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APPROPRIATE ICD THERAPY IN DILATED CARDIOMYOPATHY DEPENDING ON ITS AETIOLOGY

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INFLUENCE of LEFT VENTRICULAR EJECTION FRACTION DYNAMICS on FREQUENCY of ICD SHOCKS (I)

Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) Trial, Chicago, 449 patients

Objective:

to evaluate the effect of LVEF change on outcome in the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial

Inclusion criteria:

- ✓ **nonischemic cardiomyopathy with LVEF<36%**
- ✓ **history of symptomatic heart failure**
- ✓ **presence of significant ventricular ectopic activity**

Results:

- ✓ **patients whose LVEF improved had reduced mortality compared to patients whose LVEF decreased (HR 0.09; 95% CI 0.02-0.39; p = 0.001)**
- ✓ **survival free of appropriate shocks was not significantly related to LVEF improvement during follow-up at least 90 days (90 – 730 days)**

Schliamser JE at al. Heart Rhythm 2013 Jun;10(6):838-46

INFLUENCE of LEFT VENTRICULAR EJECTION FRACTION DYNAMICS on FREQUENCY of ICD SHOCKS (II)

123 patients with DCM, mean LV EF 23 ± 6% (9-35%)
mean follow-up 74 month

Aims: to assess the incidence and prognostic significance of left ventricular (LV) function improvement in patients with non-ischaemic dilated cardiomyopathy (DCM) and prophylactic implantable cardioverter-defibrillator (ICD).

Criteria of LV function improvement:

✓ increase of LV ejection fraction of more than 5% to more than 35%

✓decrease LV end-diastolic diameter of at least 5 mm

Results:

✓ LV function improvement after prophylactic ICD implant was found in 24%, recent onset DCM with symptoms ≤9 months as the only significant predictor of LV function improvement [OR: 6.89; 95%CI: 2.43-21.99, p = 0.0002]

✓ total mortality was higher in patients without vs. with LV function improvement [HR: 3.75; 95%CI: 1.14-12.31, p = 0.0034], while the incidence of appropriate ICD therapies was similar in both groups (HR: 1.15; 95% CI: 0.57-2.33, p = 0.70)

✓ the incidence of appropriate ICD therapies decreased to ~1% per year after LV function improvement had occurred

Grimm W. et al. Europace, 2013 Nov;15(11):1594-600

European Heart Journal
doi:10.1093/eurheartj/ehv316

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

7.1.2.1 Trials of implantable cardioverter defibrillator therapy in dilated cardiomyopathy

A number of trials have compared ICD therapy alone or in combination with CRT against placebo or amiodarone in patients with DCM.[64,151–154,313,316,317,354] Most were conducted in an era when best medical therapy evolved to include ACE inhibitors, beta-blockers and MRAs.[358] The first RCTs of ICD therapy were underpowered to detect clinically meaningful differences in survival, and in some cases (e.g. DEFINITE) the overall mortality rate was lower than anticipated before enrolment. Follow-up was relatively short in some studies and, as in other settings, the relation of appropriate shocks to prognosis is still uncertain. No study has prospectively investigated the benefit of ICDs in specific aetiological subgroups of DCM.

OBJECTIVE

to study the frequency and causes of appropriate ICD/CRT-D shocks in patients with dilated cardiomyopathy (DCM) depending on its aetiology

STUDY GROUP (I)

dilated cardiomyopathy as a syndrome

- ✓ **LV end-diastolic diameter more than 5.5 cm**
- ✓ **LV ejection fraction less than 35%**

exclusion criteria

- Myocardium infarction or acute coronary syndrome
- Congenital and valvular heart diseases (except nonsignificant atrial septal defect)
- Infective endocarditis
- Thyrotoxicosis
- LV hypertrophy >14 mm, hypertrophic cardiomyopathy
- Systemic autoimmune diseases and vasculitis
- Verified amyloidosis, sarcoidosis
- Storage diseases
- Lymphoproliferative diseases
- Chemotherapy with anthracyclines
- Heart surgery last two months (including angioplasty and RF ablation)
- Patient failure

METHODS

- medical history, clinical examination
- standard blood examination (including thyroid function)
- ECG
- Holter monitoring
- Echo-CG
- measurement of the anti-heart antibodies (ELISA):
  - antigen-specific anti-nuclear antibodies
  - IgG to the antigens of endothelial cell
  - IgG to the antigens of cardiomyocyte
  - IgG to the antigens of smooth muscle
  - IgG to the antigens of conduction heart system

- viral genome detection in the blood (real-time PCR)
- endomyocardial biopsy of the RV/ intraoperative LV biopsy (n=36)
  - virus detection (real-time PCR)
  - morphological study with hematoxylin-eosin, Van Gieson, PAS staining, congo red
  - immunohistochemistry in some cases

