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THE LEFT VENTRICULAR NONCOMPACTION SYNDROME IN 50 ADULTS: clinical variants, follow-up and outcomes

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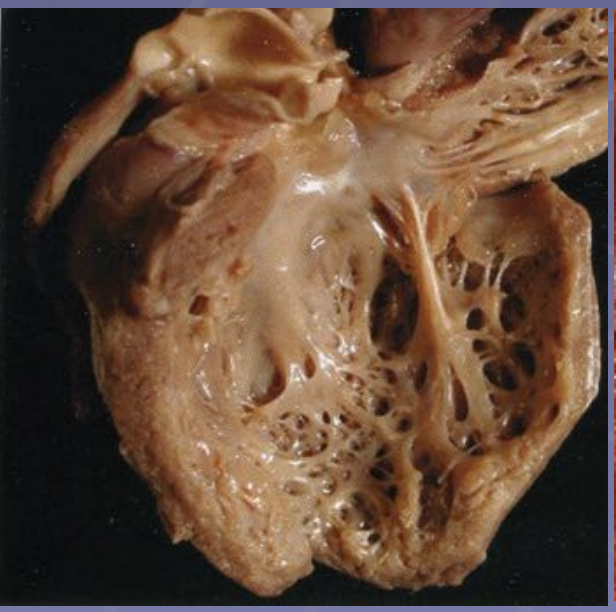
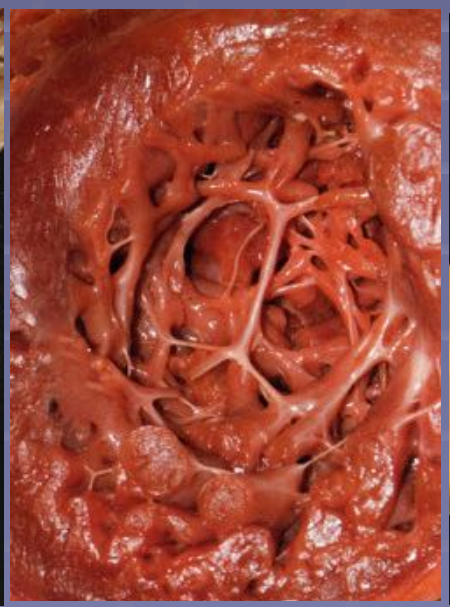
DEFINITIONS and EPIDEMIOLOGY

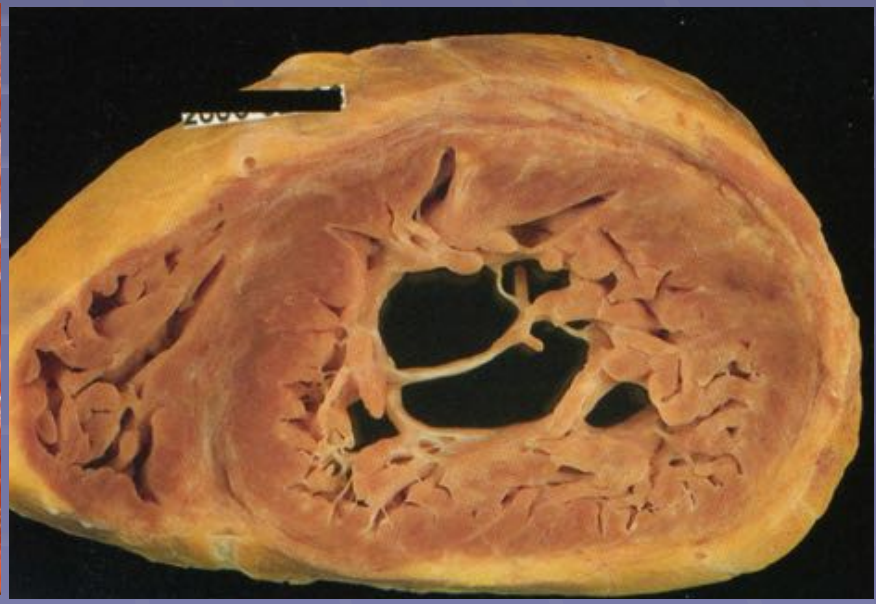
The myocardial noncompaction is a genetically heterogeneous cardiomyopathy characterized by a pattern of prominent trabecular meshwork and deep intertrabecular recesses not connected with coronary blood flow and predisposing to thrombosis

Noncompaction cardiomyopathy – myocardial noncompaction with LV systolic dysfunction

- 0,05%; 141 patients - C.Stöllberger (Vienna, 1995-2011), 210 papers in this problem
- 100 patients from 36 933 who was examined using Echo-CG (1994-2006)
- 3% from 960 patients with CHF
- 1330 papers in Medline (1990-2015)
- 229 patients – SIEG-register (Sicilia)
- 73 patients (incl. children) – Bologna (1994-2006)
- 58 patients (incl. 9 children) – Rotterdam
- 63 patients – Berlin (2008)







A.Burke, F. Tavora. Practical cardiovascular pathology. 2011

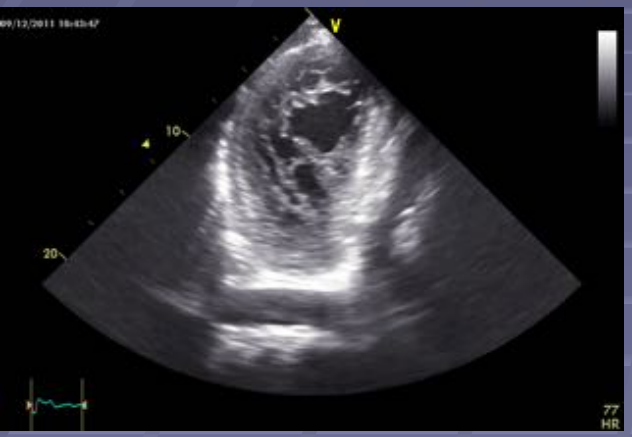
OBJECTIVE

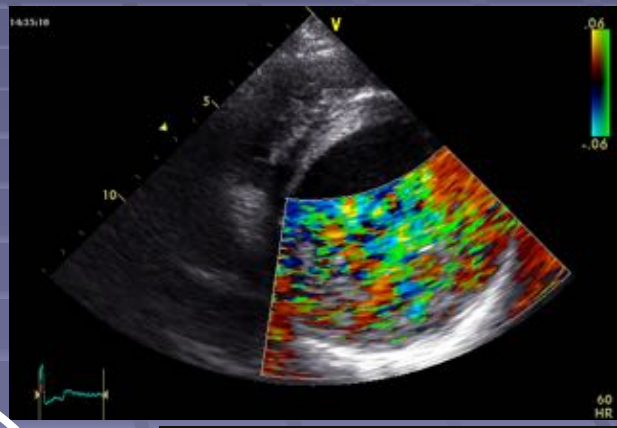
to study clinical variants, follow-up and outcomes of the left ventricular noncompaction (LVN) syndrome in adult patients

