

RESHAPE-HF2

David Zemánek

II. interní klinika

kardiologie a angiologie

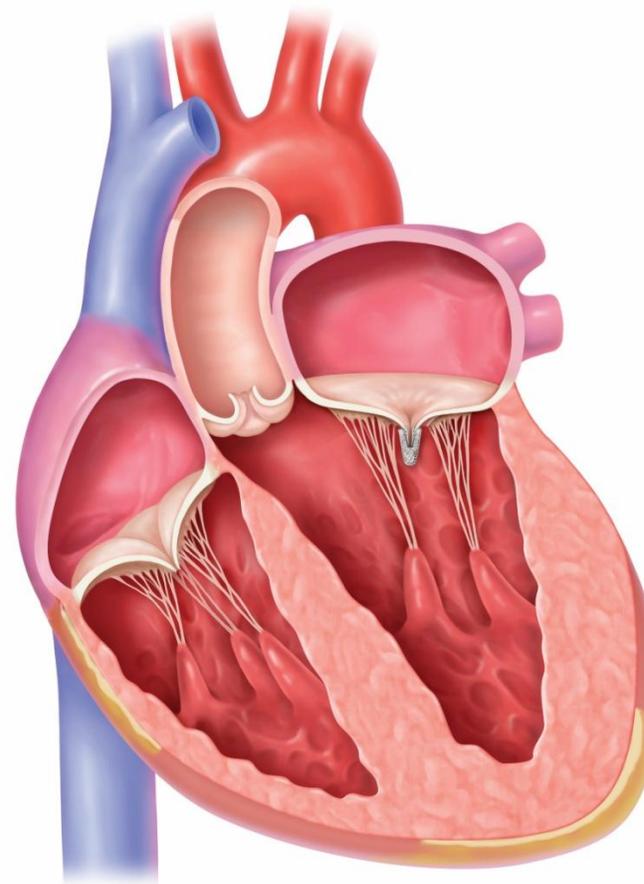
Komplexní kardiovaskulární centrum

VFN a 1. LF UK Praha



Mitral transcatheter edge-to-edge repair (M-TEER)

- Vychází z chirurgické techniky Alfieriho spočívající ve vytvoření dvou ústí
- Princip katetrizační intervence:
 - transeptální přístup
 - jícnové 3-D ECHO
- Největší zkušenosti MitraClip (EVEREST I, EVEREST II, **COAPT**, **MITRA-FR**, ...)
- Další zkušenosti Pascal