- myocardial scintigraphy with ^{99}Tc-MIBI (n=10)
- multi-slice computed tomography of the heart (MSCT, n=64)
- magnet resonance imaging of the heart (MRI, n=16)
- coronary angiography (n=41)
- geneticist, DNA-diagnostic

STUDY GROUP (II)

mean follow-up 18,5 [6,0; 31,5] month

ICD/ CRTD group

32 patients (21 male)
mean age 47.3±12.3 yars

ICD	n=19
CRT-D	n=13

29 patients (90.6%) – primary prevention of SCD

Comparison group (DCM with LV EF < 35%)

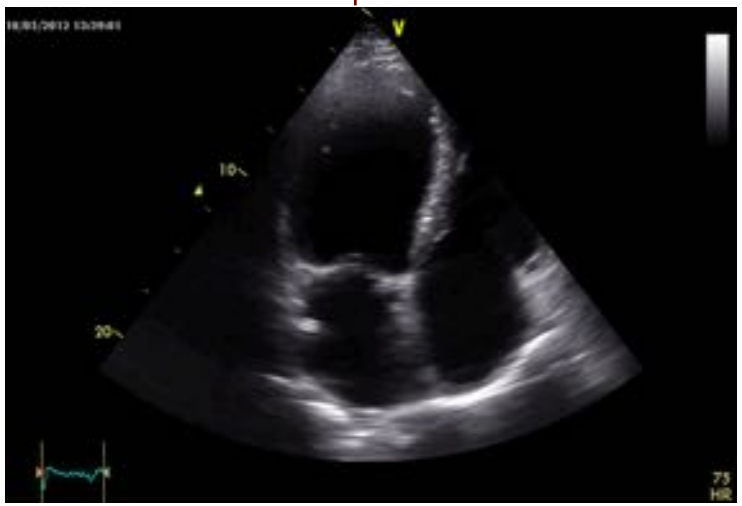
65 patients (44 male)
mean age 45.6±13.1 years

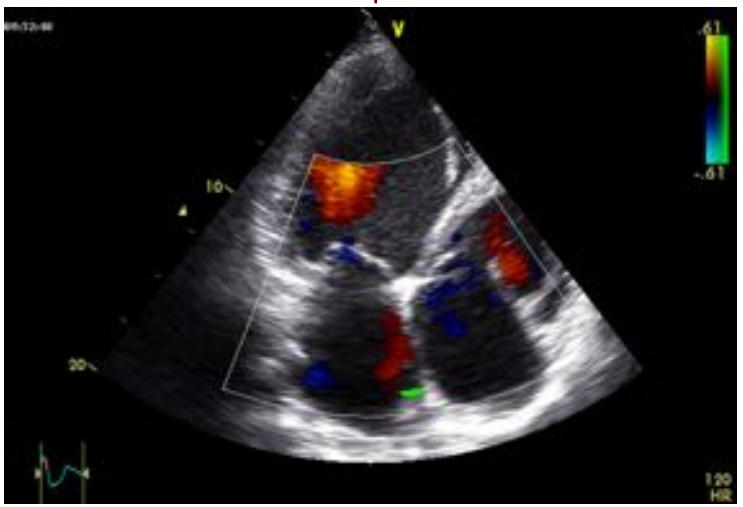
no patients with history of sustained VT/ VF

n=5 (15.6%)	reconstructive surgery with mitral valve replacement	n=8 (12.3%)

STUDY GROUP (III)

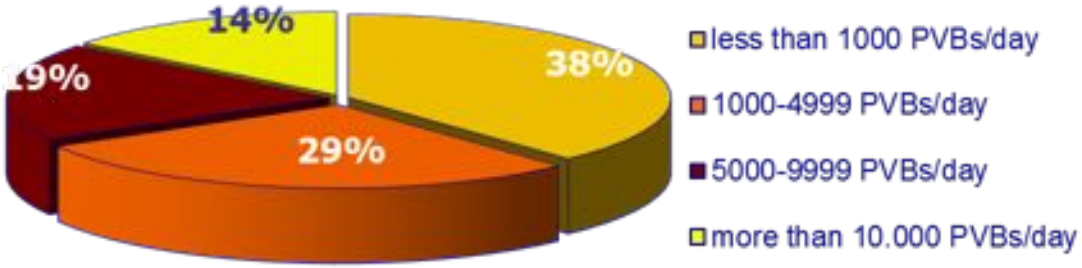
ICD / CRT-D	parameters	comparison group
2.7±0.8	NYHA class	3.0±0.9
6.7±0.8 cm	LV end-diastolic diameter	6.9±0.9 cm
204.9±104.2 ml	LV end-diastolic volume	219.4±83.9 ml
156.6±88.3 ml	LV end-systolic volume	169.3±73.4 ml
24.8±10.0%	LV ejection fraction	24.2±7.7%
609.1±175.7 Hg mm	dp/dt	765.3±405.0 Hg mm
11.0±4.2 cm	VTI	9.5±4.0 cm
110.1±35.9 ml	LA volume	109.3±54.7 ml
90.0±38.6 ml	RA volume	84.0±51.0 ml
3.4±0.7 cm	RV diameter	3.1±0.7 cm
50.4±14.7 Hg mm	PA systolic pressure	46.3±16.3 Hg mm