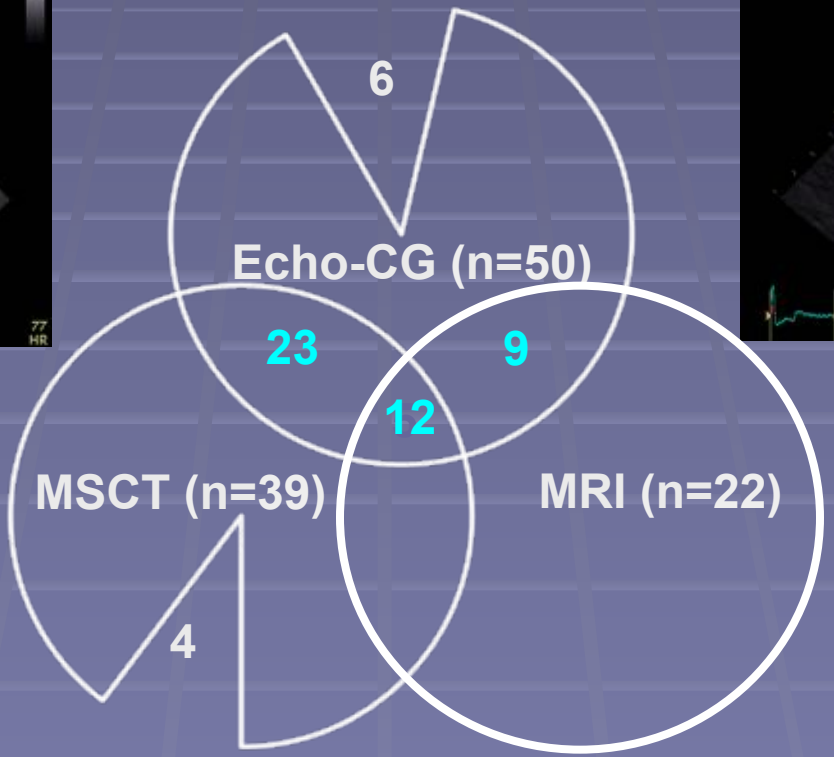
INCLUSION CRITERIA

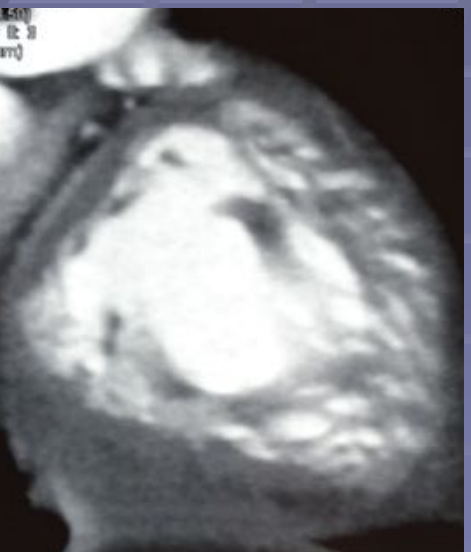
mistake initial diagnosis in 82%

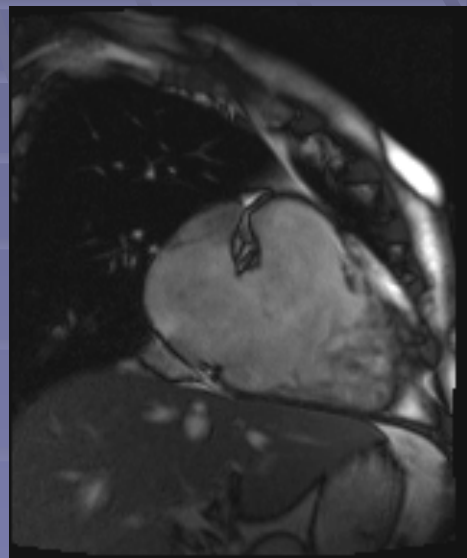
- two layers of the myocardium with a ratio of non-compact and compact parts 2:1 (Echo-CG) or 2,3:1 (MRI / MSCT)
- a synchronous motion of non-compact and compact layers
- end-diastolic visualization more than 3 trabeculae in the left ventricle
- end-diastolic blood flow into the intertrabecular spaces





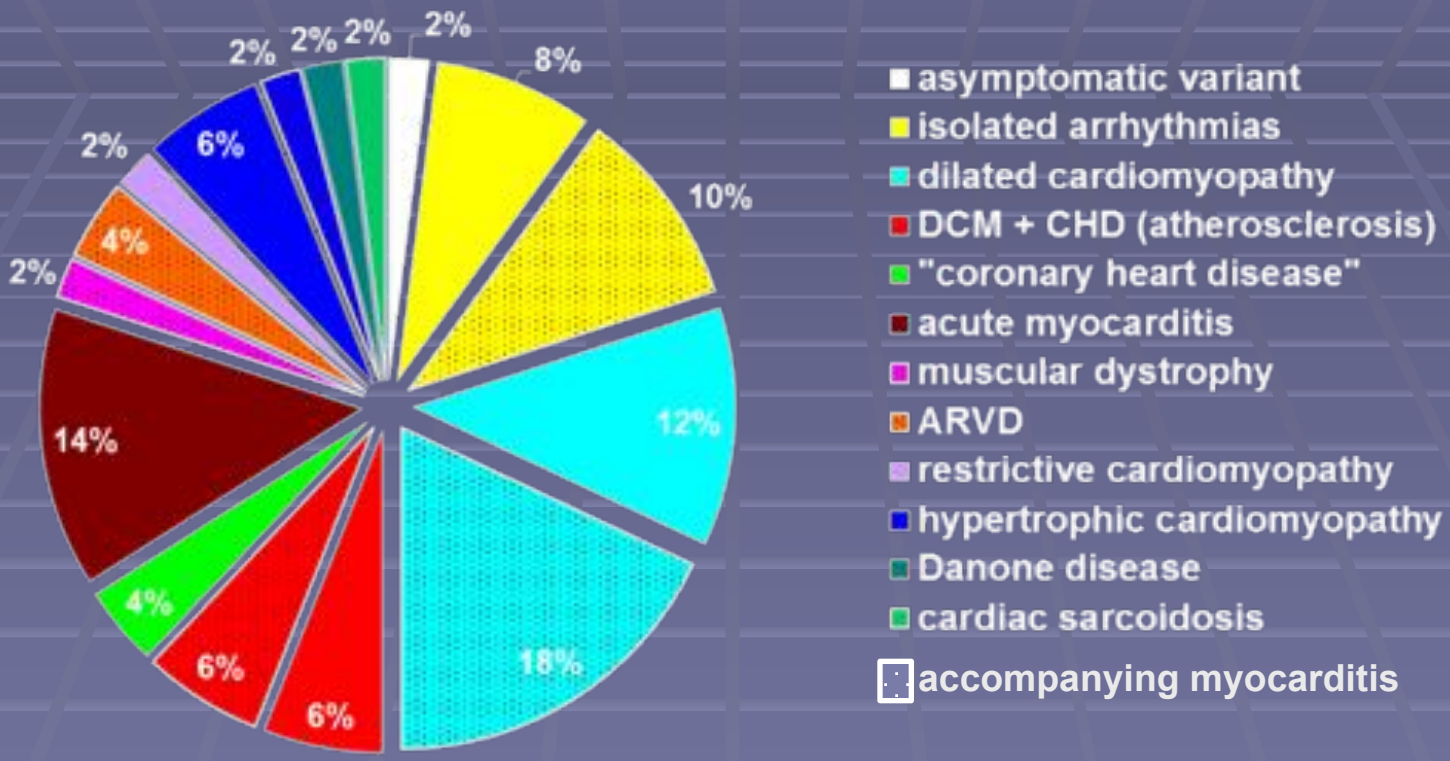






STUDY GROUP

n=50, 28 male, mean age 42,8±14,9 (18 - 76) years
family history in 9 patients (18%)



additional studies

morphological study of the myocardium (n=14, incl. EMB in 10 patients)
anti-heart antibodies and viral genome (real-time PCR) study
genetic examination with mutations detection in 10% of patients

- *MyBPC3* (n=3)
- *DSP* (n=1)
- *LAMP* (n=1)

НК – недостаточность кровообращения, ФК – функциональный класс, ЖЭ - желудочковая экстрасистолия, ЖТ – желудочковая тахикардия, МА – мерцательная аритмия