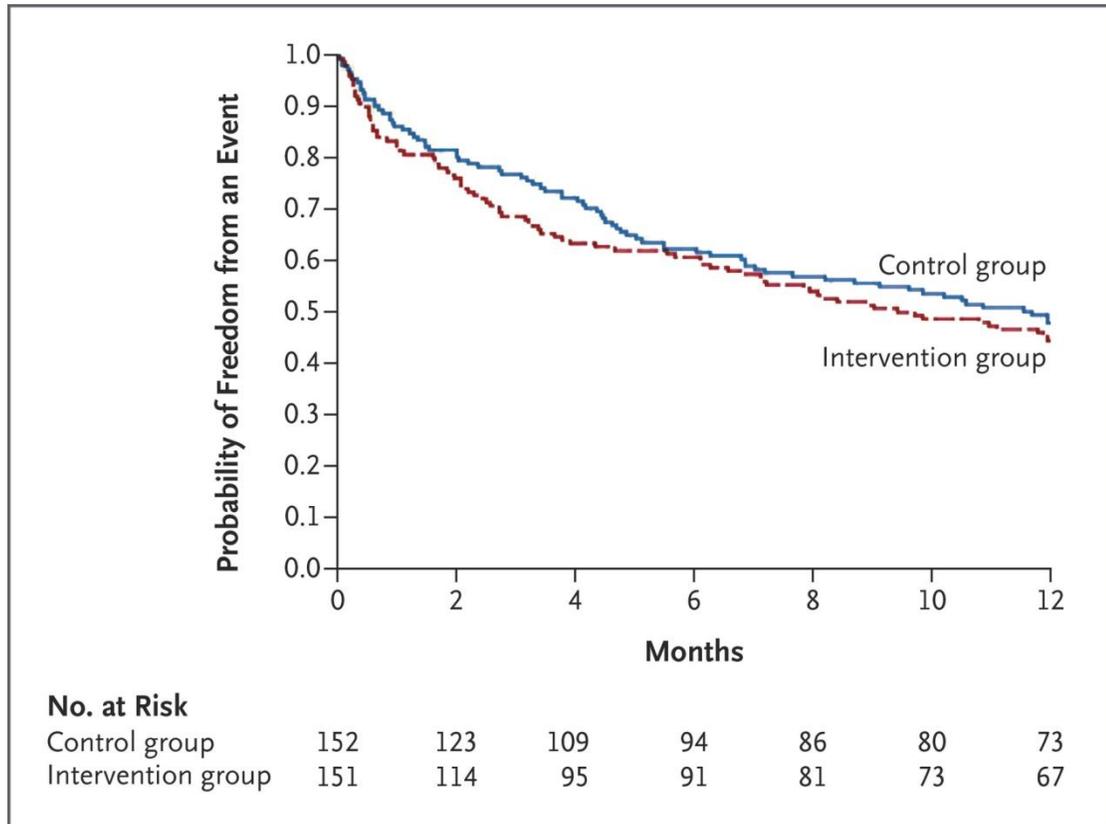


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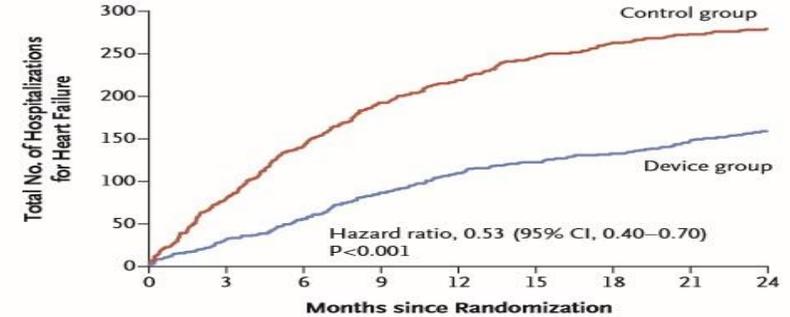
Studie MITRA-FR a COAPT

MITRA FR



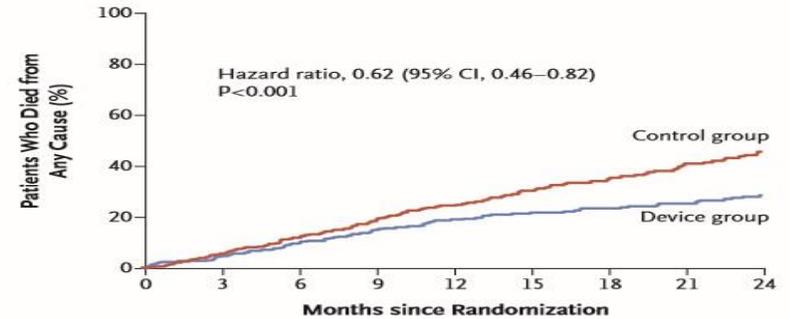
COAPT trial

Hospitalization for Heart Failure



No. at Risk	0	3	6	9	12	15	18	21	24
Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

Death from Any Cause



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Device group	302	286	269	253	236	191	178	161	124



What COAPT and MITRA-FR tell us?

	MITRA-FR	COAPT
Baseline clinical characteristics		
Age, year	70 ± 10	72 ± 11
NYHA class, %		
I	0	0.2
II	32.9	39.0
III	58.5	52.5
IV	8.6	8.3
Surgical risk		
STS score ≥8%		42.7%
EuroSCORE II, median and IQR	6.2 (3.5–11.0)	
Baseline echocardiographic characteristics		
Mitral regurgitation severity, %		
Moderate (EROA 20-29 mm ²)	52	14
Moderate-to-severe (EROA 30-39 mm ²)	32	46
Severe (EROA > 40 mm ²)	16	41
EROA, mm ²	31 ± 10	41 ± 15
LV end-diastolic volume index, mL/m ²	135 ± 35	101 ± 34
LV ejection fraction, %	33 ± 7	31 ± 7

