VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

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Ten-year follow-up of patients with unexplained left ventricular systolic dysfunction evaluated by endomyocardial biopsy

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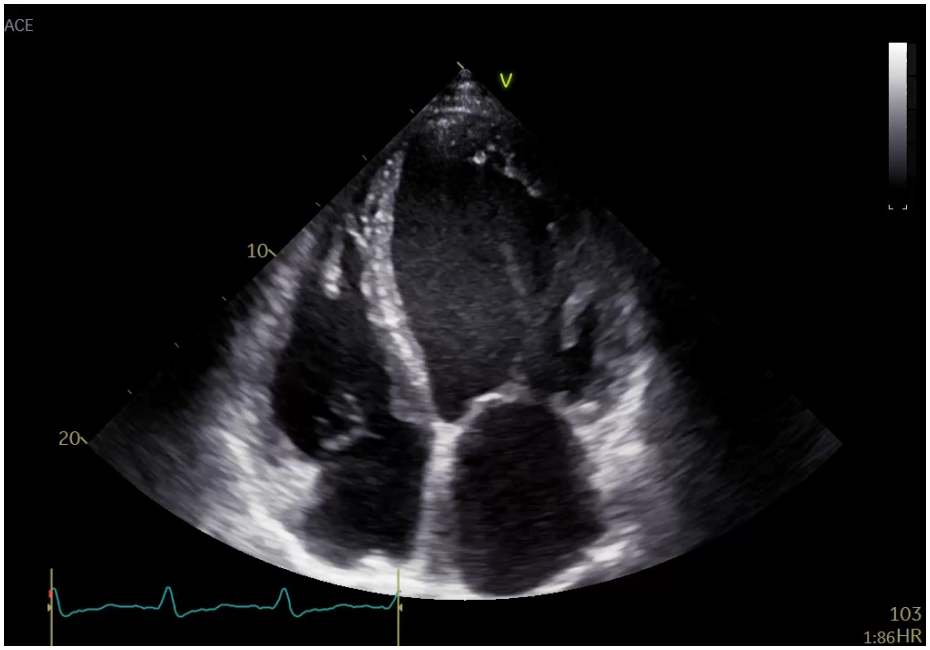
Recent-onset left ventricular systolic dysfunction

Characterized by reduced left ventricular (LV) function, as assessed by imaging techniques, commonly resulting in heart failure (HF)