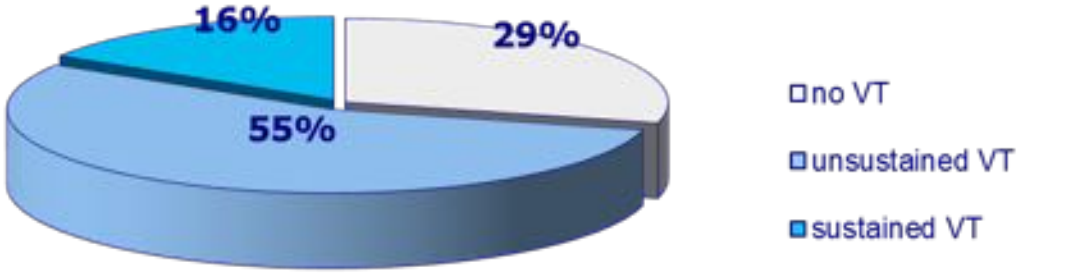




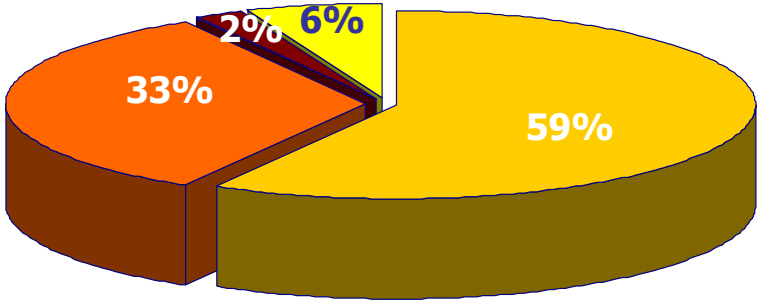
VENTRICULAR ARHHYTHMIAS in TWO GROUPS

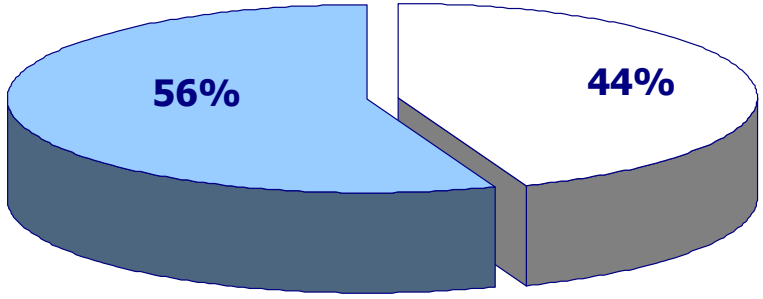
ICD / CRT-D





comparison group

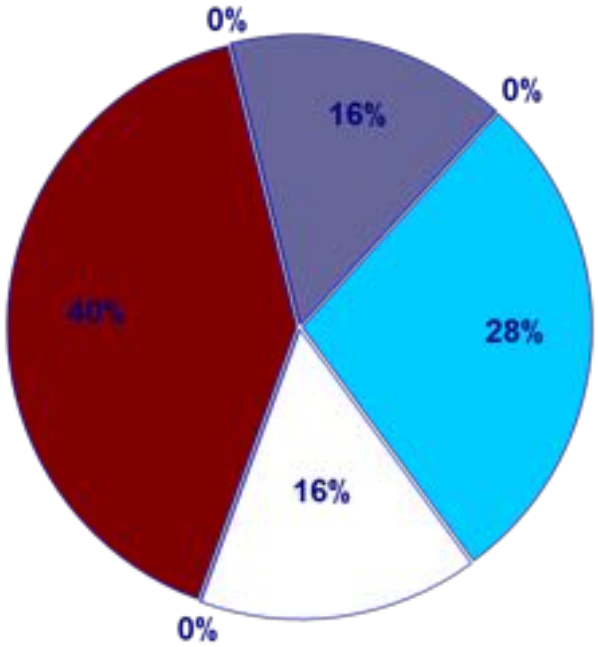




71.4%	amiodarone	55.4%
81.5%	β-blockers	72.3%
51.7%	β-blockers + amiodarone	35.4%

