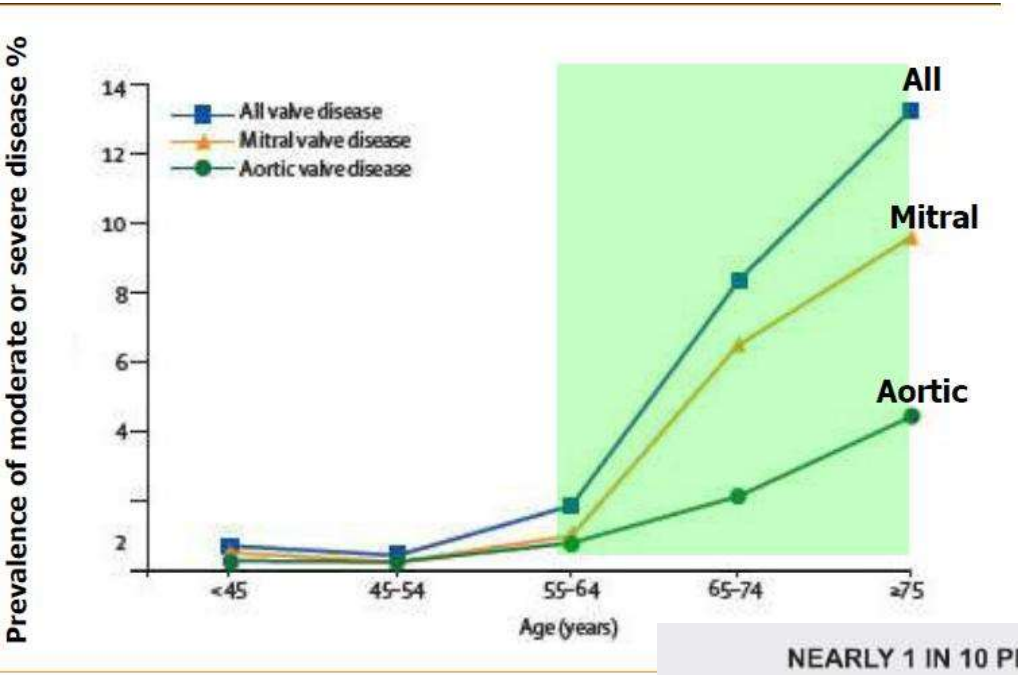
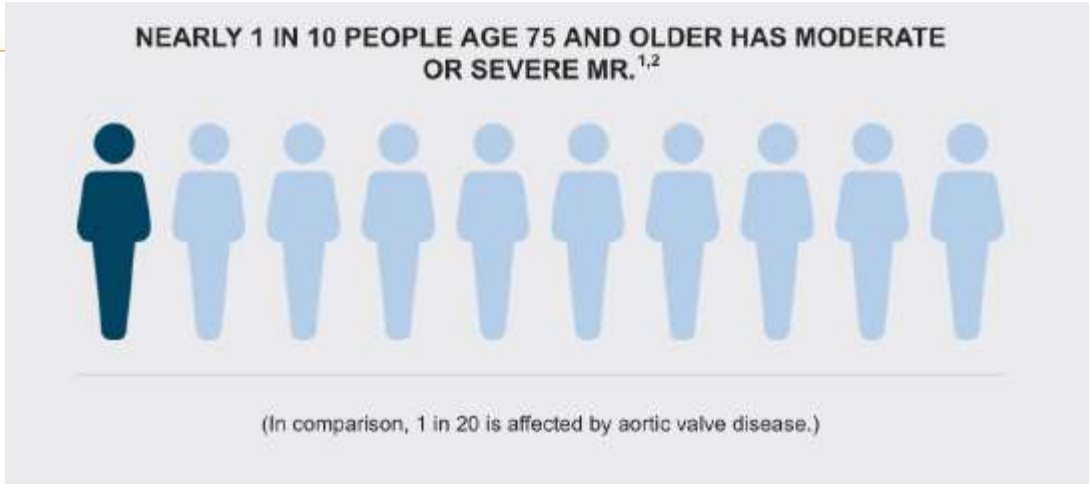
Střednědobé výsledky po intervenčních výkonech na mitrální chlopni

J. Januška, D. Krausová

Nemocnice Podlesí a.s.

Prevalence postižení Mi chlopně

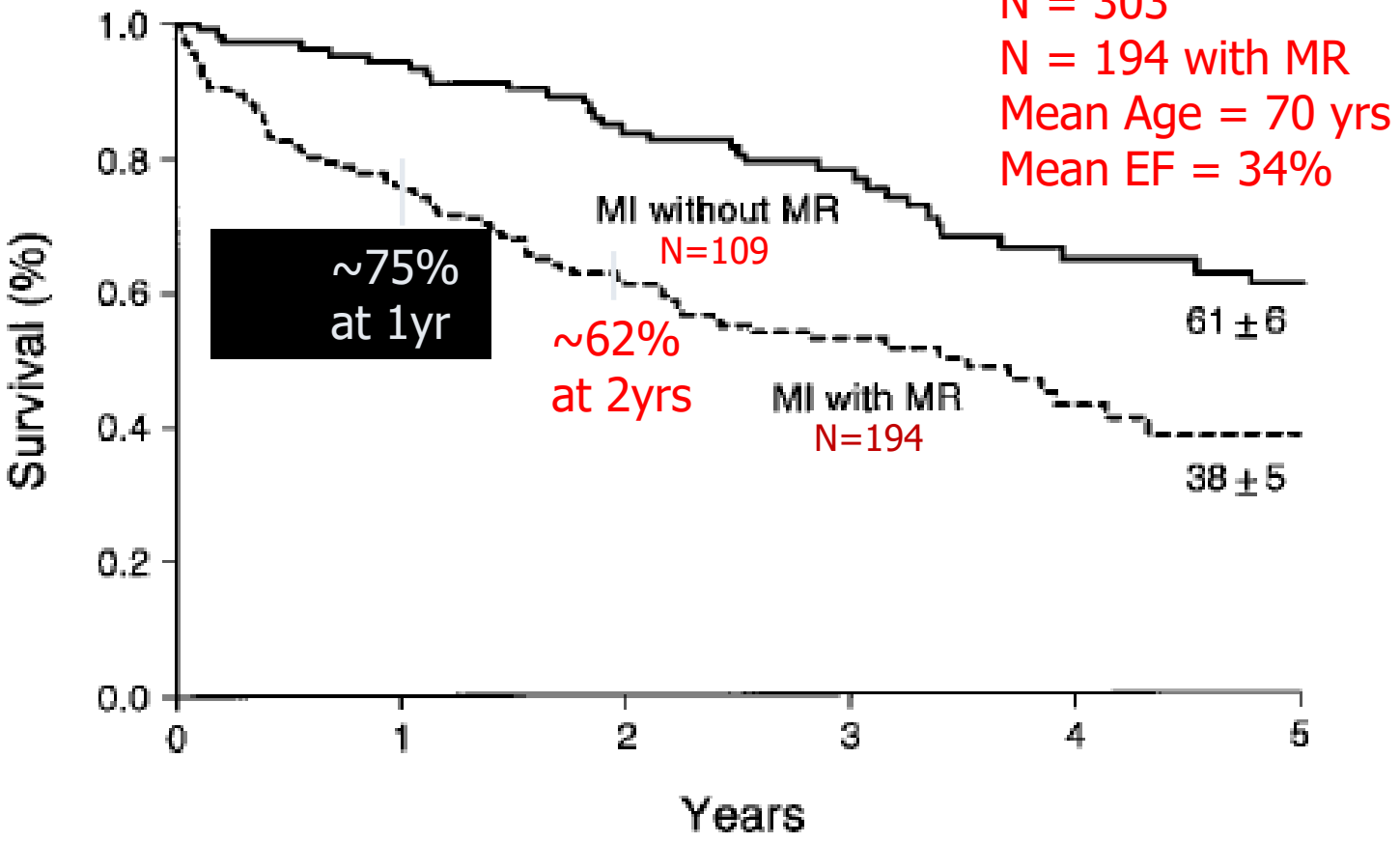




Source: Nkomo et al. Burden of valvular heart diseases: a population-based study, Lancet 2006; 368: 1005–11.

*Nkomo: 1.7% prevalence (population based studies); US Census Bureau 2016: 248M adults

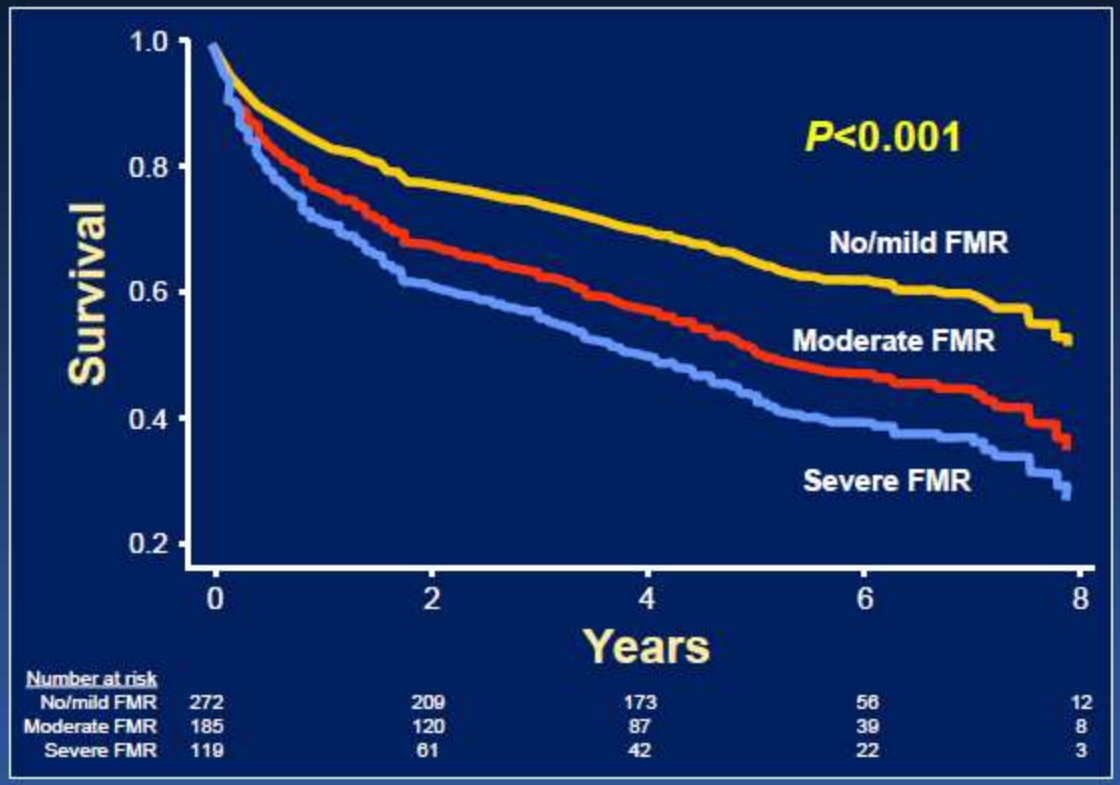
Funkční Mi regurgitace po IM



Grigioni et al. Circulation; 2001

Prognostic Utility of FMR

Prospective study of 576 pts with HFrEF; 47% died during median 5-year FU; severe FMR in 21%, mod FMR in 32%