Variable long-term prognosis

Endomyocardial biopsy (EMB) recommended in selected cases



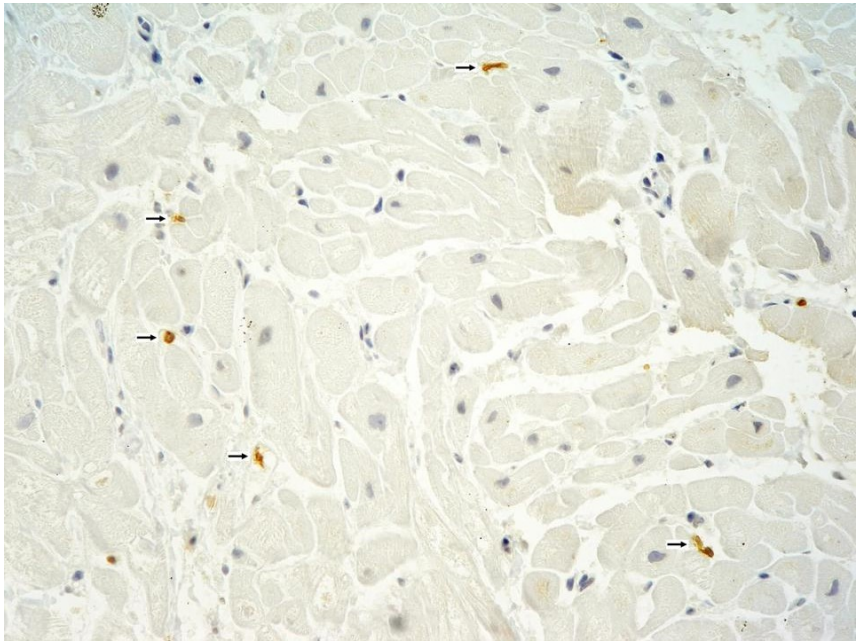


Image Archive: General University Hospital,

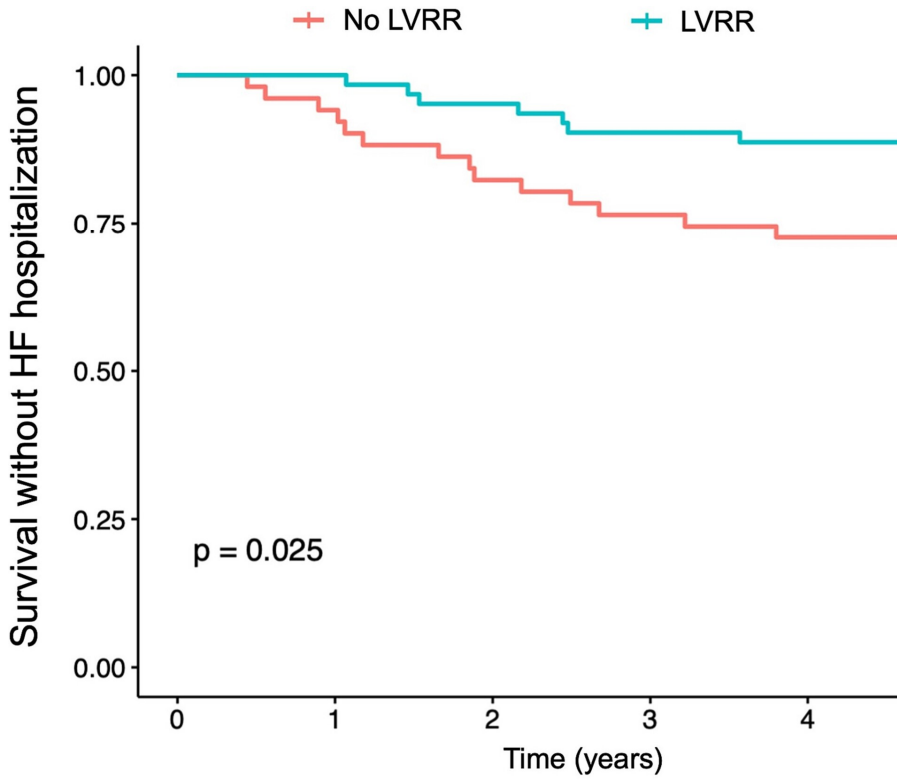
Left ventricular reverse remodelling

ecrease in chamber volume and change of geometry associated with improvem
LV systolic and diastolic function

everal definitions:

- LVEDDi decrease ≥ 10% or LVEDDi ≤ 33 mm/m2
- LVESV reduction ≥ 15%
- LVEF increase > 10%

eft ventricular reverse remodelling (LVRR)
chievement with guideline-directed therapy
nked to prognosis