	MITRA-FR	COAPT
Procedural characteristics and outcomes ^a		
Procedural success, % ^a	96	98
Procedural complications, % ^a	14.6	8.5
Number of clips, % ^b		
1 Clip	46	36
2 Clips	45	55
3 Clips	9	8
4 Clips	0	0.3
Post-procedural MR ≥ moderate-to-severe (3+), % ^a		
End of procedure	9	5
1 year post-procedure	17	5
2 years post-procedure		0.9
1-Year outcomes		
1-Year mortality, %		
Intervention	24.2	19.1 (P < 0.001)
Control	22.4	23.2
1-Year heart failure hospitalization, %		
Intervention	48.7	35.9 (P < 0.001) ^c
Control	47.4	67.9 ^c
1-Year mortality or heart failure hospitalization		
Primary outcome		
Intervention	54.6 (P = 0.53)	33.9 (P < 0.001)
Control	51.3	46.5



RESHAPE-HF2

(A Clinical Evaluation of the Safety and Effectiveness of the MitraClip System in the Treatment of Clinically Significant Functional Mitral Regurgitation)

- Randomizovaná multicentrická investigátořní studie
- Zařazeno 505 pacientů
- Primární cíl:
 - redukce KV úmrtí + hospitalizace
 - redukce hospitalizací pro HF
 - zlepšení kvality života podle KCCQ-OS

BACKGROUND

Whether transcatheter mitral-valve repair improves outcomes in patients with heart failure and functional mitral regurgitation is uncertain.

METHODS

We conducted a randomized, controlled trial involving patients with heart failure and moderate to severe functional mitral regurgitation from 30 sites in nine countries. The patients were assigned in a 1:1 ratio to either transcatheter mitral-valve repair and guideline-recommended medical therapy (device group) or medical therapy alone (control group). The three primary end points were the rate of the composite of first or recurrent hospitalization for heart failure or cardiovascular death during 24 months; the rate of first or recurrent hospitalization for heart failure during 24 months; and the change from baseline to 12 months in the score on the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS; scores range from 0 to 100, with higher scores indicating better health status).

RESULTS

A total of 505 patients underwent randomization: 250 were assigned to the device group and 255 to the control group. At 24 months, the rate of first or recurrent hospitalization for heart failure or cardiovascular death was 37.0 events per 100 patient-years in the device group and 58.9 events per 100 patient-years in the control group (rate ratio, 0.64; 95% confidence interval [CI], 0.48 to 0.85; $P=0.002$). The rate of first or recurrent hospitalization for heart failure was 26.9 events per 100 patient-years in the device group and 46.6 events per 100 patient-years in the control group (rate ratio, 0.59; 95% CI, 0.42 to 0.82; $P=0.002$). The KCCQ-OS score increased by a mean (\pm SD) of 21.6 ± 26.9 points in the device group and 8.0 ± 24.5 points in the control group (mean difference, 10.9 points; 95% CI, 6.8 to 15.0; $P<0.001$). Device-specific safety events occurred in 4 patients (1.6%).