Severe FMR was an independent predictor of long-term mortality after MV adjustment for clinical variables

HR [95%CI] = 1.61 [1.22, 2.12], *P*=0.001

and after MV adjustment for clinical, echo, biomarker and medication variables

HR [95%CI] = 1.38 [1.03, 1.84], *P*=0.03

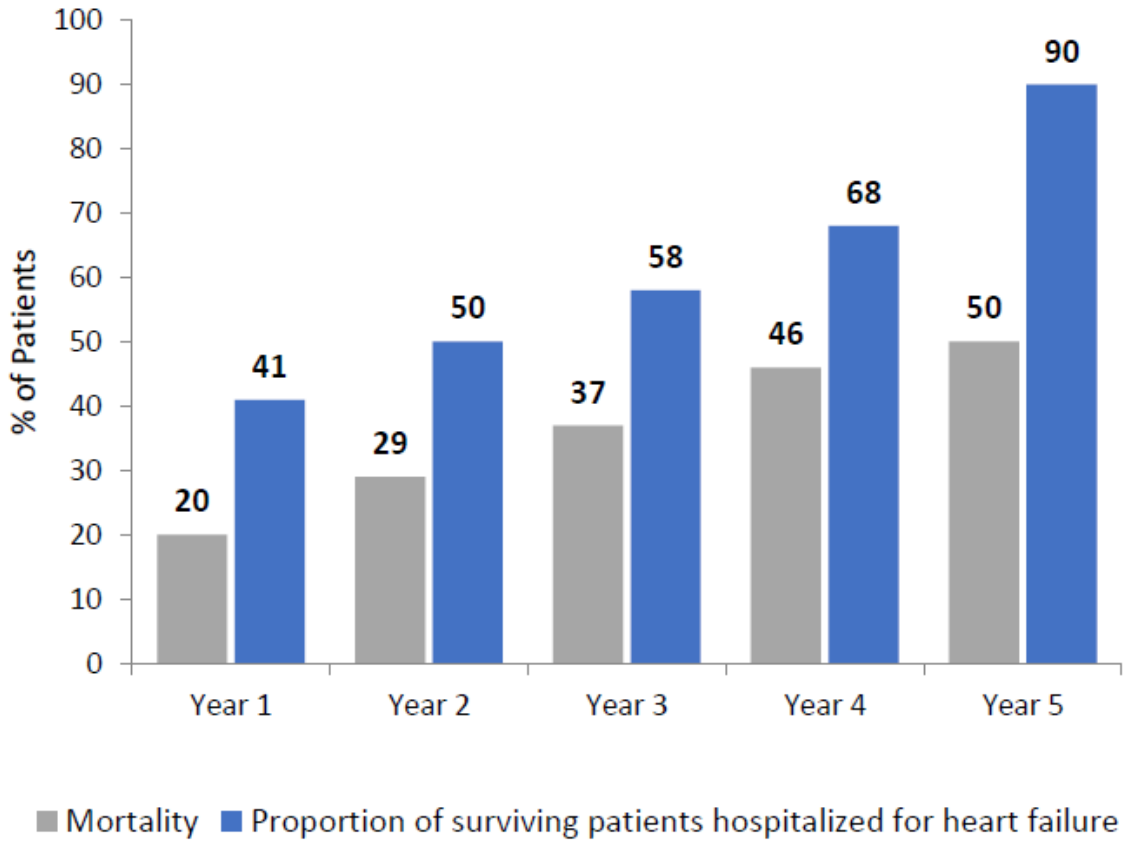
Goliasch G et al. *EHJ* 2018;39:39-46

Mortalita a morbidita Mi insufficience

20%
One year mortality rate

50%
Five year mortality rate

Very high
Rate of heart failure hospitalization

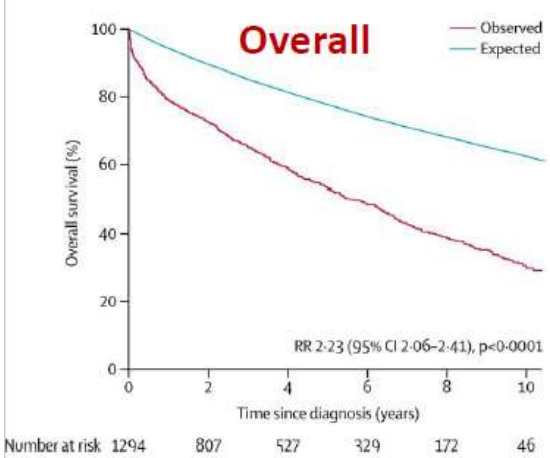


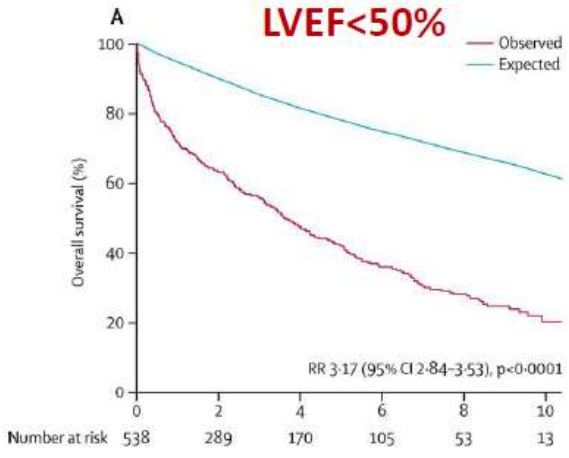
Goel et al. Journal of the Amercian College of Cardiology. 2014;63:185-186.

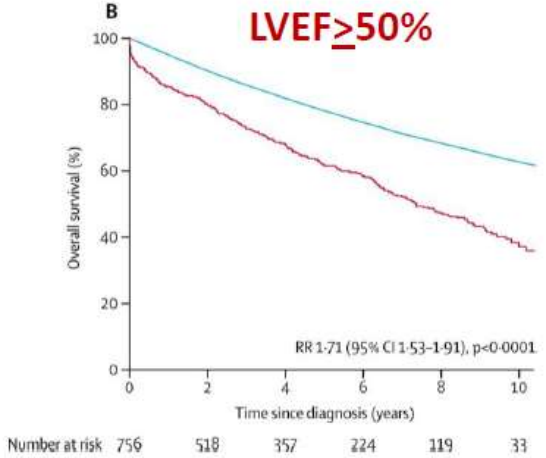
Přežívání pacientů s Mi insufficiencí

1294 community residents (median age 77 yrs [IQR 66–84]) with moderate or severe isolated mitral regurgitation in Olmsted County

Survival after diagnosis of isolated moderate or severe MR compared to expected survival of the general Olmsted County population of same age and sex







	Primary MR	Secondary MR
Mortality	RR 1·73 [1·53-1·96]	2·72 [2·48-3·01]
HF at 5-yrs	48%	78%
Mitral surgery	29%	5%

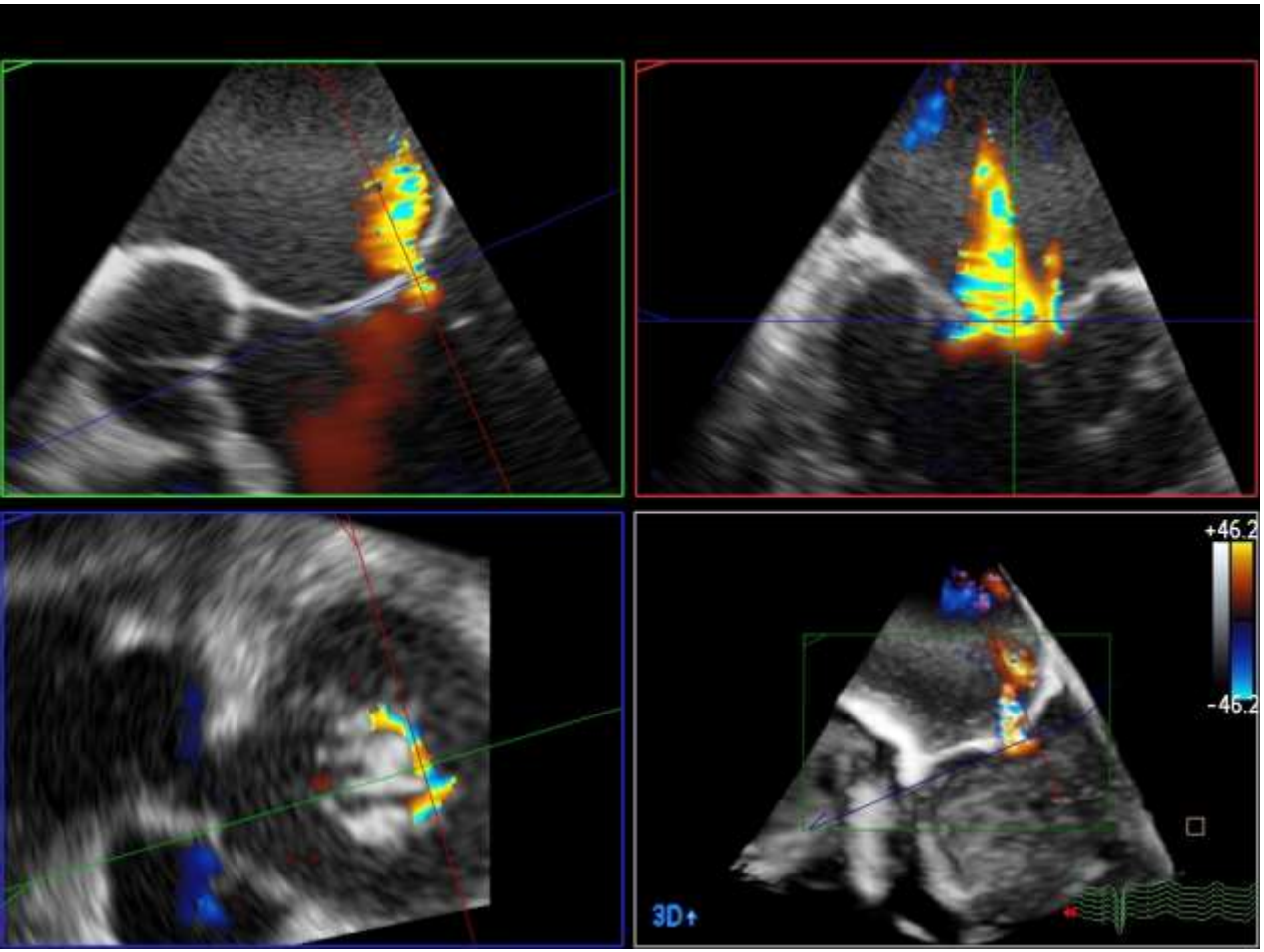
Dziadzko et al. Lancet 2018; 391: 960–69