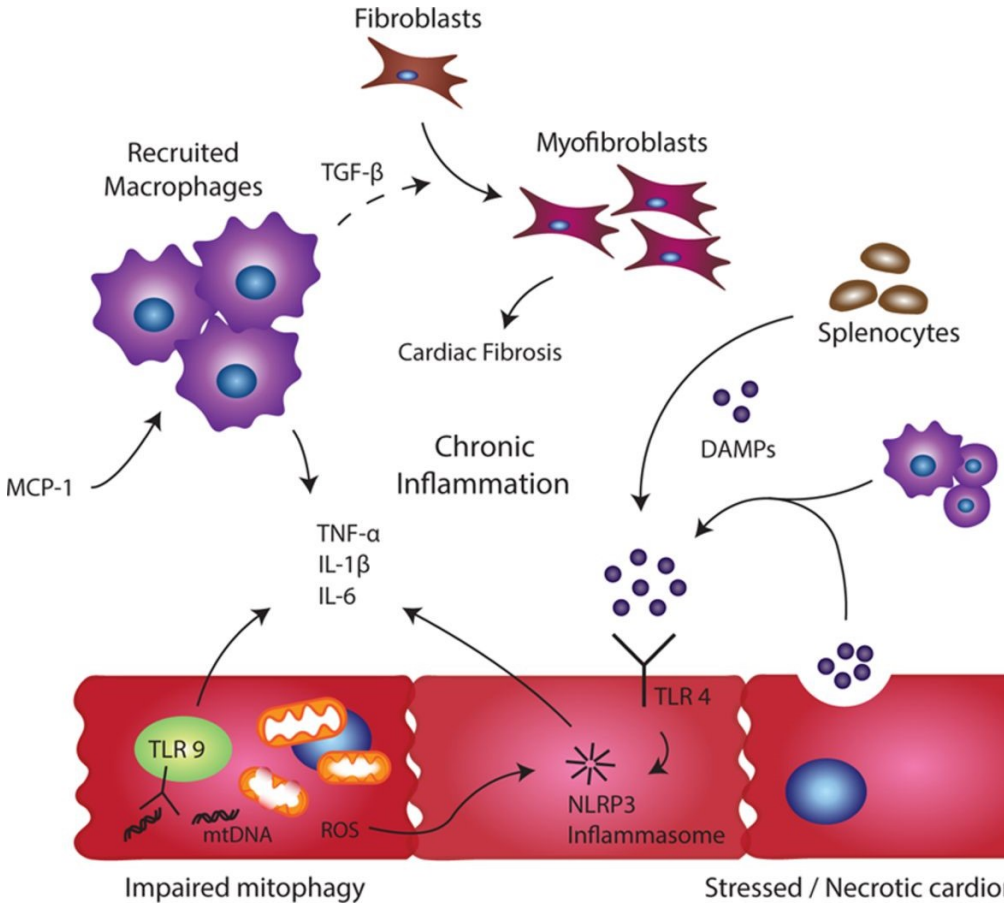


Kuchynka et al, ESC Heart Fail, 2024, 11(2):8

Subclinical systemic inflammation in heart failure

Significant role in HF pathophysiology,
both innate and adaptive immunity involved

Important role of macrophages participating
in response to myocardial damage,
including release of pro-inflammatory
cytokines, contributing to activation
of RAAS and sympathetic system