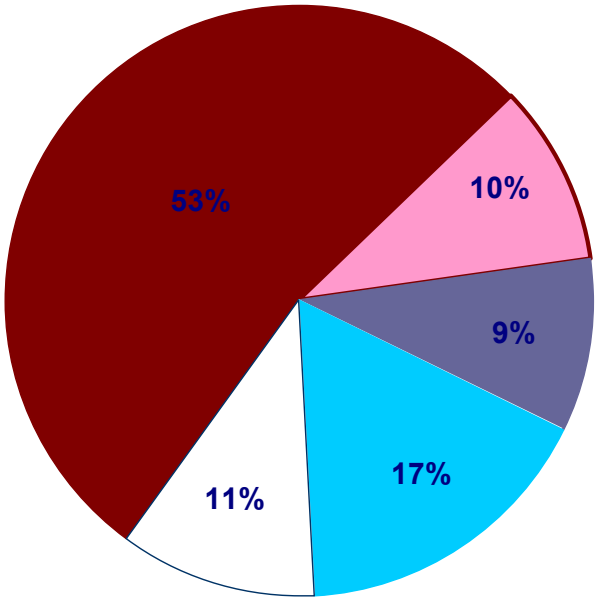
AETIOLOGY of DILATED CARDYOMYOPATHY

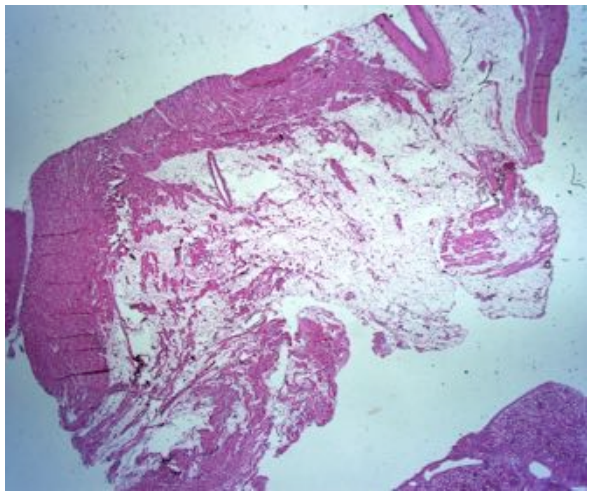
ICD / CRT-D

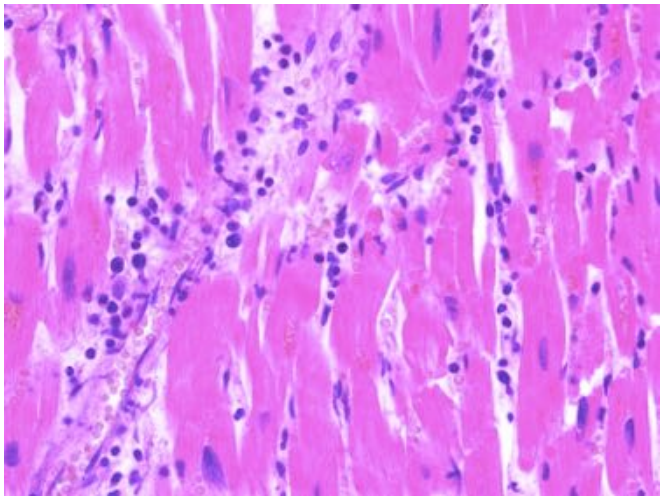


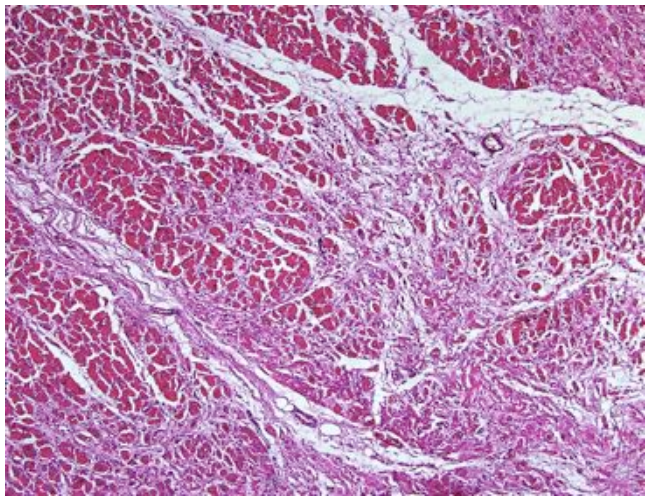
- definite myocarditis
- probable myocarditis
- genetic cardiomyopathy
- genetic cardiomyopathy + myocarditis
- idiopathic DCM