ECHOCARDIOGRAPHIC PARAMETERS

LV end-diastolic diameter 6.1±0.8 cm

LV end-diastolic volume 160.7±76.3 (61-501) ml

LV end-systolic volume 108.6±70.1 (19-386) ml

LV ejection fraction 34.6±14.0%

LA diameter 4.3±0.8 cm

LA volume 95.1±37.4 (43-180) ml

RA volume 72.5±40.7 (34-255) ml

RV diameter 2.9±0.6 cm

PA systolic pressure 37.0±17.8 Hg mm

IVS 10.1±3.0 mm

LV back well 9.9±1.9 mm

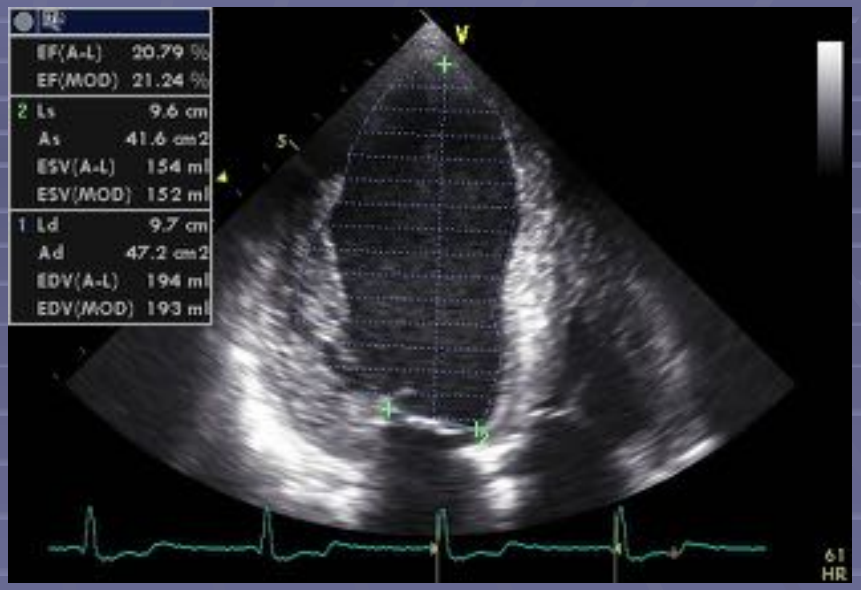
mitral annulus diameter 3.5±0.4 cm

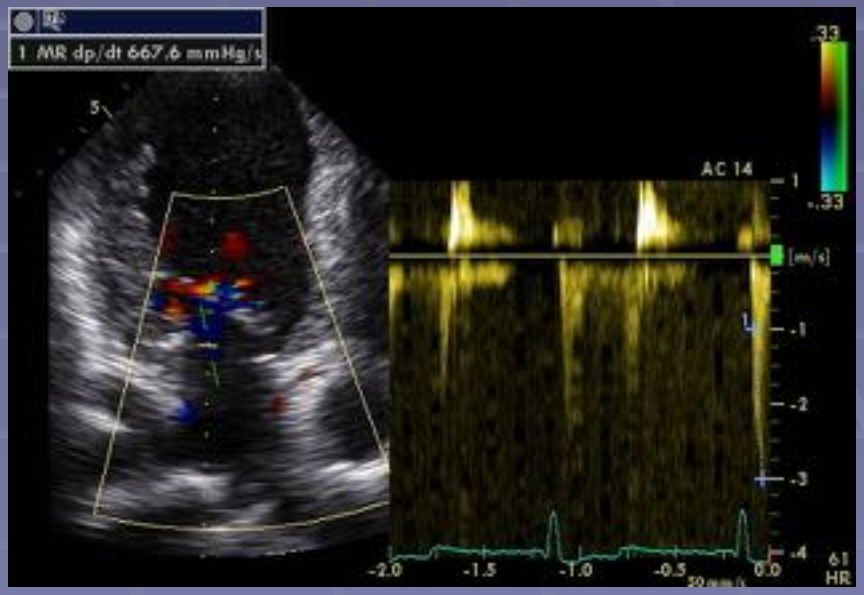
mitral regurgitation1.0 [0.5; 2.0] degree

tricuspid regurgitation 1,0 [0.5; 1.0] degree

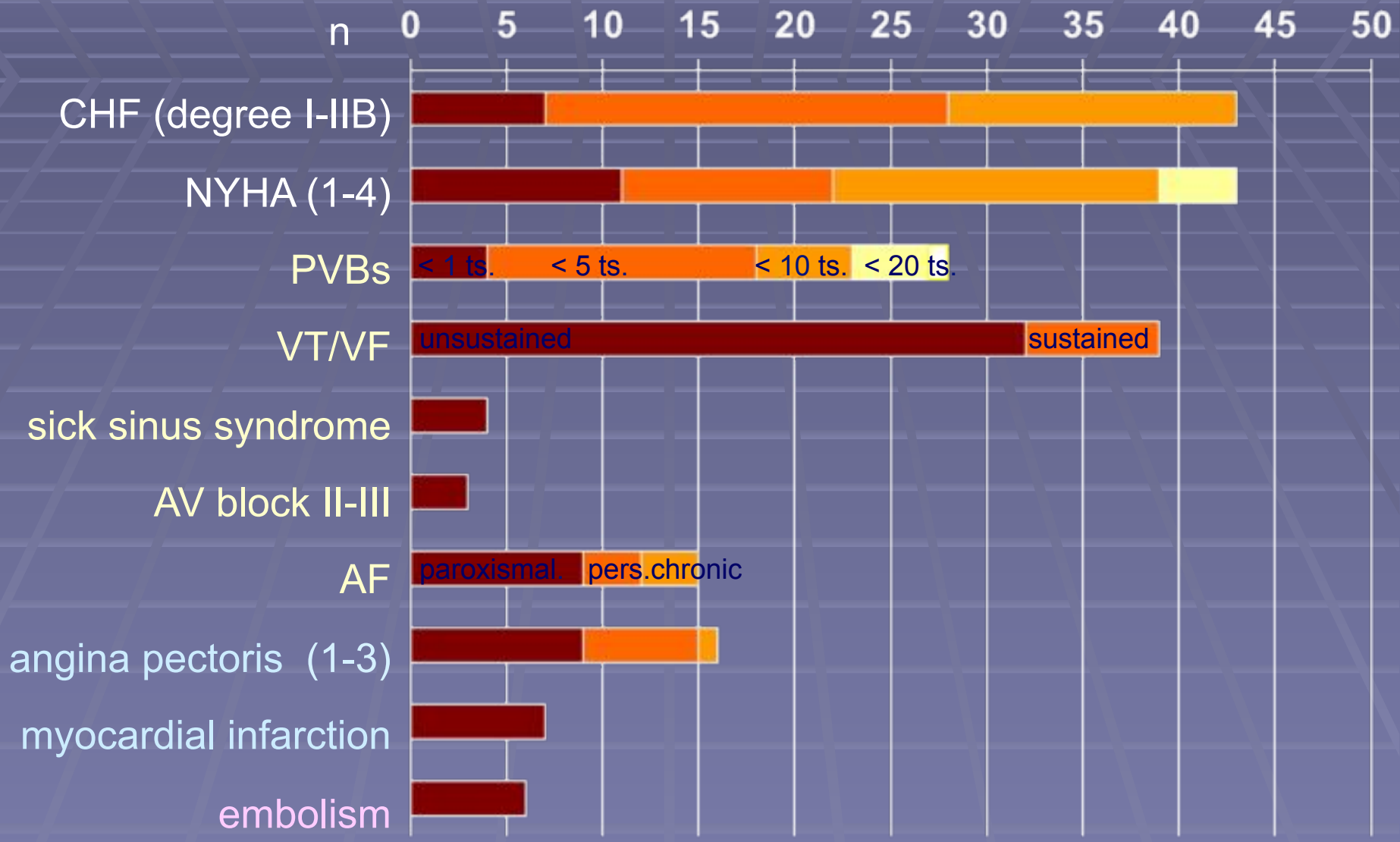
dp/dt 745.8±244.9 Hg mm

VTI 11.1±4.1 cm





CLINICAL MANIFESTATIONS OF VENTRICULAR NONCOMPACTION

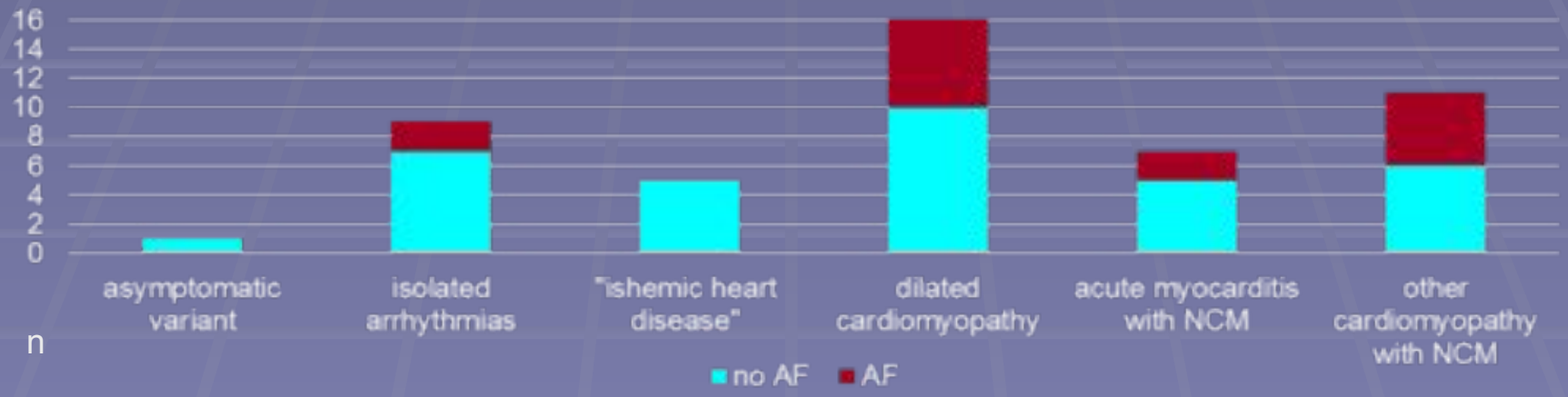


ATRIAL FIBRILLATION in MYOCARDIAL NONCOMPACTION

- **frequency is 30%**
- sustained forms (persistent and chronic) are most frequent than paroxysmal form (3 : 2)
- embolic events had 13.3% patients with AF (versus 8.6% without AV, p > 0.05)
- amiodarone received 73.4% of patients
- RF ablation in one patients was not effective