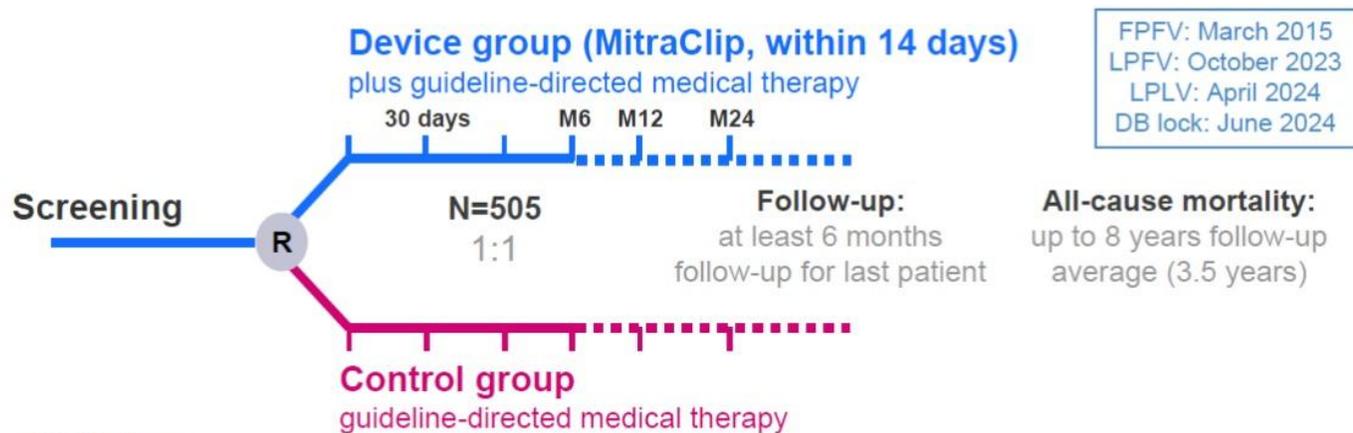
CONCLUSIONS

Among patients with heart failure with moderate to severe functional mitral regurgitation who received medical therapy, the addition of transcatheter mitral-valve repair led to a lower rate of first or recurrent hospitalization for heart failure or cardiovascular death and a lower rate of first or recurrent hospitalization for heart failure at 24 months and better health status at 12 months than medical therapy alone. (Funded by Abbott Laboratories; RESHAPE-HF2 ClinicalTrials.gov number, NCT02444338.)



RESHAPE-HF2

- Randomizovaná studie srovnávající M-TEER a optimální farmakologickou léčbu u pacientů se sekundární mitrální regurgitací



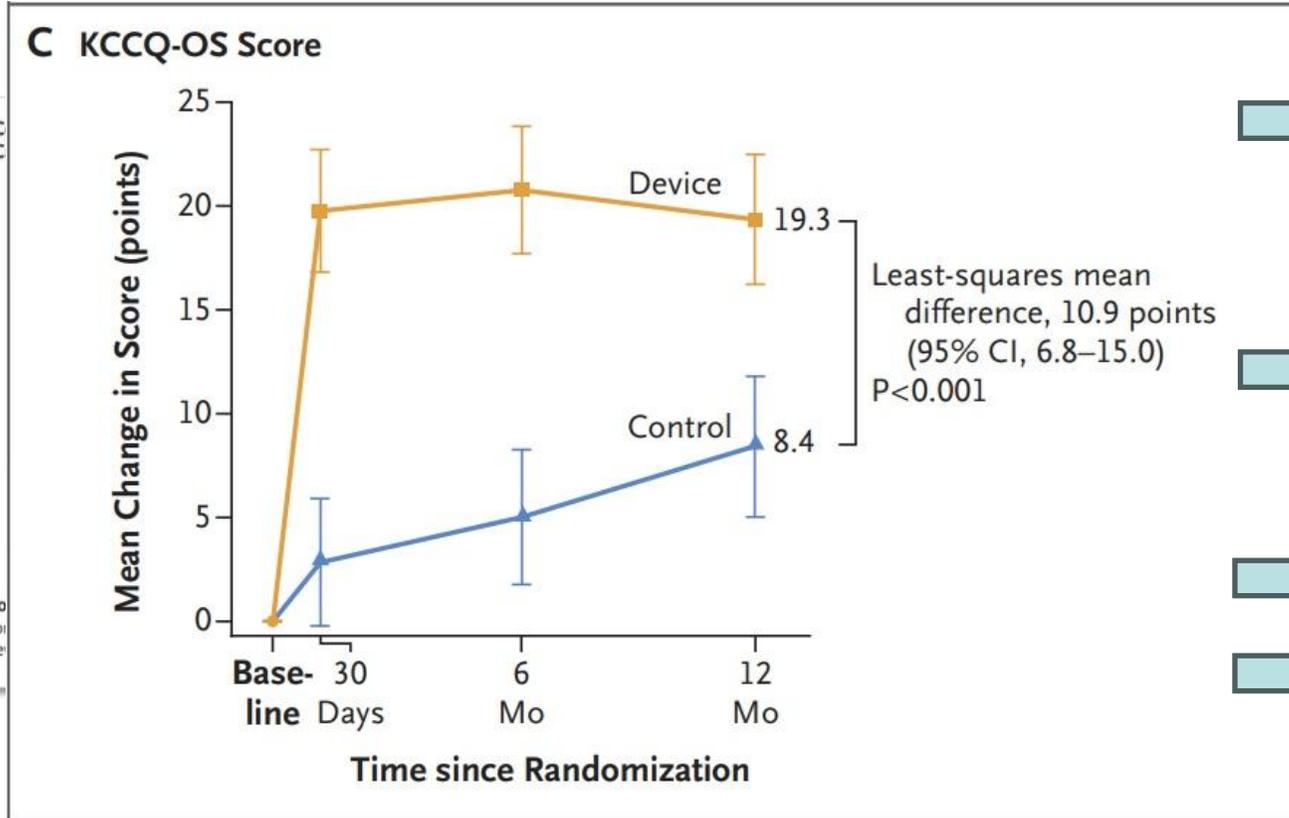
Statistics:

- **Primary EPs:**
 - (i) Recurrent events of CV death & HHF
 - (ii) Recurrent events of HHF
 - (iii) KCCQ (change BL to 12mo)
 - **Secondary EPs:**
 - 6MWT-distance (change BL-12mo) (Hochberg)
 - ACM (all available FU)
 - NYHA class I/II (24mo)
 - Recurrent hospitalization (any)
 - Grade 2+ or less MR (12mo)
- Alpha = 0.05**
Significance level controlled using Hochberg procedure

Table 1. Baseline Demographic and Clinical Characteristics of the Patients with Heart Failure and Moderate-to-Severe Functional Mitral Regurgitation.*

Characteristic	Device Group (N = 250)	Control Group (N = 255)
Age — yr	70.0±10.4	69.4±10.7
Male sex — no. (%)	195 (78.0)	211 (82.8)
Diabetes — no. (%)	91 (36.4)	85 (33.3)
Hypertension — no. (%)	141 (56.4)	127 (49.8)
Previous myocardial infarction — no. (%)	144 (57.6)	135 (52.9)
Previous PCI — no. (%)	118 (47.2)	125 (49.0)
Previous CABG — no. (%)	69 (27.6)	64 (25.1)
Previous stroke or TIA — no. (%)	29 (11.6)	30 (11.8)
Peripheral vascular disease — no. (%)	38 (15.2)	27 (10.6)
History of atrial fibrillation or flutter — no. (%)	118 (47.2)	125 (49.0)
Body-mass index†	27.0±4.3	26.7±4.3
Nonischemic cause of cardiomyopathy — no. (%)	88 (35.2)	88 (34.5)
NYHA functional class — no. (%)		
II	59 (23.6)	65 (25.5)
III	150 (60.0)	153 (60.0)
IV	41 (16.4)	36 (14.1)
Hospitalization for heart failure within previous year — no. (%)	165 (66.0)	168 (65.9)
Systolic blood pressure — mm Hg	112±16	113±16
Median NT-proBNP level (IQR) — pg/ml‡	2651 (1630–4918)	2816 (1306–5496)
Median BNP level (IQR) — pg/ml§	556 (312–1018)	406 (231–874)
Median 6-minute walk distance (IQR) — m	300 (220–382)	310 (200–378)
Estimated glomerular filtration rate — ml/min/1.72 cm ²	54.9±19.0	56.7±23.3
Median KCCQ-OS score (IQR) — points¶	42.2 (28.3–62.0)	44.3 (25.8–64.2)
Median left ventricular ejection fraction (IQR) — %	32 (26–37)	31 (25–37)
Median left ventricular end-diastolic volume (IQR) — ml	200 (153–249)	206 (158–250)
Severity of mitral regurgitation — no. (%)		
Grade 3+	141 (56.4)	141 (55.3)
Grade 4+	109 (43.6)	114 (44.7)
Median effective regurgitant orifice area (IQR) — cm ²	0.23 (0.20–0.30)	0.23 (0.19–0.29)
Median regurgitant volume (IQR) — ml	35.4 (28.9–43.9)	35.6 (28.2–42.5)