comparison group

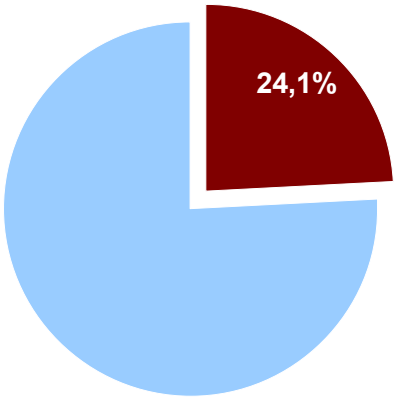




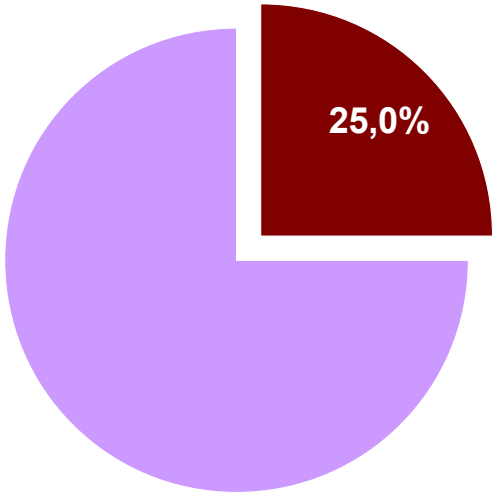




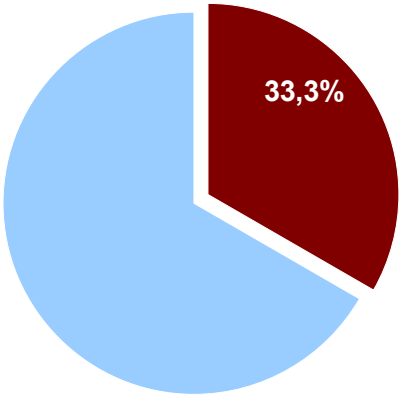
APPROPRIATE ICD/ CRTD SHOCKS



primary prevention



total

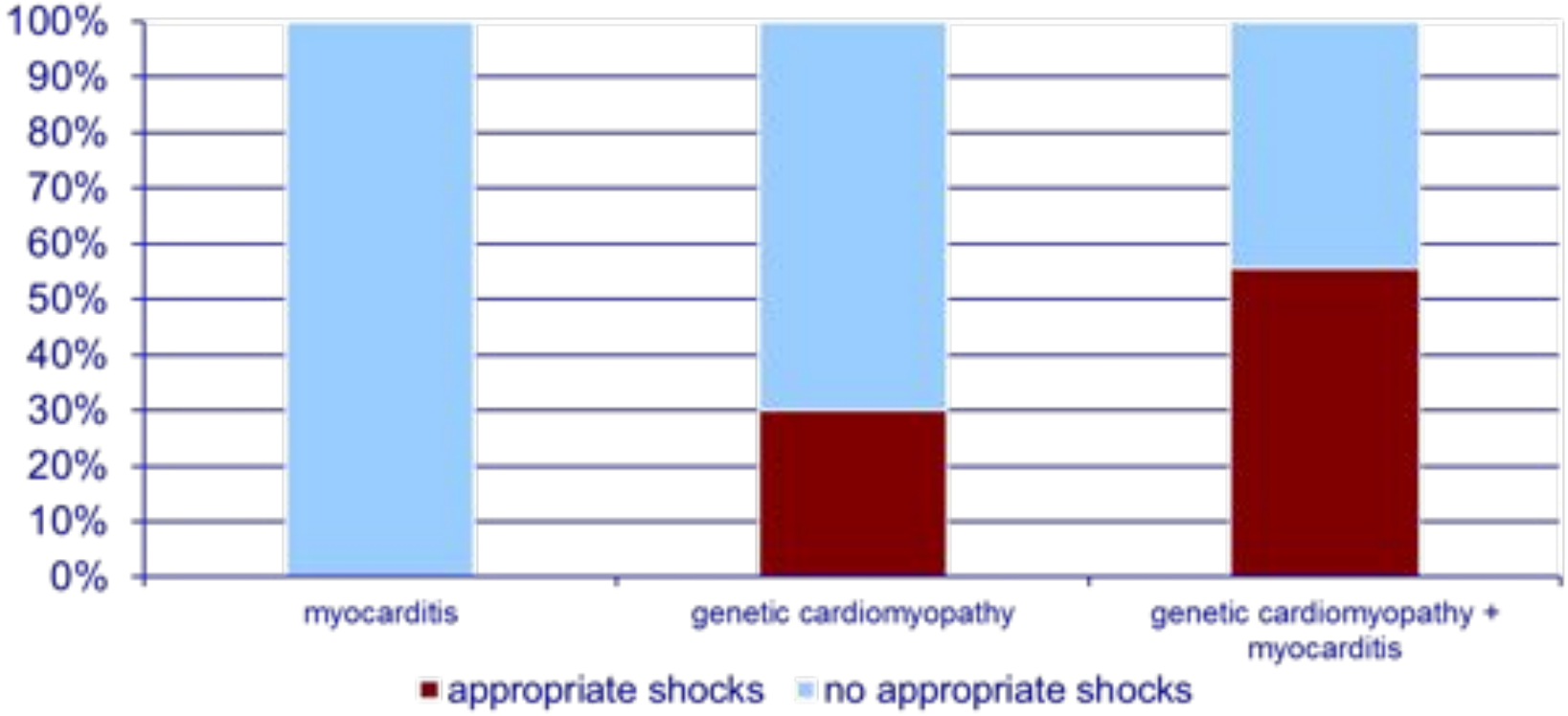


secondary prevention

Immediate causes of appropriate ICD/ CRTD shocks (sustained VT/ VF)

- ✓ the myocarditis development in patients with previously stable (noncompaction) cardiomyopathy (n=2)
- ✓ urgent abdominal surgery (n=1)
- ✓ unjustified cancel amiodarone, its replacement by digoxin (n=2)
- ✓ amiodarone-associated thyrotoxicosis (n=1)
- ✓ terminal stage of heart failure (n=2)

APPROPRIATE ICD/ CRTD SHOCKS DEPENDING on DCM AETIOLOGY



genetic forms of DCM

