mm/m^2)	33±5	38±6	<0.001
LVESDI (mm/m^2)	27±5	32±6	<0.001
LVEDVI (ml/m^2)	69±13	118±37	<0.001
LVESVI (ml/m^2)	44±12	86±36	<0.001
Significant FMR (%)	21%	45%	<0.001
RFP (%)	19%	34%	<0.001
Beta-blockers (%)	82%	82%	0.957
ACE-inhibitors-ARBs (%)	91%	93%	0.327
ICD - CRT implantation (%)	12	20	0.004

R E S U L T S

- MDCM were less symptomatic than DCM
- MDCM initially improved under optimal therapy, then were stable at mid-term, followed by a progression in the long term approaching the IDCM patients

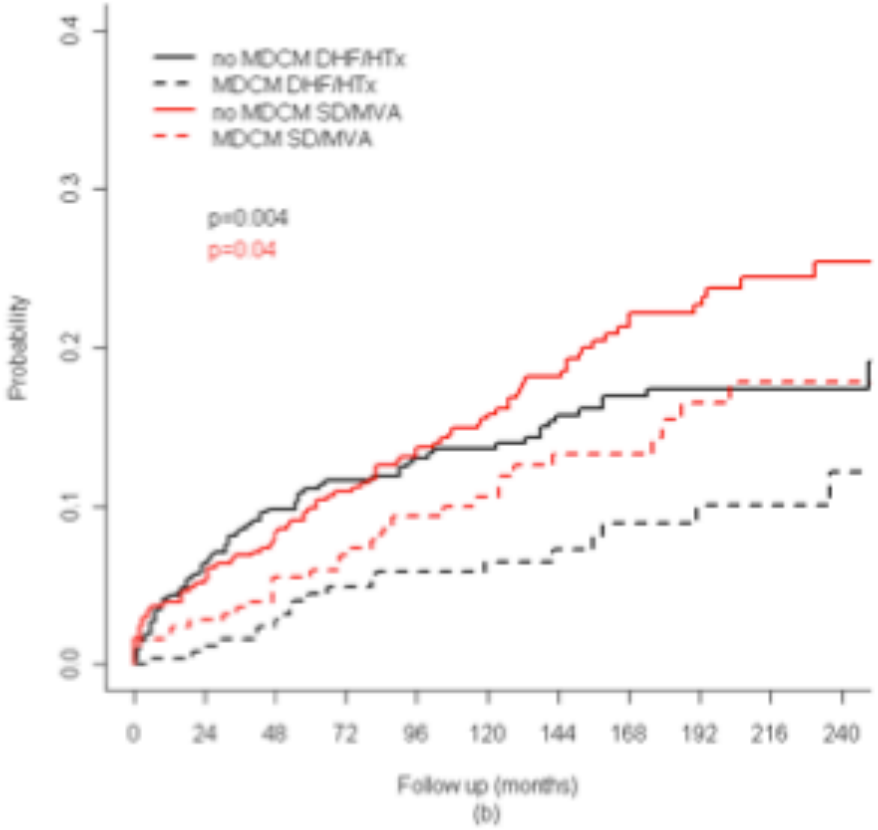


R E S U L T S



- ✓ At 10 years follow-up, **all-cause mortality/heart transplant** was **21%** in MDCM **and 39%** in DCM (p<0.001)

R E S U L T S



- ✓ **DHF /HTx** and **SD/MVA** rates were **significantly less frequent in MDCM** (p=0.004 and p=0.04, respectively)
- ✓ Notably, **MDCM condition did not** emerged as an independent predictor for any pre-specified study end-points **at multivariable analysis**

C O N C L U S I O N S

MDCM identifies a **consistent subgroup of DCM** patients **initially** characterized by an **apparent less adverse** evolution and **later** by a long time progression **similar to IDCM**

Therefore, **most of MDCMs** may be **considered as a DCM** discovered **in an early phase**, usually presenting a more benign long-term outcome

However, the possibility of a **distinct phenotypic expression associated with an unfavourable prognosis** cannot be excluded in selected cases

Further studies are **warranted** to investigate the characteristics potentially helpful in the **identification o**f these **higher-risk MDCM** patients for which **early genetic testing** could be considered


Grazie