AF	associated factors	p	not AF
4.6 ± 0.8 cm	LA diameter	0.107	4.2 ± 0.8 cm
108.9 ± 46.9 ml	LA volume	0.077	87.9 ± 29.9 ml
93.9 ± 16.0 ml	RA volume	0.015	61.9 ± 4.0 ml
20.0%	sick sinus syndrome	0.047	2.9%
60.0%	myocarditis	> 0.05	58.8%

frequency of AF in different clinical variants of myocardial noncompaction

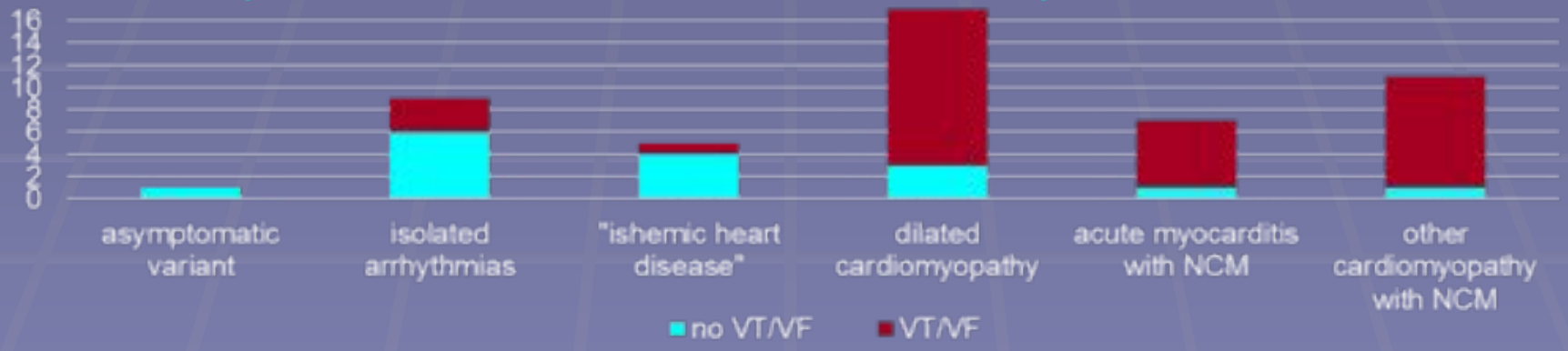


VT/VF in MYOCARDIAL NONCOMPACTION

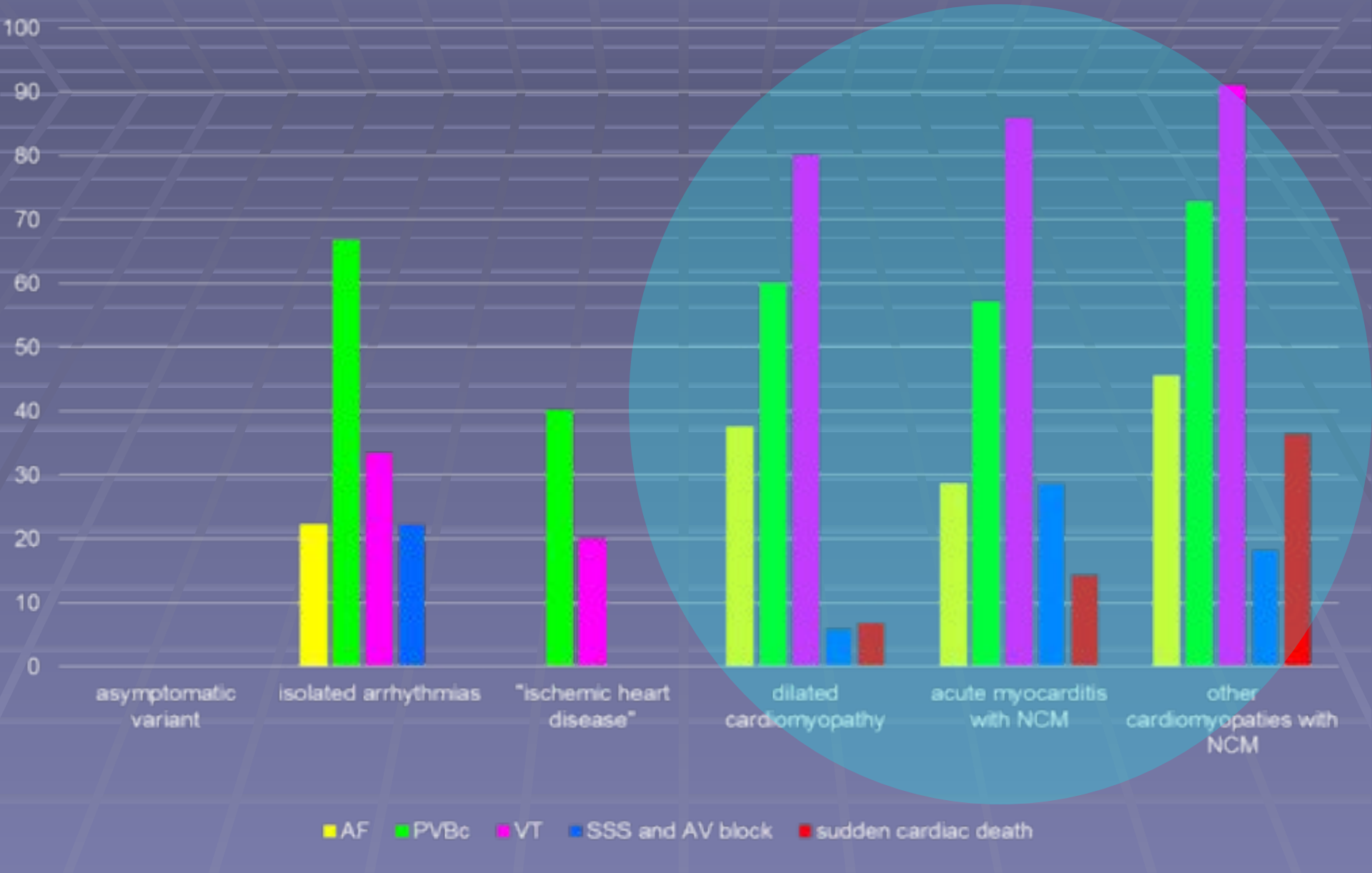
- **frequency of nonsustained VT is 64%** (incl. «torsade de pointe» in one patient)
- **frequencyof sustained VT is 14%, rate of VF is 5%** (only in the patients with variants «DCM + myocarditis» and NCM in association with other cardiomyopathy
- amiodarone received 92.9% of patients
- RFA of VT in one patient was not effective

VT/VF	associated factors	p	no VT/VF
2.75 [2; 3]	NYHA functional class	0.018	1 [0.25; 2.75]
9.4%	AB block II-III degree	0.211	0
119.7 ± 25.8 ms	QRS duration	0.010	101.4 ± 19.0 ms
31.8 ± 14.2%	LV ejection fraction	0.042	40.4 ± 12.6%
3.1 ± 0,6 cm	RV diameter	0.046	2.7 ± 0.6 cm
71.9%	myocarditis	0.008	31.3%
15.6%	mortality	0.098	0

frequency of VT/VF in different clinical variants of myocardial noncompaction

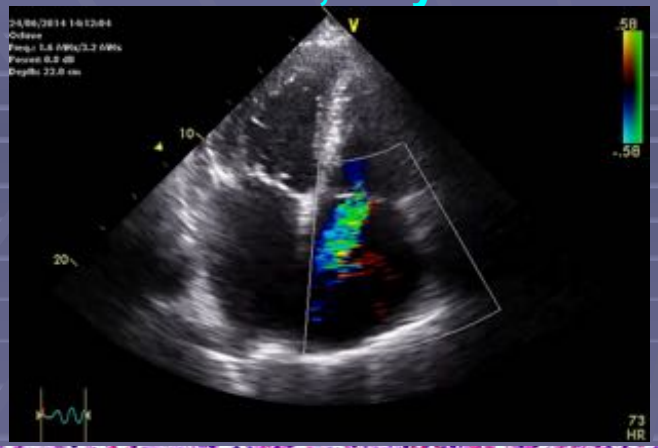


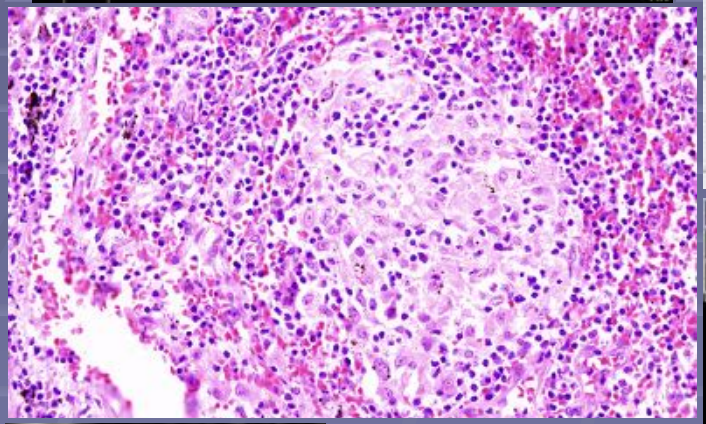
FREQUENCY of ARRHYTHMIAS in DIFFERENT CLINICAL VARIANTS of MYOCARDIAL NONCOMPACTION