Hodnocení mitrální regurgitace

Table 3 **Grading the severity of secondary mitral regurgitation by echocardiography**

	MR Severity*		
	Mild	**Moderate**	**Severe**
Qualitative			
MV morphology	Normal leaflets with mild tenting	Leaflets with moderate tenting	Severe tenting and movement restriction with leaflet coaptation reduced to leaflet tips or locally absent
Colour flow MR jet	Small	Moderate penetration of the aliasing jet	Large jet with profound LA penetration of the aliasing jet
Flow convergence zone†	None or small	Intermediate	Large
CW signal MR jet	Low density or incomplete duration	May be dense or holosystolic	Dense and holosystolic, low velocity and triangular
Semiquantitative			
Vena contracta width, mm	<3	Intermediate	≥7 (>8 for biplane)‡
Pulmonary vein flow§	Systolic dominance§ (may be absent with restrictive filling or atrial fibrillation)	Systolic blunting is non-specific§	Systolic flow reversal§
Mitral inflow§	A-wave dominant§‖	Variable§	E-wave dominance (non-specific§)
Quantitative			
EROA, mm^2	Not established	Not established	≥20
Regurgitant volume, ml	Not established	Not established	≥30
LV and LA size and systolic PAP#	Variable	Variable	Variable

Měření PISA



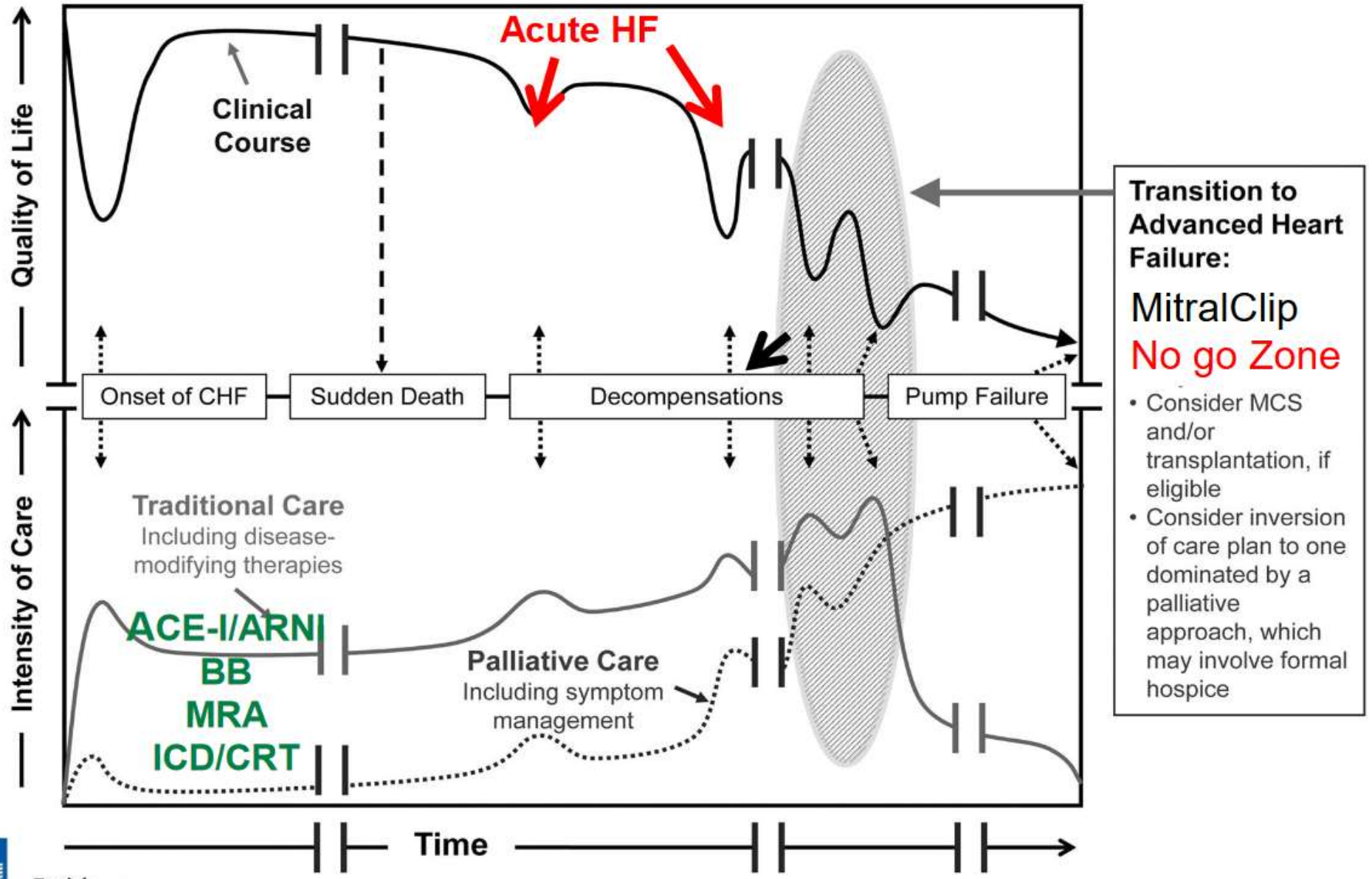
Konvenční PISA

EROA 0,16 cm2

3D PISA

EROA 1,12 cm2

Průběh srdečního selhání



Zurich

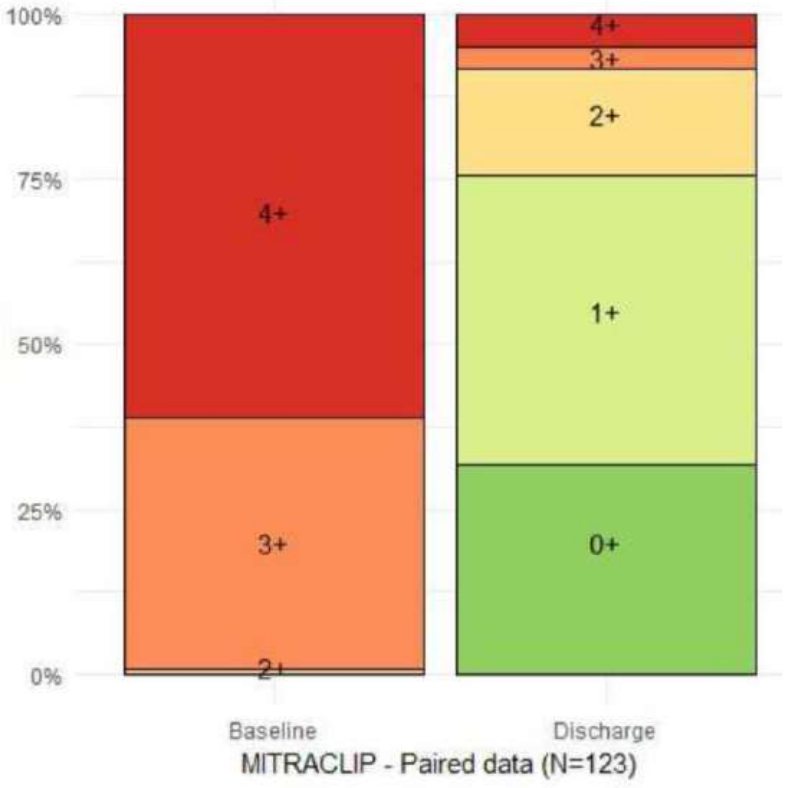
mod Ruschitzka HFA 2018, Allen Circulation 2012, Lanken AJRCC 2008