RESHAPE-HF2



Subgroup	Device no. of patients (annualized rate [no. of events/ total no. of patient-yr])	Control no. of patients (annualized rate [no. of events/ total no. of patient-yr])	Rate Ratio for Hospitalization for Heart Failure or Death from Cardiovascular Causes (95% CI)
Sex			
Male	195 (37.7 [120/318])	211 (58.2 [185/318])	0.66 (0.47–0.92)
Female	55 (34.4 [31/90])	44 (64.5 [40/62])	0.56 (0.30–1.03)
Age			
≥70 yr	140 (39.6 [90/227])	143 (64.7 [130/201])	0.63 (0.42–0.94)
<70 yr	110 (33.9 [61/180])	112 (53.1 [95/179])	0.64 (0.42–0.97)
Body-mass index			
≥30	52 (29.4 [25/85])	49 (59.2 [42/71])	0.49 (0.27–0.91)
<30	197 (39.4 [126/320])	203 (59.8 [183/306])	0.68 (0.48–0.94)
LVEF			
≥30%	151 (34.5 [82/249])	137 (44.5 [89/200])	0.79 (0.53–1.18)
<30%	99 (41.1 [65/158])	118 (75.6 [136/180])	0.55 (0.36–0.85)
Cause of heart failure			
Nonischemic	88 (39.0 [55/141])	88 (77.8 [98/126])	0.51 (0.33–0.79)
Ischemic	162 (36.1 [96/266])	167 (50.0 [127/254])	0.74 (0.50–1.09)
Estimated GFR			
≥50 ml/min/1.73 m ²	143 (30.7 [73/238])	149 (43.5 [104/239])	0.72 (0.45–1.13)
<50 ml/min/1.73 m ²	103 (44.8 [74/165])	103 (88.2 [120/136])	0.52 (0.36–0.75)
BNP or NT-proBNP			
≥Median	124 (49.5 [98/198])	121 (76.4 [123/161])	0.68 (0.47–0.99)
<Median	122 (25.6 [52/203])	129 (46.2 [97/210])	0.54 (0.34–0.87)
Previous cardiac-resynchronization			
Yes	77 (34.1 [43/126])	68 (72.9 [70/96])	0.49 (0.31–0.77)
No	172 (38.4 [108/281])	187 (54.6 [155/284])	0.71 (0.50–1.03)
Severity of mitral regurgitation			
Severe, grade 4+	109 (35.7 [61/171])	114 (75.2 [118/157])	0.48 (0.32–0.72)
Moderate to severe, grade 3+	141 (38.1 [90/236])	141 (48.0 [107/223])	0.81 (0.54–1.23)
NYHA functional class			
III or IV	191 (37.9 [121/319])	189 (70.3 [185/263])	0.56 (0.41–0.76)
I or II	59 (34.1 [30/88])	65 (34.8 [40/115])	0.91 (0.42–1.98)
Left ventricular end-diastolic volume			
High, >227 ml	80 (37.0 [50/135])	88 (74.8 [98/131])	0.49 (0.30–0.80)
Medium, >170 to 227 ml	83 (46.0 [63/137])	85 (63.1 [77/122])	0.78 (0.48–1.25)
Low, ≤170 ml	87 (28.1 [38/135])	82 (39.4 [50/127])	0.70 (0.40–1.23)
Effective regurgitant orifice area			
High, >0.27 cm ²	84 (42.3 [58/137])	75 (89.0 [89/100])	0.51 (0.32–0.82)
Medium, >0.21 to 0.27 cm ²	75 (40.2 [47/117])	84 (47.3 [61/129])	0.81 (0.46–1.44)
Low, ≤0.21 cm ²	76 (30.2 [39/129])	84 (47.4 [64/135])	0.66 (0.39–1.12)
Hospitalization for heart failure within 12 mo before randomization			
Yes	165 (36.7 [99/270])	168 (71.0 [179/252])	0.53 (0.37–0.75)
No	85 (38.0 [52/137])	87 (35.9 [46/128])	1.05 (0.62–1.79)