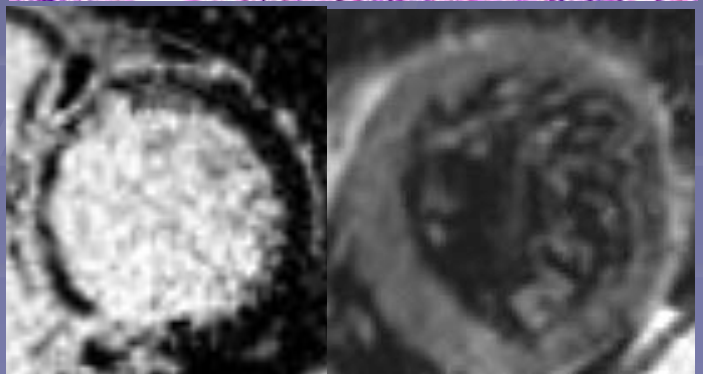


MYOCARDIUM NONCOMPACTION, RESTRICTIVE and HYPERTROPHIC CARDIOMYOPATIES in ONE FAMILY MEMBERS

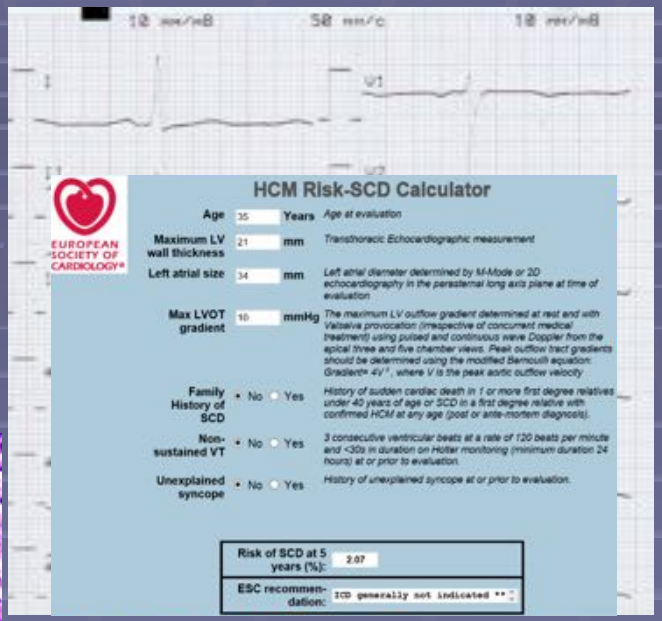
father, 64 years

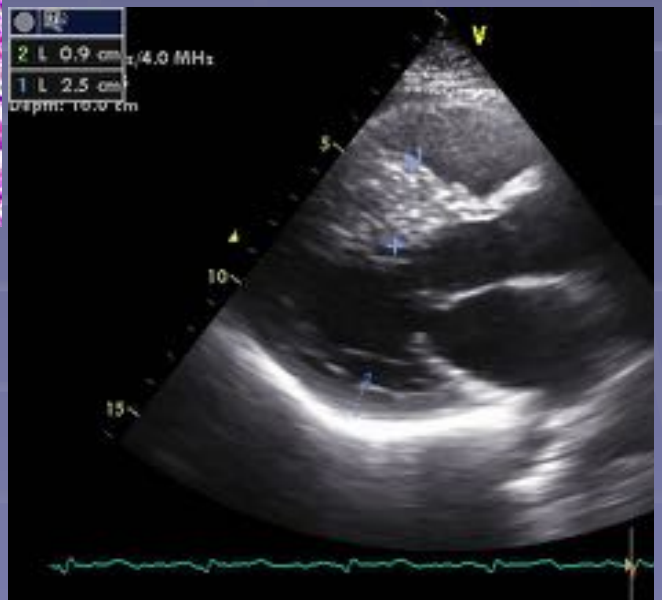




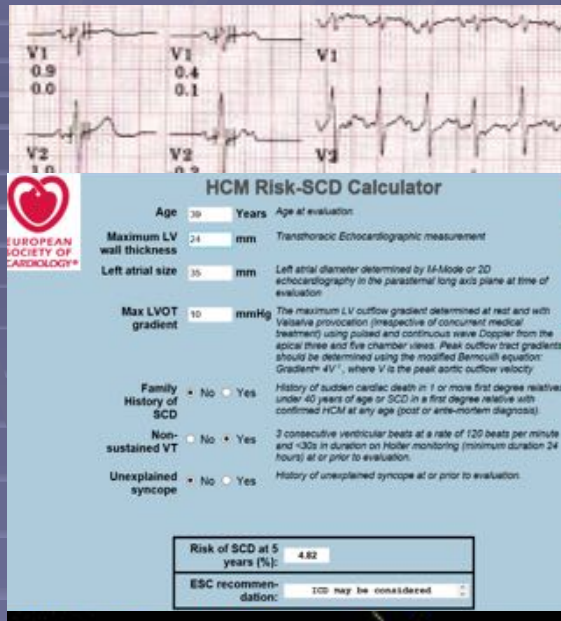


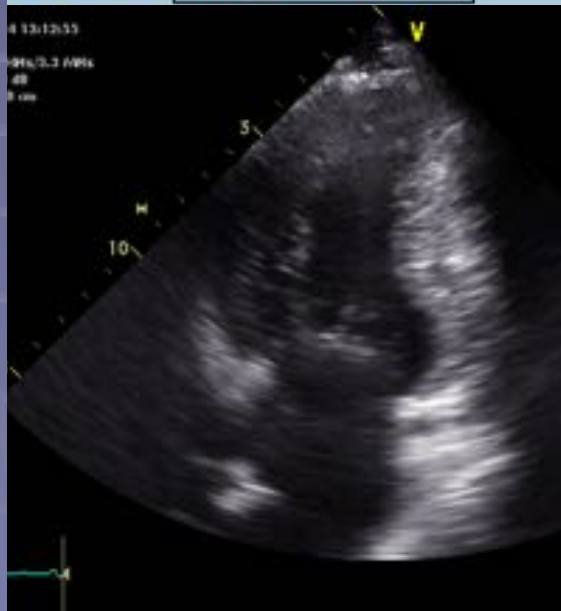
daughter, 35 years





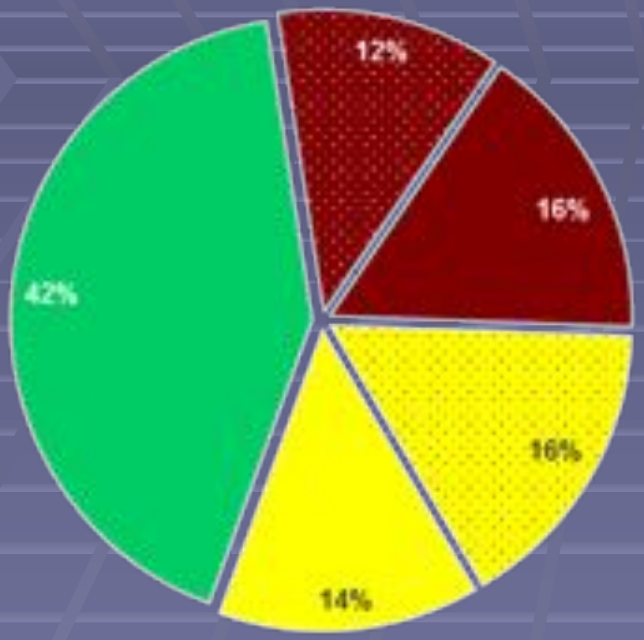
son, 39 years





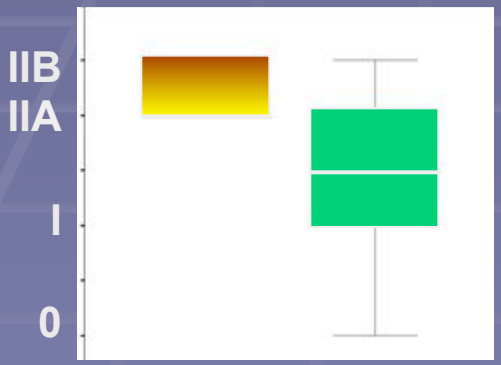
FREQUENCY and MANIFESTATIONS of the MYOCARDITIS in MYOCARDIAL NONCOMPACTION