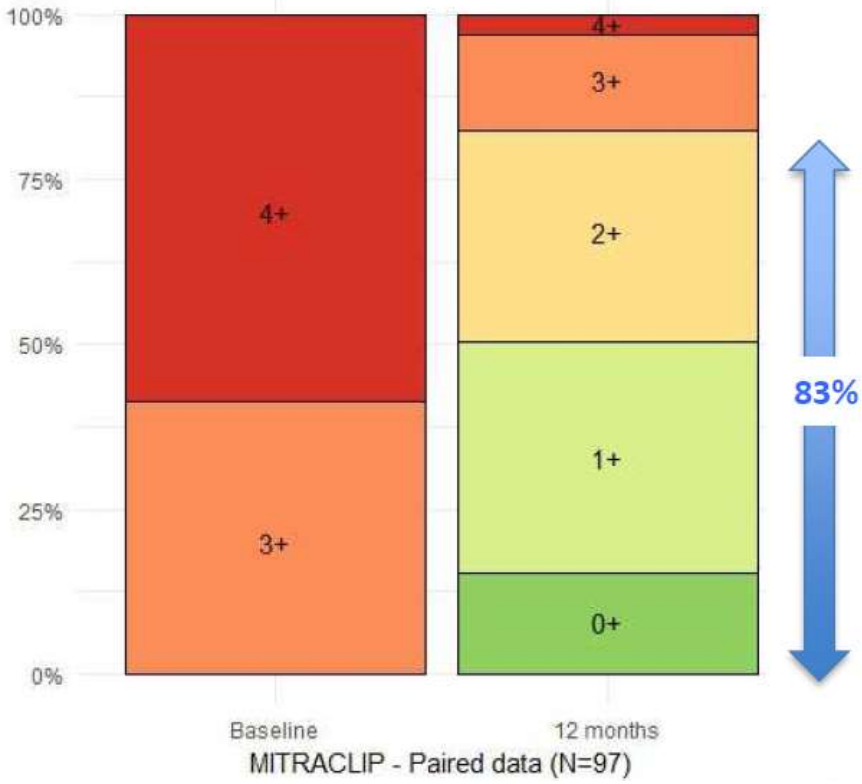
Srdeční selhání - studie

	MITRA-FR	COAPT	RESHAPE-HF-2
N patients	290+ pts @ 22 sites	614 pts @ 85 NA sites	380 pts @ 50 EU sites
Control arm	GDMT ± CRT	GDMT ± CRT	GDMT ± CRT
FMR grade	Severe (EROA >20mm² + Rvol >30mL) by ECL	≥3+ (EROA ≥30mm² &/or Rvol >45mL by ECL)	≥3+ (EROA ≥30mm² &/or Rvol >45mL-ECL)
NYHA class	II - IV	II, III, or ambulatory IV	III or ambulatory IV
Other inclusion	HF hosp within 12 months; *not eligible for MV surgery*	HF hosp within 12 months or BNP ≥300 pg/ml or nT-proBNP ≥1500 pg/ml within 12 months; ***MV surgery not local SOC***	HF hosp <12 mos or BNP ≥350 pg/ml or nT-proBNP ≥1400 pg/ml <90 days; *ineligible for MV surgery*
LVEF	≥15% - ≤40%	≥20% - ≤50%	≥15% - ≤40%
LV volumes	-	LVESD ≤70 mm	LVEDD ≥55 mm
Efficacy endpoint	Death or HF hosp at 12 mos	HF hospitalization 12 months	Death or HF hosp 12 mos
Safety endpoint	-	SLDA, device embolizations, endocarditis/MS/device-related complications requiring non-elective CV surgery, LVAD, OHT	All-cause mortality, stroke, MI, new renal replacement therapy, non-elective CV surgery for device related complications
Duration Follow-up	2 years	5 years	1 year