- ✓ unverified (n=4)
- ✓ family dilated cardiomyopathy (n=1)
- ✓ TTR amyloidosis (n=1)
- ✓ Emery-Dreifuss muscular dystrophy (n=1)
- ✓ unverified muscular dystrophy (n=1)
- ✓ left ventricular noncompaction syndrome (n=11)

RESULTS of ENDOMYOCARDIAL BIOPSY in PATIENTS with CLINICAL DIAGNOSIS ARVD

ARVD diagnosis according diagnostic criteria (1998),
EMB od right ventricle, Italy, Padova

30 patients (17 female, 47±17 years)

ARVD (n=15)

13 ICD

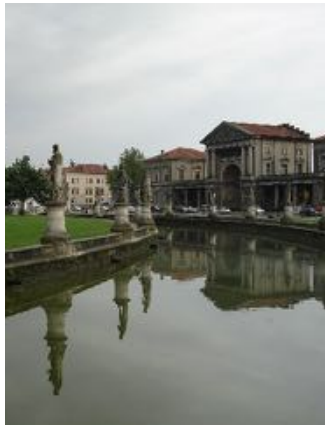
ICD shocks in 47%

active myocarditis (n=15)

1 ICD

no arrhythmia

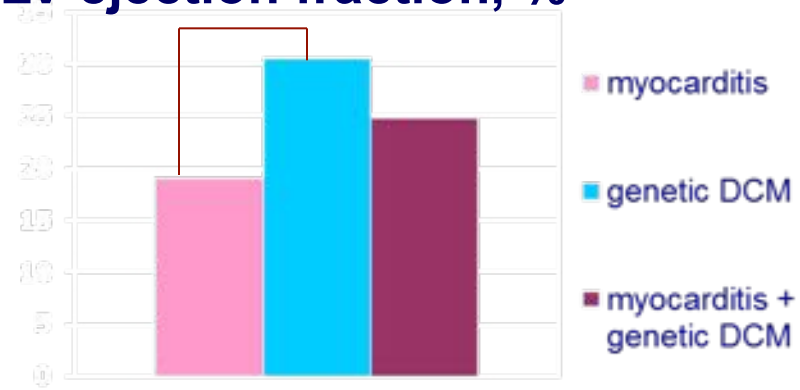
follow-up 21±8 month



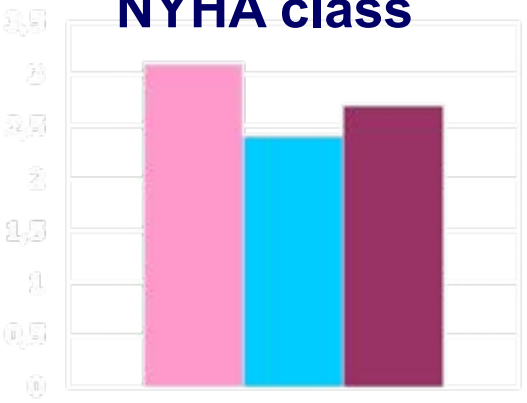
Pieroni M. et al. J Am Coll Cardiol. 2009 Feb 24; 53(8): 681-9