n=50



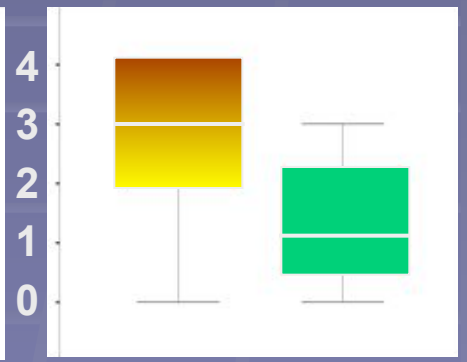
- no myocarditis
- biopsy proved myocarditis (virus-positive)
- biopsy-proved myocarditis (virus-negative)
- clinically proved myocarditis (virus-positive)
- clinically proved myocarditis (virus-negative)

CHF degree



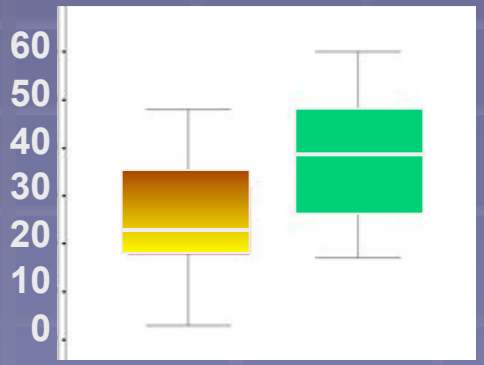
p=0.013

NYHA functional class



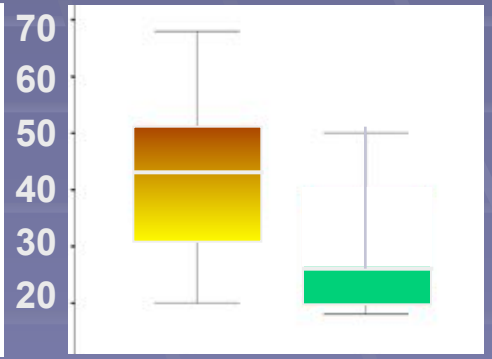
p=0.015

LV EF, %



p=0.013

systolic PA pressure, Hg mm

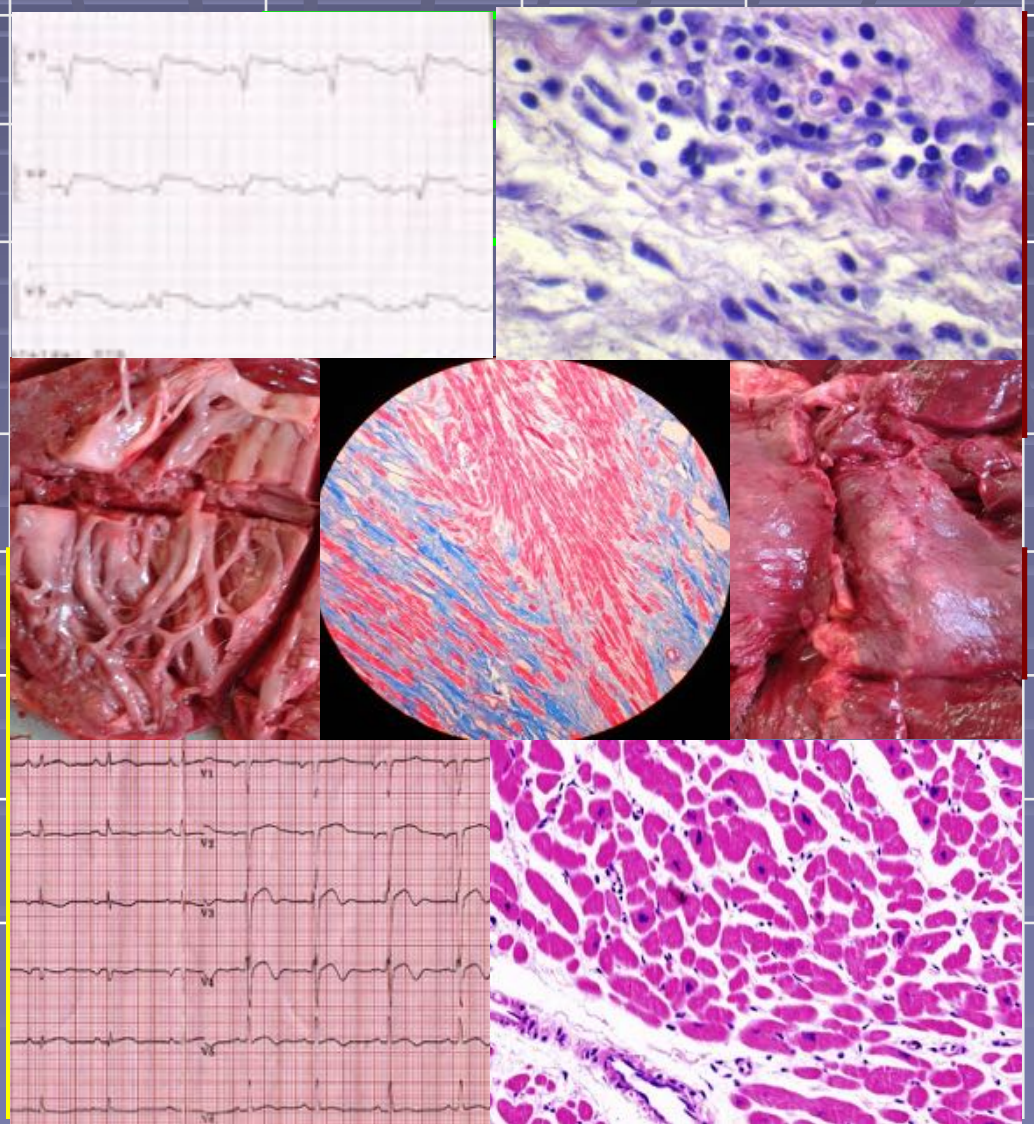


p=0.002

MIOCARDIAL INFARCT in PATIENTS WITH NONCOMPACTION

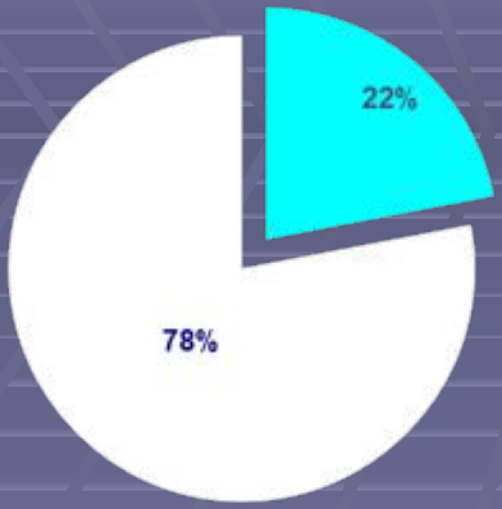
n=8 (16% of patients)

patient	angina	ECG	Tn	coronary stenoses	LV thrombosis	other embolism	myocarditis	outcomes
M, 39 y.	no	STEMI	+					transplan-tation
M, 40 y.	no	STEMI	+					ICD
F, 30 y.	yes	STEMI	+					
F, 37 y.	no	???	???					death
F, 62 y.	no	QS	+					ICD
M, 72 y.	no	Q	+					angioplasty
M, 30 y.	no	Q	???					interrupted death, ICD
M, 42 y.	no	Q	+					