Mitra France

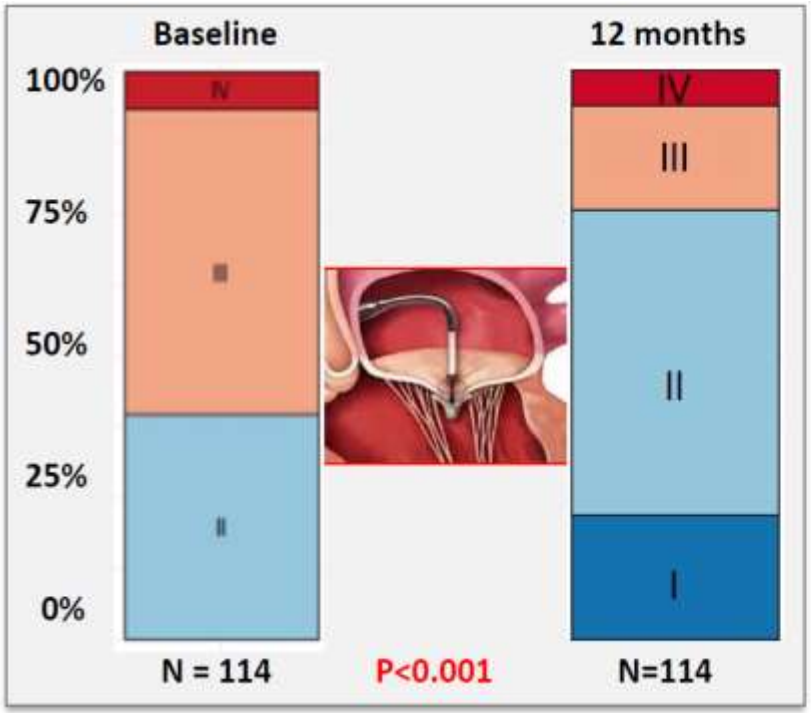
Reziduální Mi regurgitace

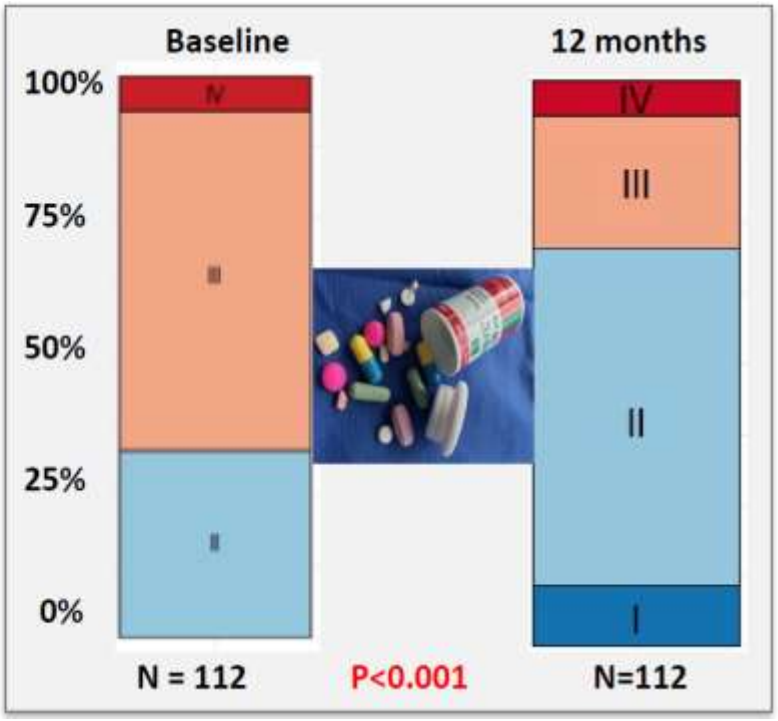




Mitra France

NYHA – nesignifikantní rozdíl mezi MitraClip a konservativní

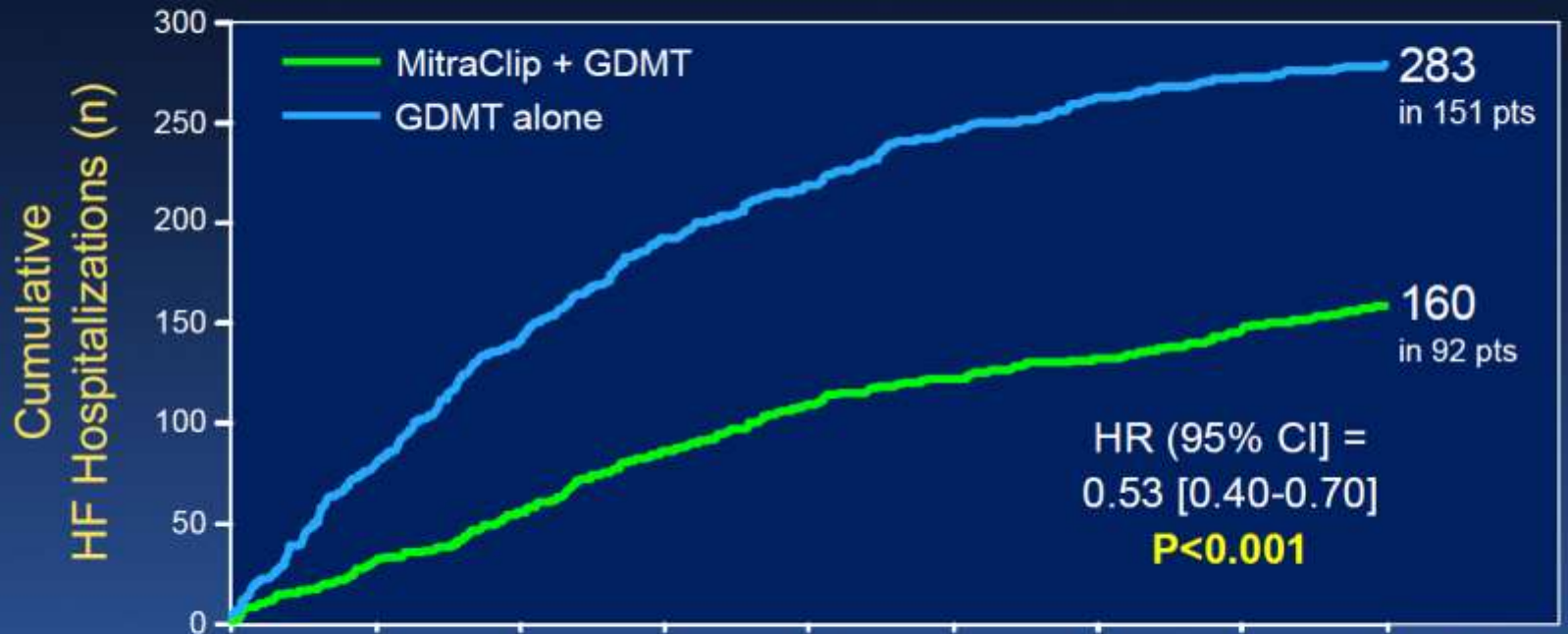




COAPT TRIAL

Primary Effectiveness Endpoint

All Hospitalizations for HF within 24 months



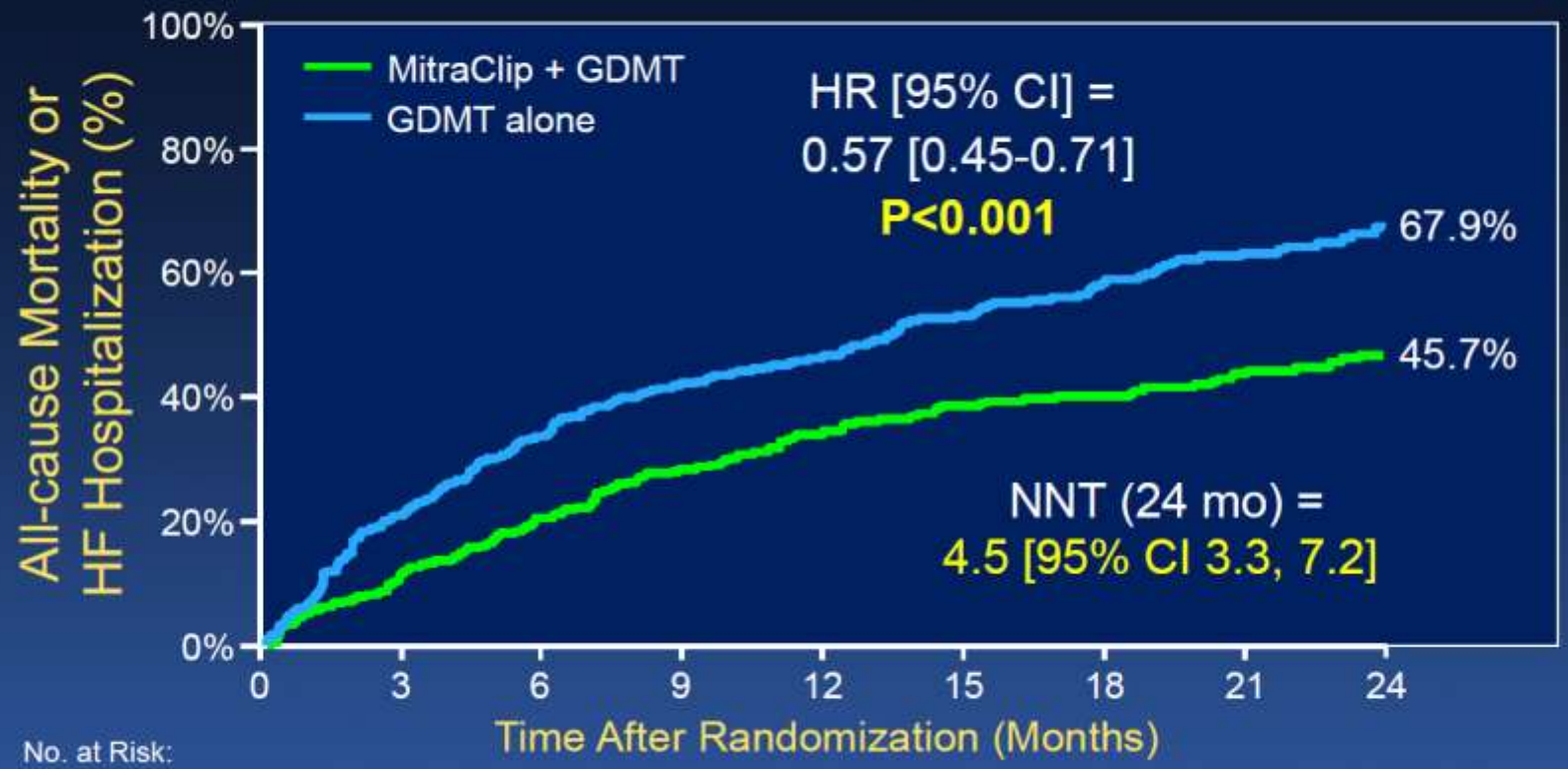
Median [25%, 75%] FU = 19.1 [11.9, 24.0] mos

No. at Risk:

MitraClip	302	286	269	253	236	191	178	161	124
GDMT	312	294	271	245	219	176	145	121	88

COAPT TRIAL

Death or HF Hospitalization

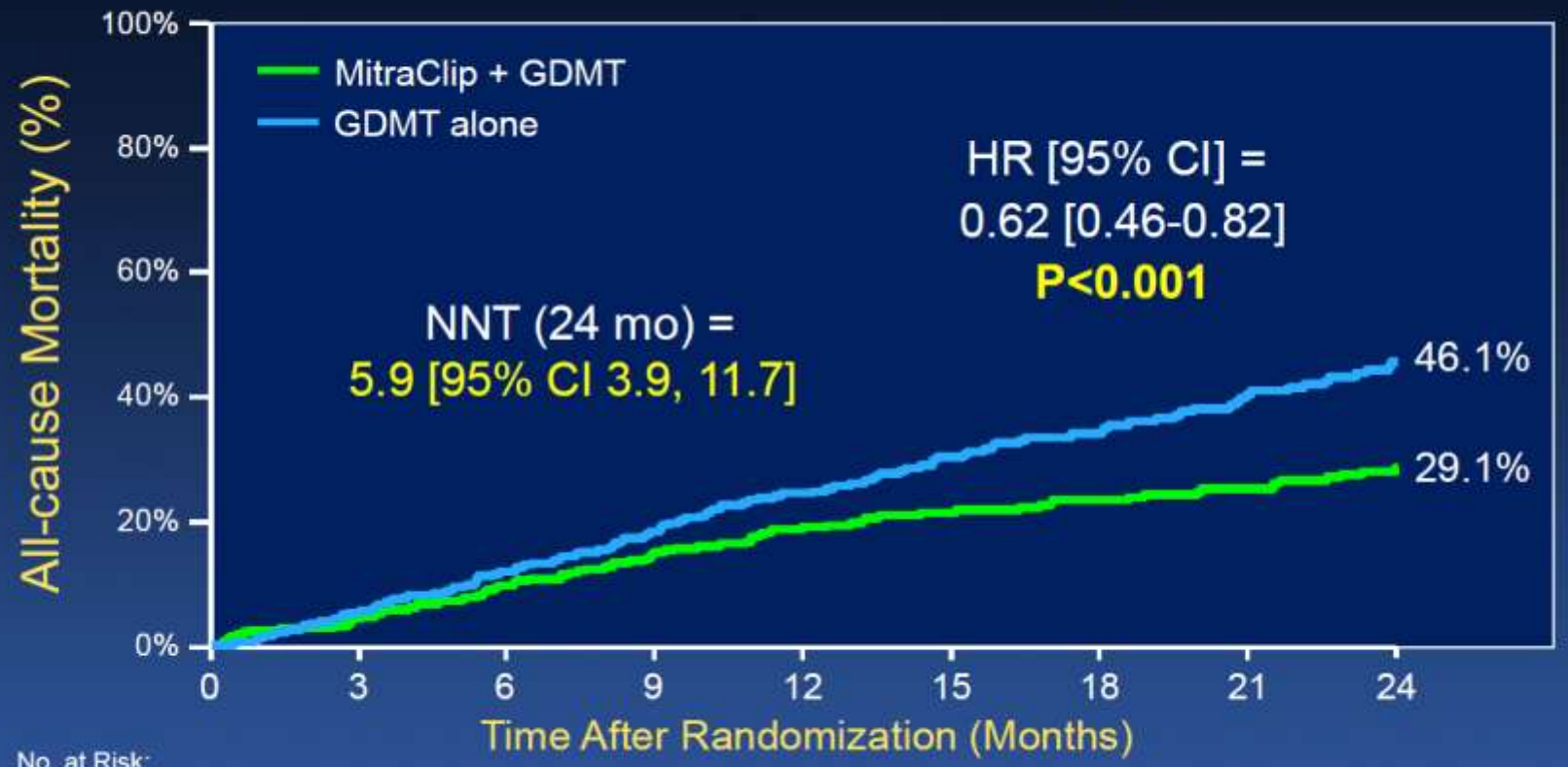


No. at Risk:

MitraClip + GDMT	302	264	238	215	194	154	145	126	97
GDMT alone	312	244	205	174	153	117	90	75	55

COAPT TRIAL

All-cause Mortality



No. at Risk:									
MitraClip + GDMT	302	286	269	253	236	191	178	161	124
GDMT alone	312	294	271	245	219	176	145	121	88

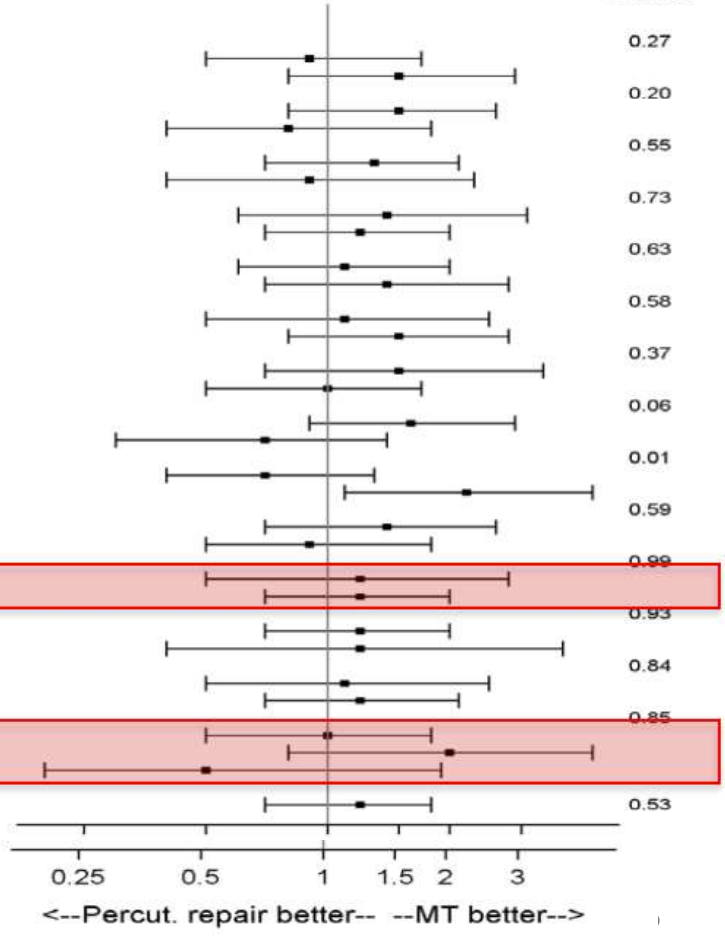
Sekundární mitrální regurgitace

Secondary MR, Symptomatic, hospitalization within 12 m	Mitra.fr 	Coapt 
Support	Academic	Abbott
N	288	430 → 614
EF	15 to 40%	20 to 50%
ERO	20 mm^2	40 mm^2
Number of centers	37	≈ 100
Roll-in Procedure/site	5	3
Enrollment	Dec 2013 → march 2017 3.2 years	Aug 2012 → June 2017 4.8 years
Enrollment / center	8.3 pt	6 pt
Primary Endpoint	Death + Rehosp at 1 y	Rehosp. at 2 after 1y FU
Expected Results	ESC August 2018	Quarter 4 - 2018