INITIAL PARAMETERS in ICD/CRT-D PATIENTS WITH DIFFERENT ETIOLOGY of DCM

LV ejection fraction, %



NYHA class

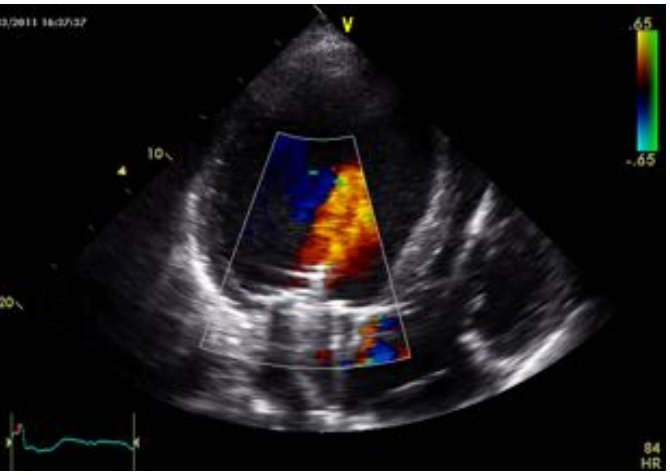


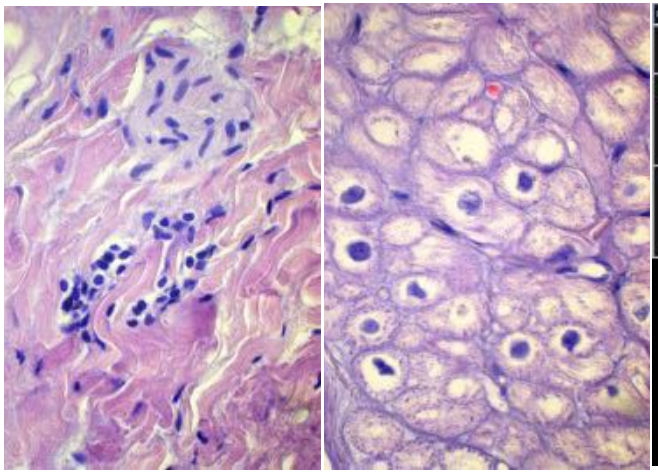
factors depending on frequency of appropriate shocks

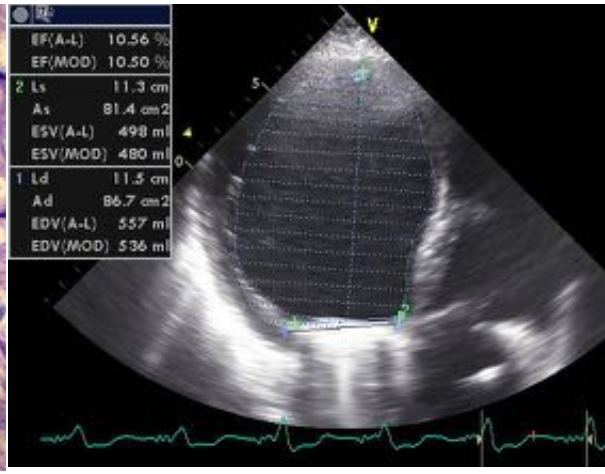
	appropriate shocks	no appropriate shocks	p
genetic DCM	100%	41.7%	0.013
NYHA class	2.2±0.9	2.9±0.7	>0.05
LV ejection fraction	31.8±11.5%	22.8±7.9%	>0.05
a poor response to therapy (LV EF increasing < 5%)	37.5%	46.7%	>0.05
a good response (>10%)	12.5%	41.7%	>0.05
nonsustained / sustained VT	75.0% / -	58.3% / 8.3%	>0.05
β-blockers	75.0%	85.0%	>0.05
amiodarone	75.0%	71.4%	>0.05

CLINICAL CASES

Case №1: male 50 y., active viral myocarditis, no shocks







Case №2: male 58 y., hypernephroma, idiopathic DCM, 2 appropriate shocks

Patient №1	parameters	Patients №2
32 month	follow-up after CRT-D	13 month
3	NYHA class	1-2
2 years	duration of DCM	1 year
7,5 cm/ 408 ml	LV end-diastolic diameter/ volume	6,3 cm/ 171 ml
17%	LV EF (initially)	25%
from 30 to 10%	LV EF (during of treatment)	42%
700 PVBs/day	PVBs/ VT	no (initially)
paroxismal	atrial fibrillation	paroxismal
betaxolol 20 mg/day	β-blockers	bisoprolol 2,5 mg/day
200 mg/ 0,25 mg	amiodarone/ digoxin	200 mg/ no (initially)