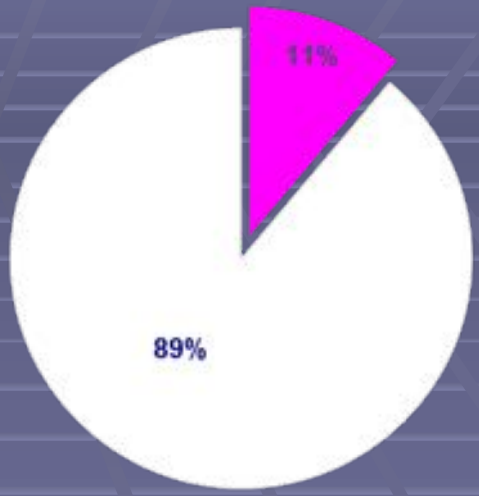
FREQUENCY of THROMBOSIS and EMBOLISM

intracardiac thrombosis



all embolic events (with one exception) developed in the absence of anticoagulants in patients with intracardiac thrombosis verified retrospectively

embolism



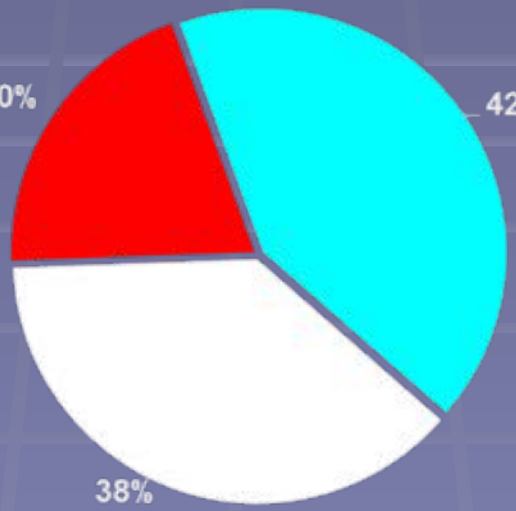
thrombosis/embolism (n=13)	risk factors	p	no thrombosis/ embolism (n=37)
3 [1.5; 3]	NYHA functional class	0.098	2 [1; 3]
IIA [I-II; IIB]	CHF degree	> 0.05	IIA [I; IIB]
30.0%	atrial fibrillation	> 0.05	27.6%
61.5%	myocarditis	> 0.05	56.8%
109.2 ± 30.0 ml	LA volume	0.084	88.8 ± 37.0 cm
6.5 ± 0.9 cm	LV end-diastolic diameter	0.063	6.0 ± 0.0 cm
29.7 ± 3.8%	LV ejection fraction	0.124	36.5 ± 14.7%
3.2 ± 0.7 cm	RV diameter	0.088	2.8 ± 0.5 cm
0 [0; 1.5]	degree of arterial hypertension	> 0.05	0 [0; 2]

INDICATIONS to the ANTICOAGULANTS ADMINISTRATION in MYOCARDIAL NONCOMPACTION

- **history or present intracardiac thrombosis**
- **embolic history**
- **atrial fibrillation**
- **LV ejection fraction less than 40%**
- microvascular ischemia (angina)?
- history or present myocardial infarct
- ICD?
- $CHADS_2$ risk factors without AF?
- LA volume more than 100 ml?
- definite diagnosis «myocardial noncompaction»?
- association noncompaction with HCM?

anticoagulants in the study group (according to the basic indications)

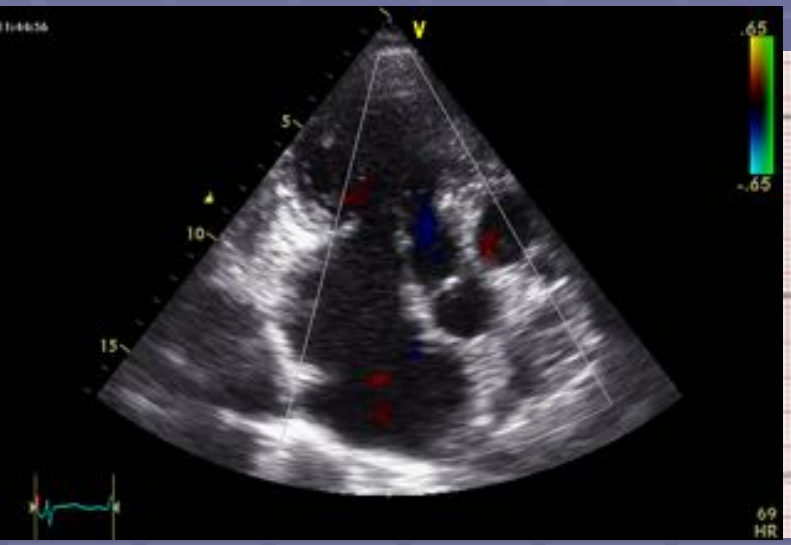
should to prescribe anticoagulants (LV EF<40%)?