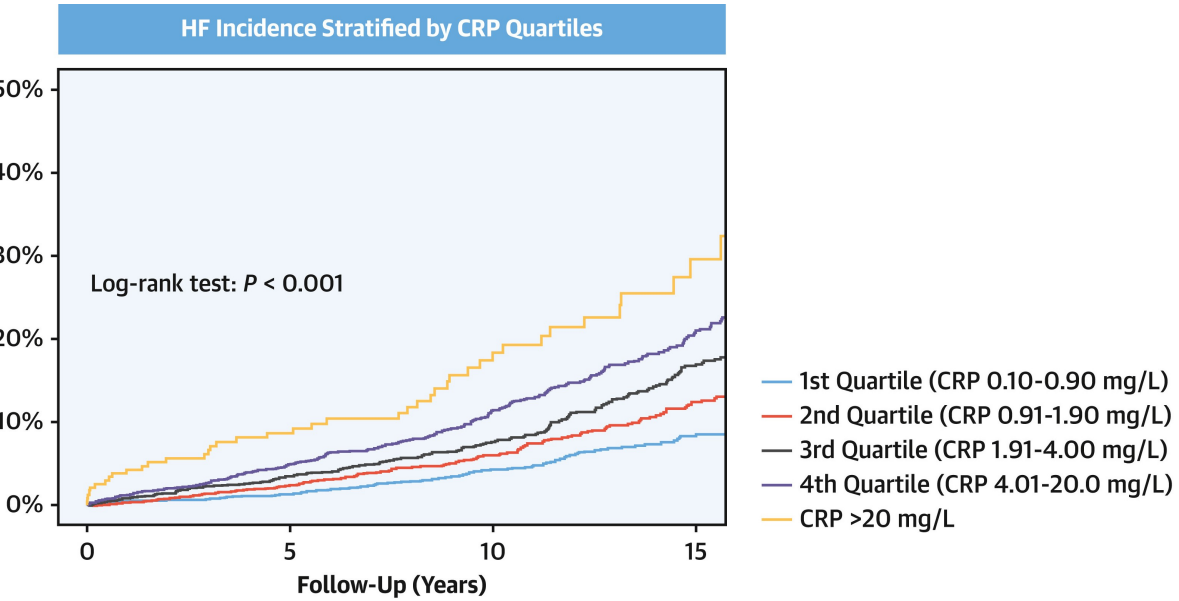


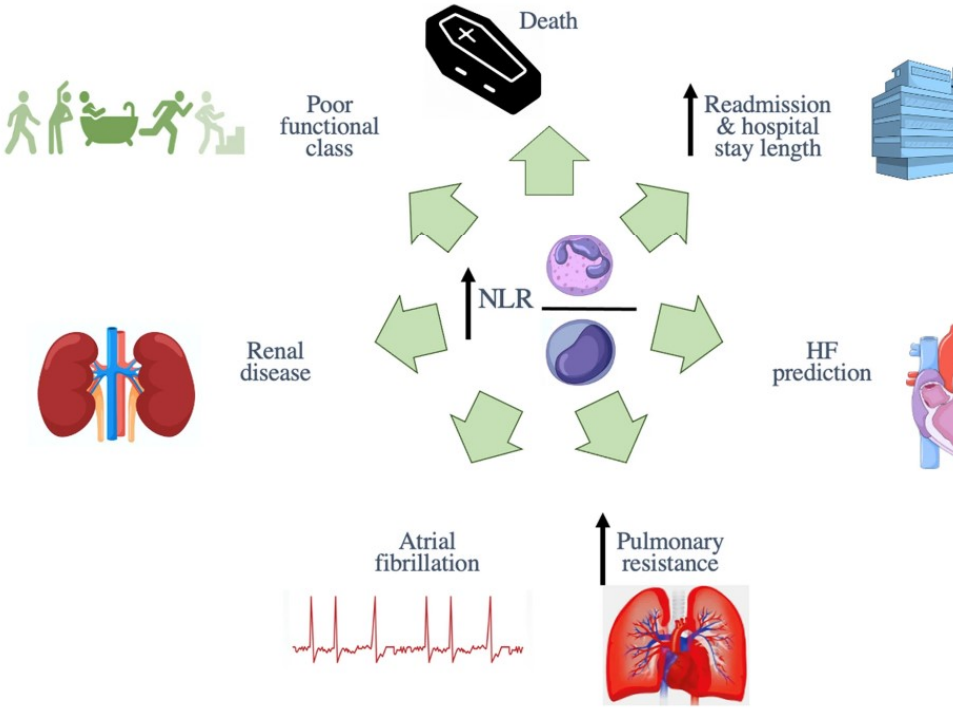
Dick et al, Circulation Research 2016, 119(1):1

Subclinical systemic inflammation in heart failure

Different biomarkers of systemic inflammation with established prognostic usefulness in cardiovascular diseases, including HF

- C-reactive protein (CRP)
- Neutrophil-to-lymphocyte ratio (NLR)
- CRP-to-lymphocyte ratio (CLR)





Burger et al, J Am Coll Cardiol. 2023, 82(5):4

Vakhshoori et al, BMC Cardiovasc Disord. 2023, 23

Aims of our study

To identify baseline predictors of ten-year mortality and heart transplantation, including EMB parameters and biomarkers of subclinical inflammation

To assess the prognostic role of LVRR after one year of guideline-directed therapy with combined end-point comprised of mortality, heart transplantation and ICD/CRT-D therapy

– Our definition of LVRR – combined presence of LVEF ≥50% or increase in LVEF ≥10% points and decrease in LV end-diastolic diameter index (LVEDDi) ≥10% or LVEDDi ≤33 mm/m²

Study cohort

- Single-centre study
- 133 patients with recently diagnosed unexplained LV systolic dysfunction (55±11 years, 72 % males) with HF symptoms lasting <6 months referred to our institution between April 2007–November 2013 for further evaluation
- In all patients, EMB was performed
- 10-year follow-up including annual echocardiography