Mitra France

Subgroup Analysis

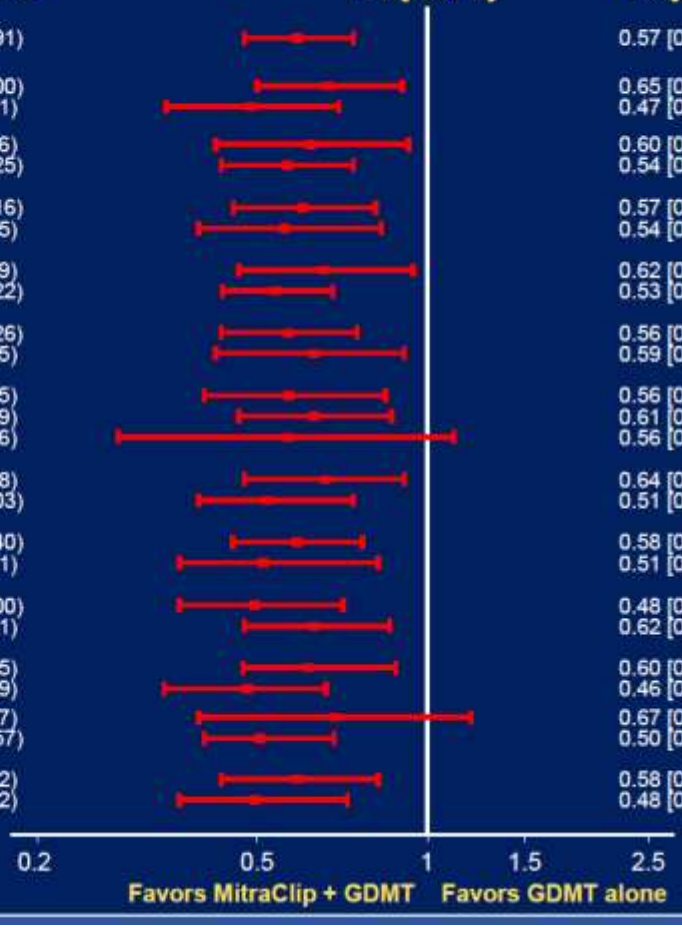
Subgroup	Percut. repair Events/N	(%)	Medical treatment Events/N	(%)	OR (95% CI)	P Value*
CENTRE SIZE						0.27
N <= 15 Randomized patients	33/73	(45.2)	35/73	(47.9)	0.90 (0.50, 1.70)	
N > 15 Randomized patients	50/77	(64.9)	43/78	(55.1)	1.50 (0.80, 2.90)	
AGE						0.20
<= 75 Yr	52/100	(52.0)	39/93	(41.9)	1.50 (0.80, 2.60)	
> 75 Yr	31/50	(62.0)	39/58	(67.2)	0.80 (0.40, 1.80)	
GENDER						0.55
Male	67/120	(55.8)	53/106	(50.0)	1.30 (0.70, 2.10)	
Female	16/30	(53.3)	25/45	(55.6)	0.90 (0.40, 2.30)	
NYHA						0.73
Class II	26/56	(46.4)	17/44	(38.6)	1.40 (0.60, 3.10)	
Class III/IV	57/94	(60.6)	61/107	(57.0)	1.20 (0.70, 2.00)	
ISCHEMIC CARDIOMYOPATHY						0.63
Yes	49/94	(52.1)	42/84	(50.0)	1.10 (0.60, 2.00)	
No	34/56	(60.7)	35/66	(53.0)	1.40 (0.70, 2.80)	
PULMONARY ARTERY PRESSURE						0.58
< 50 mmHg	23/53	(43.4)	18/44	(40.9)	1.10 (0.50, 2.50)	
≥ 50 mmHg	49/73	(67.1)	51/88	(58.0)	1.50 (0.80, 2.80)	
ATRIAL FIBRILLATION						0.37
Yes	30/49	(61.2)	24/47	(51.1)	1.50 (0.70, 3.40)	
No	46/91	(50.5)	51/99	(51.5)	1.00 (0.50, 1.70)	
PREVIOUS HOSPIT FOR CHF						0.06
< 2	53/95	(55.8)	38/87	(43.7)	1.60 (0.90, 2.90)	
≥ 2	30/55	(54.5)	40/62	(64.5)	0.70 (0.30, 1.40)	
CREATININE						0.01
< 1 5 mg/dl	31/75	(41.3)	43/85	(50.6)	0.70 (0.40, 1.30)	
≥ 1 5 mg/dl	51/72	(70.8)	34/65	(52.3)	2.20 (1.10, 4.50)	
HEMOGLOBINE						0.59
< Median	43/75	(57.3)	33/65	(50.8)	1.40 (0.70, 2.60)	
≥ Median	38/72	(52.8)	42/80	(52.5)	0.90 (0.50, 1.80)	
LVEF						0.99
< 30%	21/35	(60.0)	27/48	(56.3)	1.20 (0.50, 2.80)	
≥ 30%	62/115	(53.9)	51/102	(50.0)	1.20 (0.70, 2.00)	
TRICUSPID REGURGITATION						0.93
Mild	60/110	(54.5)	60/118	(50.8)	1.20 (0.70, 2.00)	
Moderate/Severe	19/29	(65.5)	14/23	(60.9)	1.20 (0.40, 3.80)	
LV TELEDIASTOLIC DIAMETER						0.84
< 65 mm	21/43	(48.8)	21/45	(46.7)	1.10 (0.50, 2.50)	
≥ 65 mm	62/107	(57.9)	56/105	(53.3)	1.20 (0.70, 2.10)	
MITRAL REGURGITANT ORIFICE						0.85
< 30 mm2	37/77	(48.1)	39/80	(48.8)	1.00 (0.50, 1.80)	
30-40 mm2	28/44	(63.6)	24/51	(47.1)	2.00 (0.80, 4.50)	
> 40 mm2	18/29	(62.1)	15/20	(75.0)	0.50 (0.20, 1.90)	
OVERALL	83/150	(55.3)	78/151	(51.7)	1.20 (0.70, 1.80)	0.53



COAPT TRIAL

24-Month Death or HF Hospitalization

Subgroup	MitraClip + GDMT	GDMT alone	HR [95% CI]	P [Int]
All patients	45.7% (129)	67.9% (191)	0.57 [0.45, 0.71]	
Age (median)				
≥74 years (n=317)	52.1% (78)	70.2% (100)	0.65 [0.48, 0.88]	0.13
<74 years (n=297)	37.8% (51)	65.3% (91)	0.47 [0.33, 0.66]	
Sex				
Female (n=221)	43.2% (39)	59.4% (66)	0.60 [0.40, 0.89]	0.76
Male (n=393)	47.1% (90)	73.0% (125)	0.54 [0.41, 0.71]	
Etiology of cardiomyopathy				
Ischemic (n=373)	48.1% (84)	70.0% (116)	0.57 [0.43, 0.76]	0.79
Non-ischemic (n=241)	41.1% (45)	65.2% (75)	0.54 [0.37, 0.78]	
Prior CRT				
Yes (n=224)	50.2% (55)	68.4% (69)	0.62 [0.44, 0.89]	0.54
No (n=390)	42.9% (74)	67.4% (122)	0.53 [0.39, 0.71]	
HF hospitalization within the prior year				
Yes (n=407)	44.7% (86)	67.9% (126)	0.56 [0.42, 0.73]	0.79
No (n=207)	47.6% (43)	67.8% (65)	0.59 [0.40, 0.86]	
Baseline NYHA class				
I or II (n=240)	41.1% (50)	66.9% (65)	0.56 [0.39, 0.81]	0.92
III (n=322)	46.6% (67)	65.3% (99)	0.61 [0.44, 0.83]	
IV (n=51)	68.3% (12)	84.4% (26)	0.56 [0.28, 1.12]	
STS replacement score				
≥8% (n=262)	54.1% (65)	71.4% (88)	0.64 [0.46, 0.88]	0.41
<8% (n=352)	39.2% (64)	65.0% (103)	0.51 [0.37, 0.70]	
Surgical risk status*				
High (n=423)	49.7% (95)	71.5% (140)	0.58 [0.45, 0.75]	0.69
Not high (n=188)	35.8% (32)	58.7% (51)	0.51 [0.33, 0.80]	
Baseline MR grade				
3+ (n=320)	37.5% (51)	65.3% (100)	0.48 [0.34, 0.67]	0.29
4+ (n=293)	53.4% (78)	71.4% (91)	0.62 [0.45, 0.83]	
Baseline LVEF				
≥30% (median; n=301)	44.1% (62)	61.2% (85)	0.60 [0.43, 0.84]	0.32
<30% (median; n=274)	46.4% (56)	77.8% (99)	0.46 [0.33, 0.64]	
>40% (n=103)	49.7% (22)	56.2% (27)	0.67 [0.38, 1.17]	0.31
≤40% (n=472)	44.2% (96)	71.9% (157)	0.50 [0.39, 0.65]	
Baseline LVEDV (median)				
≥181 mL (n=288)	48.9% (43)	68.0% (92)	0.58 [0.42, 0.80]	0.42
<181 mL (n=287)	41.5% (54)	69.5% (92)	0.48 [0.34, 0.67]	