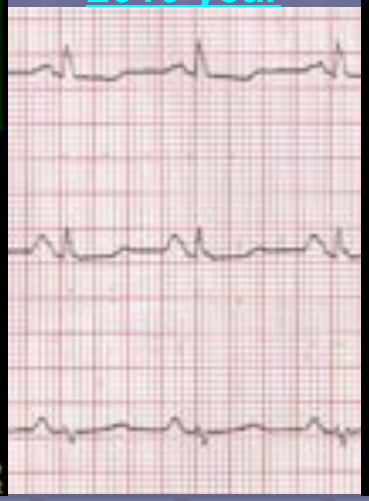
anticoagulants

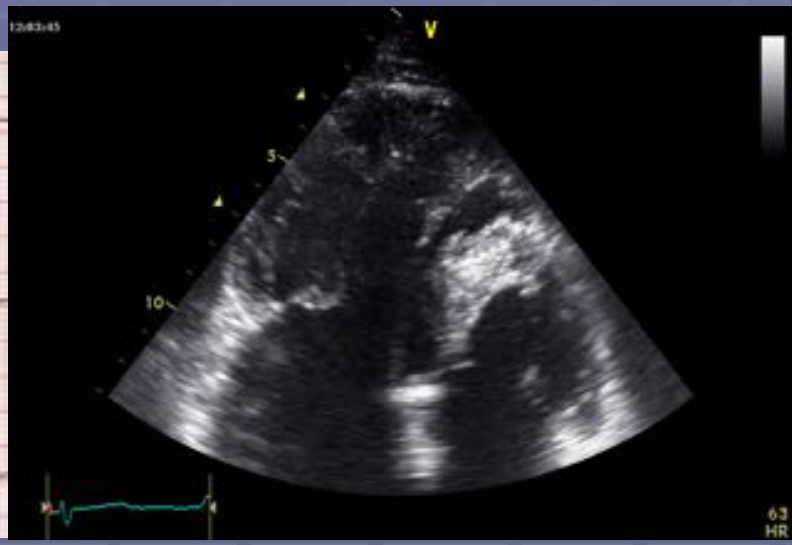
no anticoagulants

PATIENTS 37 y. HYPERTHROPHIC CARDIOMYOPATHY



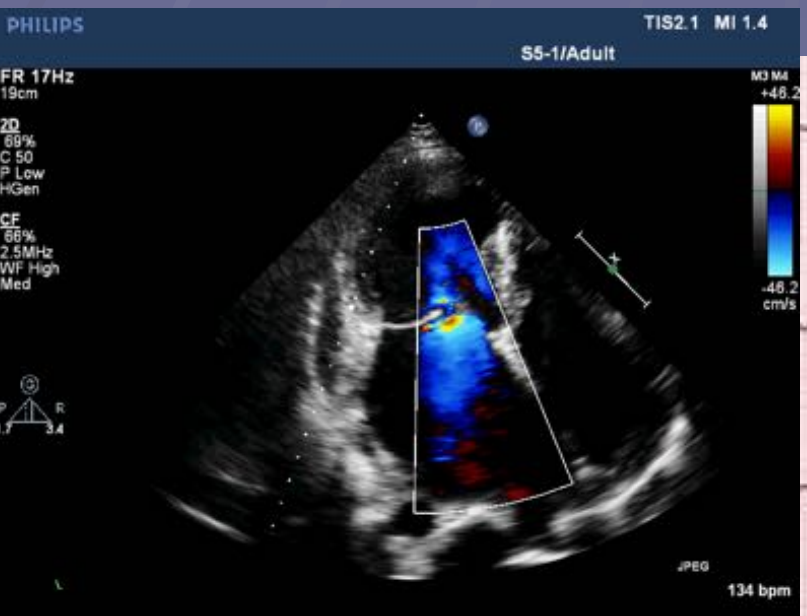
2010 year

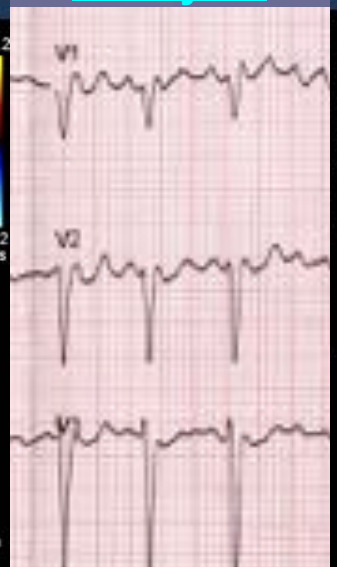


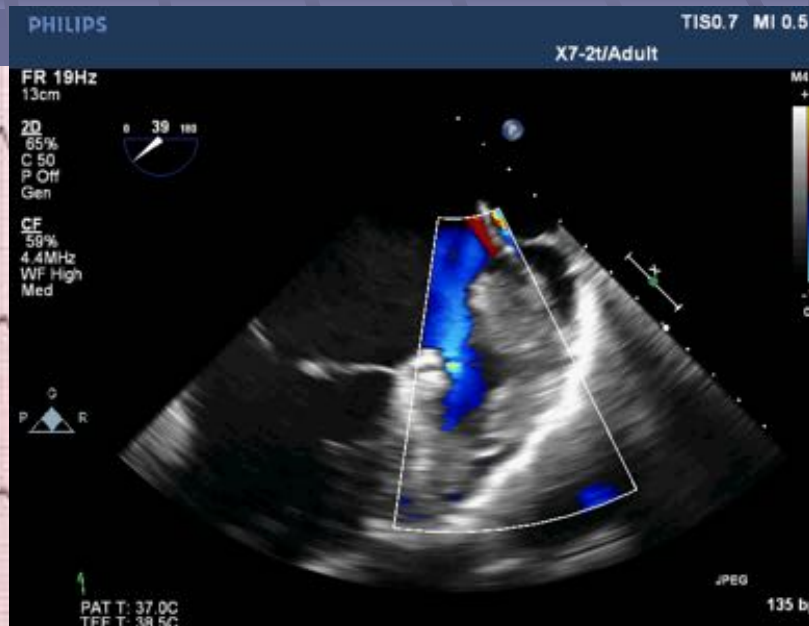


- since 2012 – paroxisms of atrial fibrillation/flutter, electrical cardioversion, long-time amiodarone therapy without effects
- 2013 – ineffective RFA, ICD due to unsustained VT

2015 year

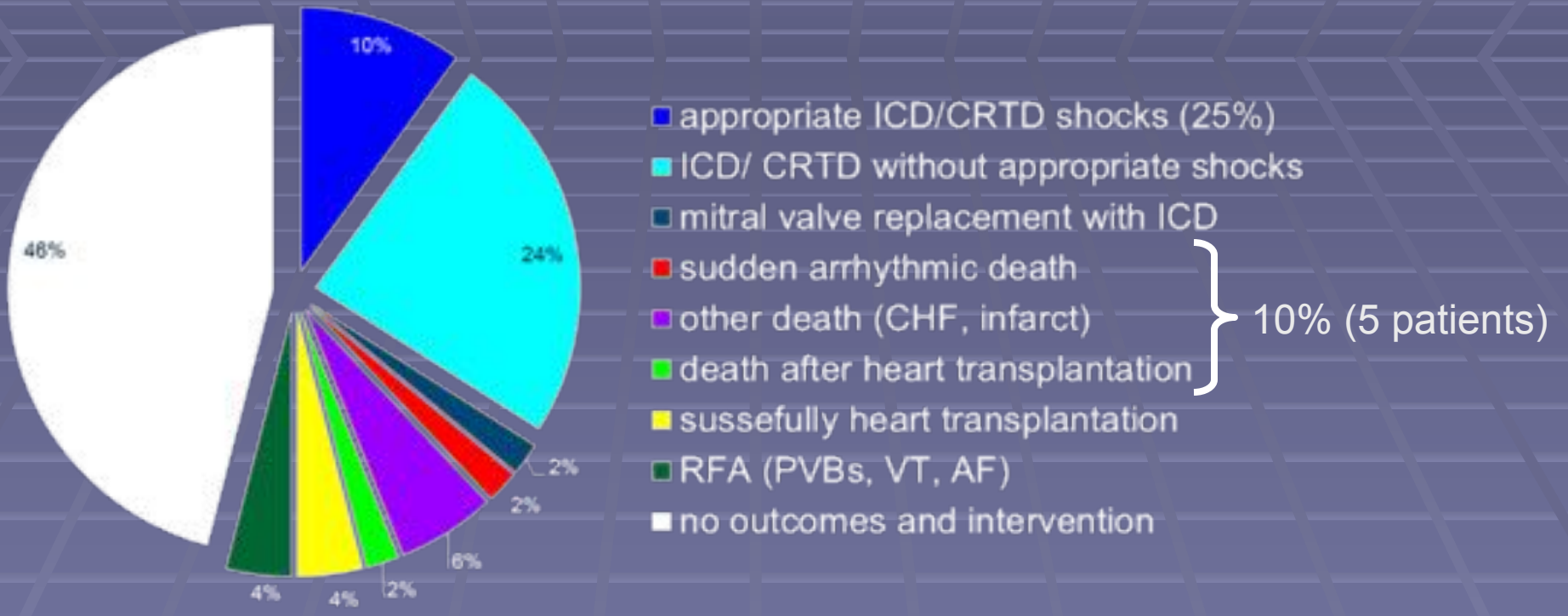






OUTCOMES and INTERVENTION in MYOCARDIAL NONCOMPACTION (n=50)

mean follow-up 12,5 [5,5; 25,5] month



drug therapy	n	%
β-blockers	32	64%
sotalol	5	10%
amiodarone	33	66%
digoxin	2	4%
ACE inhibitors	29	58%

CLINICAL CLASSIFICATION of MYOCARDIAL NONCOMPACTION

1. **Asymptomatic variant.**
2. **Isolated arrhythmic variant (with/ without myocarditis):**
   - isolated AF
   - isolated PVBs/ unsustained VT
   - sustained VT/ VF/ sudden cardiac death
   - associations of ventricular and supraventricular arrhythmias
   - associations of rhythm and conduction disturbance
3. **Ischemic variant:**
   - microvascular angina/ ischemia (with/ without myocarditis)
   - myocardial infarct (embolic, due to myocardidtis, coronary atherosclerosis)
   - association of microvascular ischemia and myocardial infarct
4. **Thromboembolic variant.**
5. **Acute myocarditis with myocardial noncompaction.**
6. **DCM (noncompaction cardiomyopathy):**
   - with myocarditis
   - without myocarditis
7. **Myocardial noncompaction in association with other cardiomyopaties/ congenital heart diseases:**
   - with hypertrophic cardiomyopathy
   - with restrictive cardiomyopathy
   - with ARVD
   - with muscular dystriphy
   - with cannelopathies (?)
   - with congenital heart disease (septal defects, pulmonary artery stenosis etc.)
8. **Mixed variants.**

Etiological variants:

1. Primary (genetic):
   - genetically verified
   - genetically unverified
2. Secondary (due to severe cardiac dysfunction)?

By severity:

1. Increased trabecularity of the myocardium (ratio of layers 1:1-1:2).
2. Myocardial noncompaction (ratio of layers 1:2 and more).

CONCLUSIONS

- LVNS in adults is vary polymorphic and is isolated only in 32% of patients
- it can be identified following clinical variants of LVNS in adults: asymptomatic, isolated arrhythmic, ischemic, tromboembolic, dilated cardiomyopathy, association with acute myocardidtis, other cardiomyopathies and mixed
- myocarditis, including viral, complicates LVNS in the half of the patients and leads to a significant deterioration of the disease
- the most typical kind of arrhythmia is the unstable VT, which is associated with significant structural changes of the heart (LV EF < 35%, QRS >120 ms); 24% of patients have life-threatening arrhythmias; the frequency of appropriate ICD/ CRTD shocks during follow-up (mean 12.5 months) is 25%
- ischemic symptoms are typical in LVNS; the rate of myocardial infarct (necrosis) was 16%, its mechanisms are, in addition to atherosclerosis, embolism and myocarditis
- embolic complications developed in 11% of patients in the presence of intracardiac thrombosis and in the absence of anticoagulation therapy; mean risk factors were severe systolic dysfunction and NYHA functional class of CHF
- the rate of mortality/ transplantation for the year follow-up was 14%; terminal heart failure, and thromboembolic complications prevail in the structure of the causes of death