Inclusion and exclusion criteria

Inclusion criteria

History of HF symptoms < 6 months

LV EF < 40% persisting after at least 1 week of conventional HF therapy

Exclusion criteria

- Significant coronary artery disease
- Pregnancy or the postpartum period
- Moderate or severe primary valvulopathy
- Haemodynamically significant congenital heart dise
- AFib or any other SV arrhythmia with >100 beats/m
- Any uncorrected metabolic or endocrine disorder
- Systemic autoimmune disease
- History of alcohol/drug abuse, cardiotoxic oncother

Clinical, ECG and laboratory characteristics

Age (years)	55 [46,61]
Gender (women)	37 (27.8%)
HF symptoms duration (days)	56 [28,123]
NYHA class I/II/III/IV (class)	4/25/45/57
Arterial hypertension	52 (39.1%)
Diabetes mellitus	17 (12.7%)
Atrial fibrillation	9 (7%)
LBBB	25 (18.7%)
BNP (pg/mL)	405 [198,789]
TnI (ug/L)	0.05 [0.03,0.16]
CRP (mg/L)	5 [2, 9]
NLR	2.55 [1.81, 3.58]

Baseline echocardiographic parameters

LVEDD (mm)	68±7
LVEDDi (mm/m^2)	34 [31,37]
LVEDV (mL)	199 [159,239]
LVEDVi (mL/m^2)	96 [83,114]
LVEF (%)	28 ±7
E/e´ ratio	12 [9,14]
Mitral regurgitation (grade)	2 [1,2.5]
LAVi (mL/m^2)	47 [37,61]
TAPSE (mm)	18 [15,21]
Tricuspid regurgitation (grade)	1 [1,1.5]
RA area (cm^2)	18 [15,22]
PASP (mmHg)	36 [27,47]

Endomyocardial biopsy findings

sitive EMB PCR focused on uses AS = 133)	69 (52%)
M focused on viruses AS = 133)	82 (62%)
sitive Dallas criteria AS = 133)	3 (2%)
sitive IH criteria for myocarditis AS = 128)	22 (17%)
A DR (NAS = 109) - grade 0/1/2/3	35/35/19/20
A (NAS = 86) -positive cells (counts)	5[2,8]
03 (NAS = 122) -positive cells (counts)	3[1,5]
68 (NAS = 85) -positive cells (counts)	1[0,3]

IH criteria for myocarditis - immunohistoch
criteria defined as ≥14 leucocytes/mm2 and ≥
CD3 positive T-lymphocytes/mm2

Predictors of ten-year mortality and transplantatio

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
RAP (mmHg)	1.125	1.050–1.206	0.001			
PASP (mmHg)	1.037	1.009–1.066	0.010			
RA area (cm²)	**1.128**	**1.071–1.188**	**<0.001**	**1.120**	**1.061–1.182**	**<0.001**
TR severity (grade)	1.482	1.013–2.168	0.043			
LA diameter (mm)	1.062	1.010–1.117	0.019			
logBNP	2.093	1.016–4.309	0.045			
CRP (mg/l)	1.055	1.007–1.106	0.024			
NLR	**1.336**	**1.091–1.636**	**0.005**	**1.363**	**1.081–1.720**	**0.009**
CLR (mg/10⁹)	1.086	1.009–1.168	0.028			
PR interval (per 1 ms)	1.012	1.001–1.023	0.031			