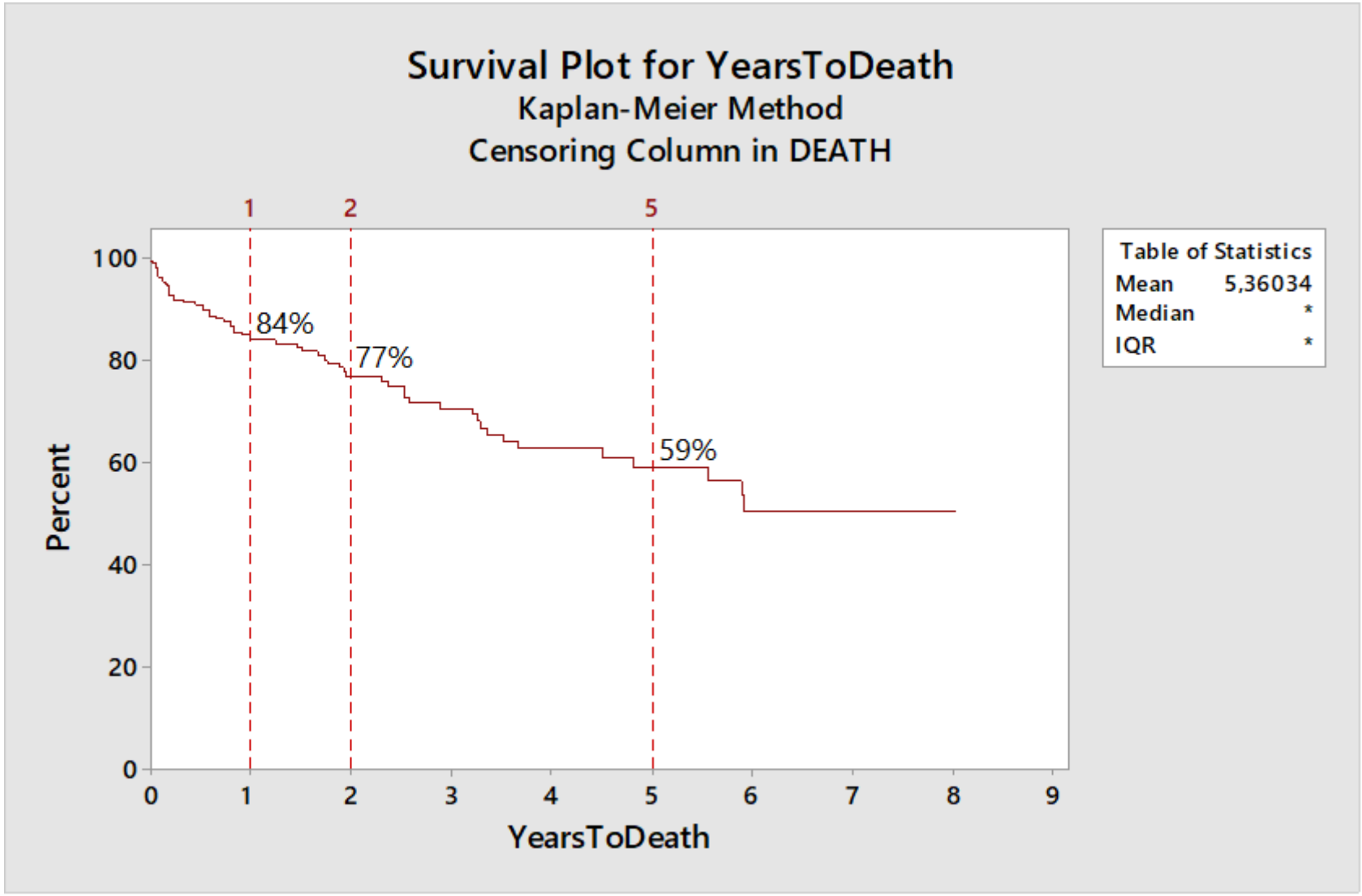
KM time-to-first event rates

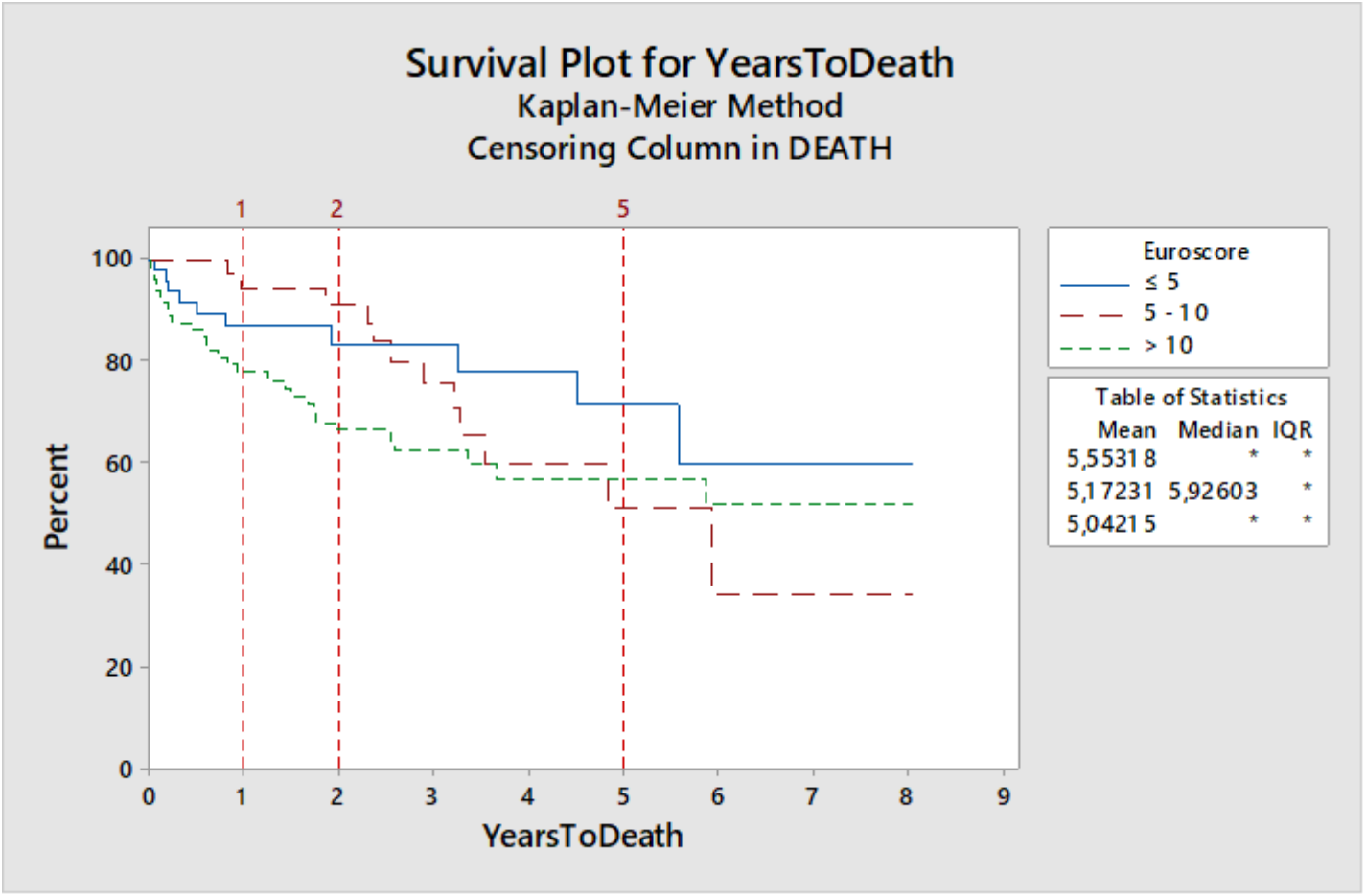
*Central eligibility committee assessment