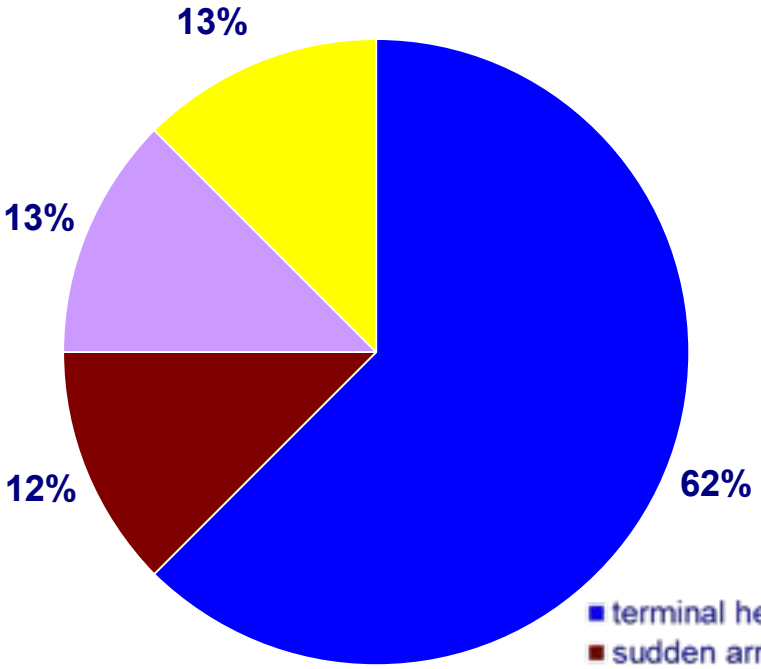
MORTALITY in TWO GROUPS

21.9% (ICD/CRT-D) vs **33.8%** (p = 0.228)

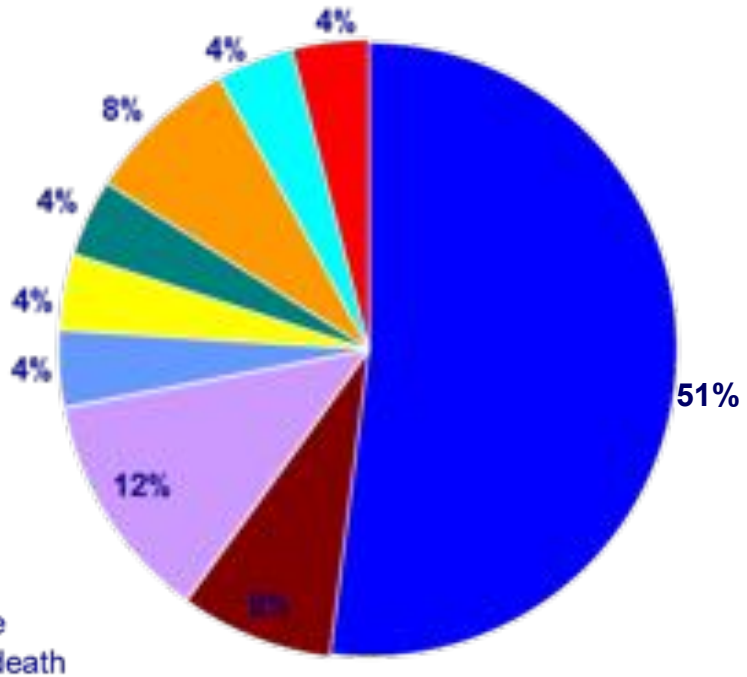
21.9% vs 40.0% (death + heart transplantation, p=0.148)

immediate causes of death

study group



comparison group



- terminal heart failure
- sudden arrhythmic death
- death in the early postoperative period
- hepatic failure
- stroke (ischemic, hemorrhagic)
- pulmonary embolism
- pneumonia
- miocardial infarct
- stomach cancer

CONCLUSIONS

in patients with different forms of DCM ICD/ CRTD implantation is reasonable and effective for prevention of sudden cardiac death (appropriate shocks in 25% by follow-up 18.5 month, incl. 24% in primary prevention group)

*** * ***

the mortality in the patient with DCM who have indication to ICD (NYHA class 2-3, LV EF < 35%) was higher than in similar patients with ICD/ CRTD (33.8% vs 21.9%, p = 0.228)

*** * ***

the patients with association of genetic DCM and myocarditis had a maximal rate of ICD/ CRTD appropriate shocks, the patients with isolated myocarditis - minimal

*** * ***

the aetiology of DCM is a more important predictor of shocks than the LV ejection fraction and NYHA class

*** * ***

immediate causes of appropriate shocks were the myocarditis development in patients with previously stable cardiomyopathy, unjustified cancel amiodarone, its replacement by digoxin, amiodarone-associated thyrotoxicosis, terminal stage of heart failure