Prognostic value of LVRR

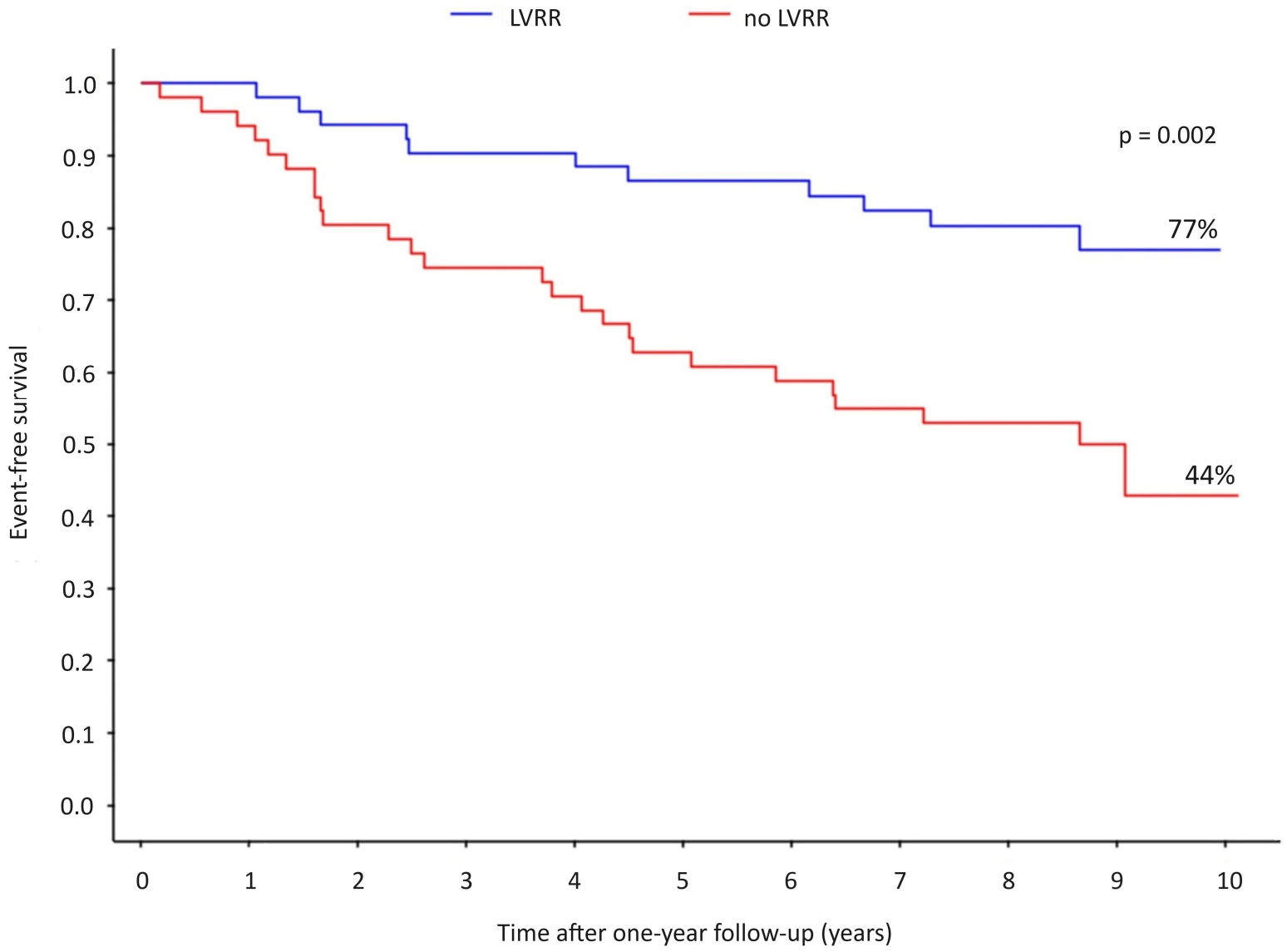
At the first year of follow-up:

- 100% angiotensin-converting enzyme inhibitors/angiotensin receptor blockers
- 98% beta-blockers
- 67% mineralocorticoid receptor antagonists

During the ten-year follow-up period:

- 36 (27%) individuals died, 4 (3%) underwent heart transplantation
- 51 HF hospitalisations in 27 (20%) individuals
- ICD and CRT-D devices implanted in 14 and 26 individuals
- 35 episodes of ICD/CRT-D therapy recorded in 13 individuals (33% of ICD/CRT-D recipients)

Prognostic value of LVRR



Conclusions

urrent optimal guideline-directed medical therapy leads to early LVRR in a gnificant portion of patients with recently diagnosed non-ischemic LVSD and its chievement is related to long-term prognosis

ight heart involvement and laboratory signs of subclinical systemic inflammation so have a strong impact on the long-term prognosis of these patients

either the presence of EMB-proved myocarditis by immunohistochemical criteria or the presence of viral agents in EMB predict outcome

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Thank you