Soubor pacientů Třinec Podlesí 12/2010 – 12/2018

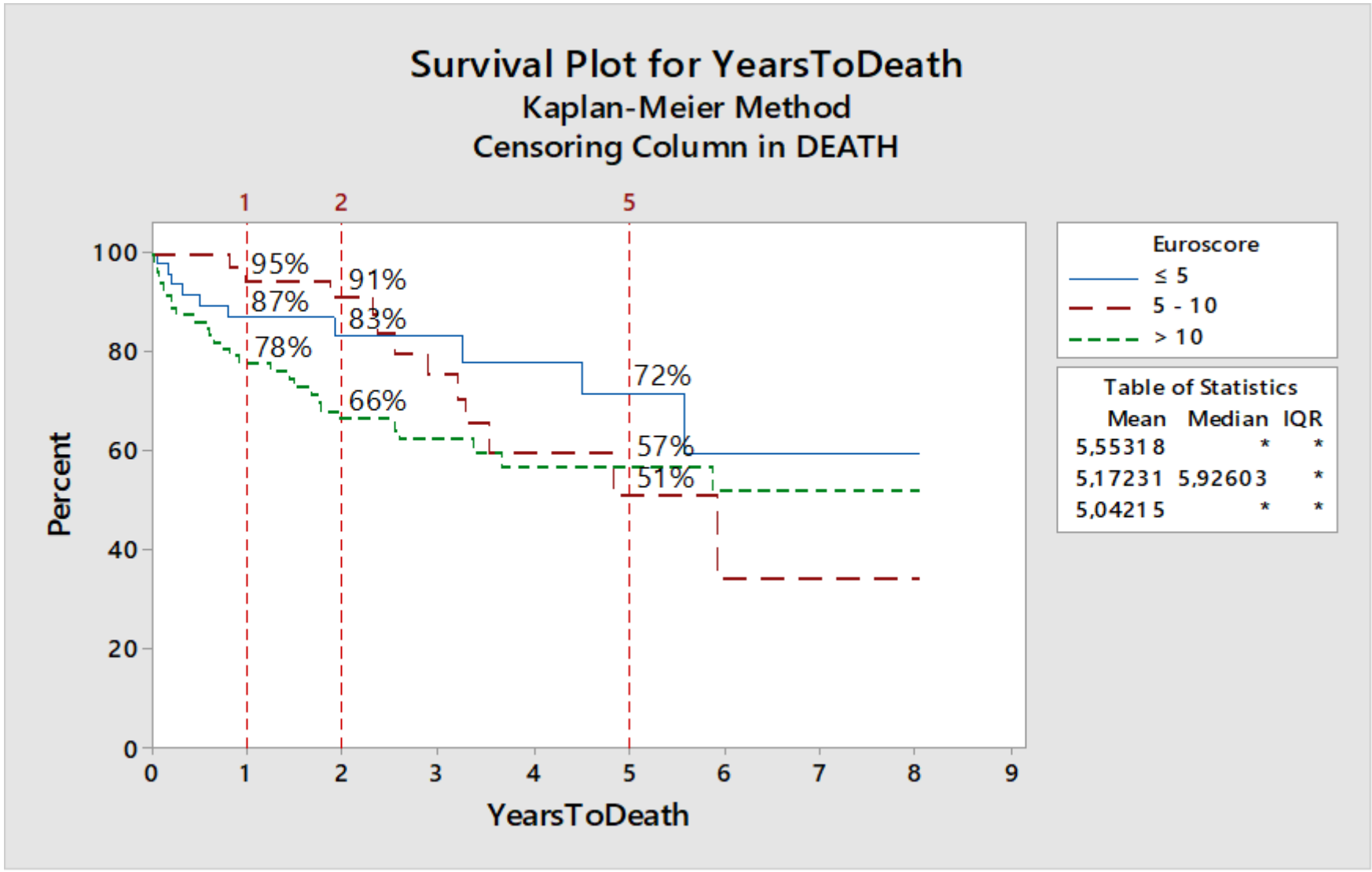
Nemocnice Podlesí
Člen skupiny AGEL

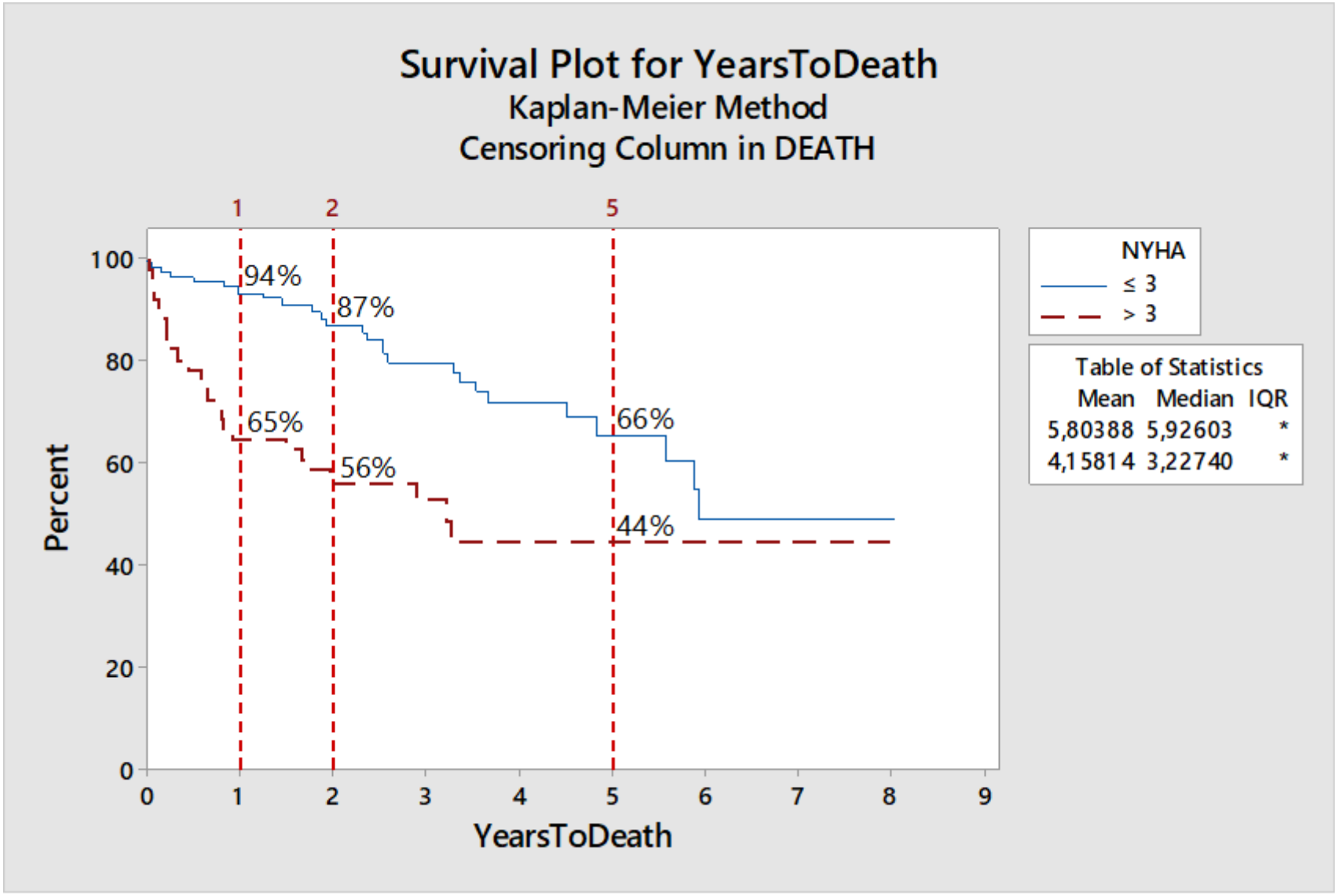
- **173 pacientů**
- **Věk 70,7 roku**
- **EF 36,1%**
- **NYHA III, IV**

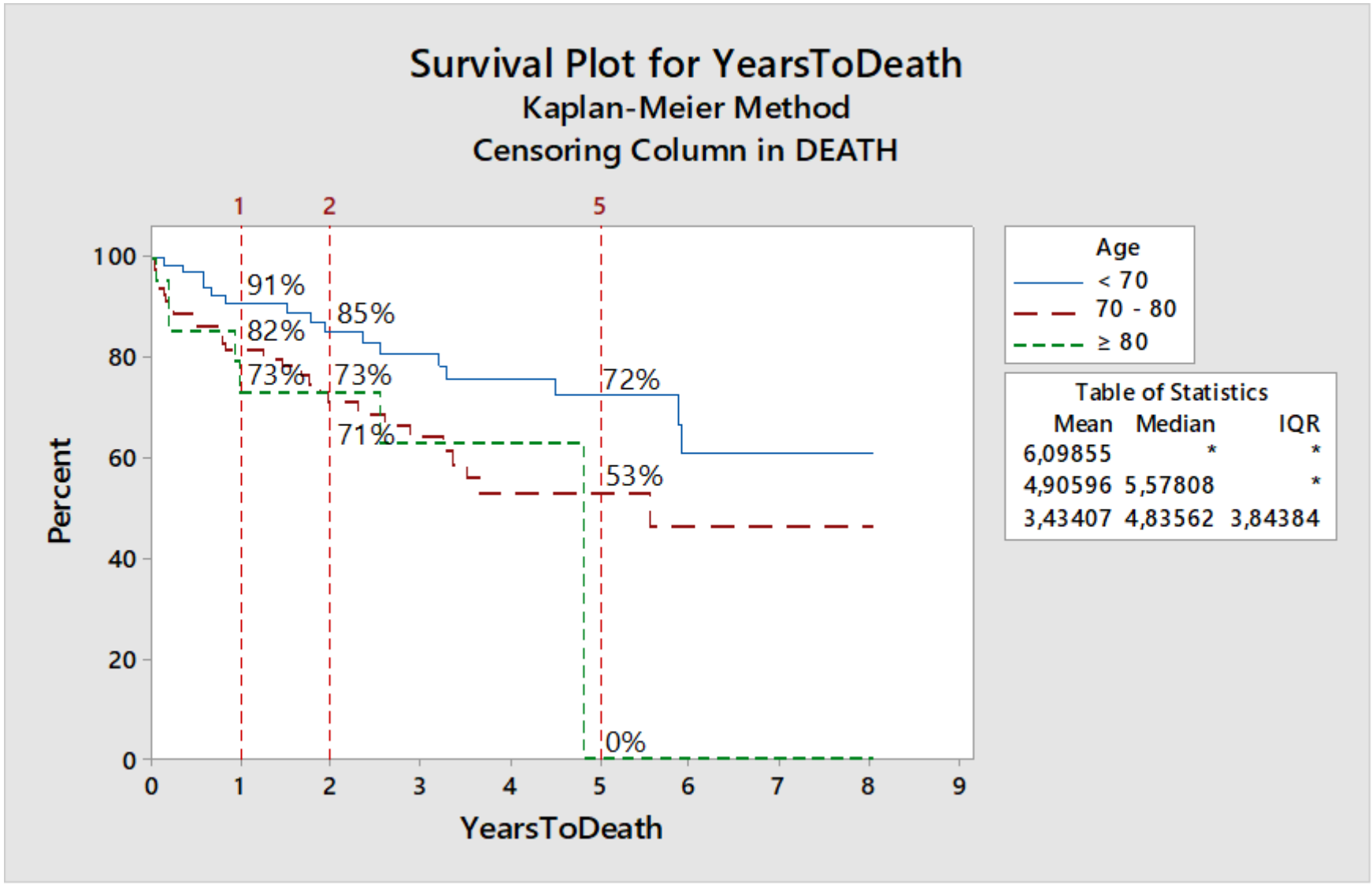

Survival Plot for YearsToDeath
Kaplan-Meier Method
Censoring Column in DEATH
1
2
5
100
80
60
40
20
0
Percent
84%
77%
59%
0
1
2
3
4
5
6
7
8
9
YearsToDeath
Table of Statistics
Mean 5,36034
Median *
IQR *



Euroscore	Survival probability after		
	1 year	2 years	5 years
≤ 5	87 %	83 %	72 %
5 - 10	95 %	91 %	51 %
> 10	78 %	66 %	57 %


Survival Plot for YearsToDeath
Kaplan-Meier Method
Censoring Column in DEATH
1
2
5
100
80
60
40
20
0
Percent
95%
91%
87%
83%
78%
72%
66%
57%
51%
0
1
2
3
4
5
6
7
8
9
YearsToDeath
Euroscore
≤ 5
5 - 10
> 10
Table of Statistics
Mean Median IQR
5,55318 * *
5,17231 5,92603 *
5,04215 * *


Survival Plot for YearsToDeath
Kaplan-Meier Method
Censoring Column in DEATH
1
2
5
94%
87%
65%
56%
66%
44%
Percent
YearsToDeath
NYHA
≤ 3
> 3
Table of Statistics
Mean Median IQR
5,80388 5,92603 *
4,15814 3,22740 *


Survival Plot for YearsToDeath
Kaplan-Meier Method
Censoring Column in DEATH
1
2
5
100
80
60
40
20
0
Percent
91%
82%
73%
85%
73%
71%
72%
53%
0%
0
1
2
3
4
5
6
7
8
9
YearsToDeath
Age
< 70
70 - 80
≥ 80
Table of Statistics
Mean Median IQR
6,09855 * *
4,90596 5,57808 *
3,43407 4,83562 3,84384

Závěrem

- **1/ plastika mitrální chlopně MitraClipem snižuje morbiditu a mortalitu i u pacientů nevhodných k operačnímu řešení**
- **2/ výkony u pacientů s terminálním srdečním selháním neprodlouží život pacientů**
- **3/ indikace katetrizačních metod v první fázi FMRI rozšíří možnost intervenční léčby u většího počtu inoperabilních pacientů**