RESHAPE-HF2

Primární a sekundární cíle

Table 2. Primary and Secondary End Points.*

End Point	Device Group (N=250)	Control Group (N=255)	Difference (95% CI) [†]	P Value [‡]
Primary End Points[§]				
Rate of the composite of first or recurrent hospitalization for heart failure or death from cardiovascular causes during 24 mo per 100 patient-yr (no. of events/total no. of patient-yr)	37.0 (151/408.6)	58.9 (225/381.9)	0.64 (0.48–0.85)	0.002 [¶]
Rate of first or recurrent hospitalization for heart failure during 24 mo per 100 patient-yr (no. of events/total no. of patient-yr)	26.9 (110/408.6)	46.6 (178/381.9)	0.59 (0.42–0.82)	0.002 [¶]
Mean change from baseline to 12 mo in the KCCQ-OS score — points	21.6±26.9	8.0±24.5	10.9 (6.8–15.0)	<0.001 [¶]
Secondary end points				
Mitral regurgitation grade ≤2+ at 12 mo — no./total no. (%)	132/146 (90.4)	43/119 (36.1)**	21.3 (10.7–45.8) ^{††}	<0.001 [¶]
Mean change in 6-min walk distance from baseline to 12 mo — m	34.0±105.9	5.1±97.6	20.5 (0.3–40.7)	0.05 ^{‡‡}
Rate of death from any cause during the complete follow-up per 100 patient-yr (no. of events/total no. of patient-yr)	17.0 (142/836.7)	18.6 (142/765.2)	0.90 (0.71–1.13)	0.37 ^{‡‡}
Rate of recurrent hospitalization for any cause during 24 mo per 100 patient-yr (no. of events/total no. of patient-yr)	48.7 (199/408.6)	61.0 (233/381.9)	0.82 (0.63–1.07)	0.15 ^{‡‡}
NYHA functional class I or II heart failure at 12 mo — no./total no. (%) ^{§§}	140/188 (74.5)	96/164 (58.5)	2.35 (1.48–3.77) ^{††}	<0.001 [¶]

Nežádoucí příhody během 24 měsíců

Table 3. Adverse Events of Interest during 24 Months in the Intention-to-Treat Population.*

Event	Device Group (N=250)	Control Group (N=255)	Hazard or Rate Ratio (95% CI) [†]	P Value
<i>no. of patients with event (estimate of event rate)</i>				
Death from any cause [‡]	51 (22.3)	67 (29.6)	0.73 (0.51–1.05)	0.09
Death from cardiovascular causes [§]	41 (17.8)	47 (20.4)	0.84 (0.55–1.28)	0.43
Death from noncardiovascular causes [§]	10 (4.5)	20 (9.3)	0.46 (0.22–0.99)	0.04
Unplanned MitraClip implantation [¶]	8 (2.0)	25 (6.5)	0.32 (0.14–0.70)	0.004
All unplanned transcatheter mitral-valve repair [¶]	8 (2.0)	38 (10.0)**	0.21 (0.10–0.44)	<0.001
Mitral-valve surgery ^{††}	1 (0.004)	2 (0.008)	0.51 (0.05–5.58)	0.57
PCI [§]	6 (0.026)	8 (0.034)	0.74 (0.26–2.12)	0.57
CABG	0	0	—	—
Stroke [§]	5 (0.022)	2 (0.008)	2.5 (0.48–12.9)	0.25
Myocardial infarction [¶]	3 (0.007)	3 (0.008)	1.02 (0.14–7.52)	0.99
LVAD implantation ^{††}	1 (0.008)	2 (0.02)	0.5 (0.05–5.49)	0.56
Heart transplantation	1	0	—	—
Implantation of ICD or CRT-D [§]	7 (1.8)	7 (1.7)	0.96 (0.35–2.66)	0.93

Souhrn

- M-TEER pomocí systému MitraClip je efektivní u pacientů se symptomatickou sekundární mitrální regurgitace ve srovnání s optimální medikamentózní léčbou
- V dnešní době je jednoznačně prokázán jeho efekt na redukci hospitalizací a zlepšení symptomů
- Doposud doporučovaná tzv. „COAPT kritéria“ budou potřebovat určitou korekci (velikost MiR dle ERO, dilatace a dysfunkce LK)
- K jednoznačnému určení pozice M-TEER v léčbě mitrální regurgitace budou potřeba ještě další studie



DĚKUJI ZA POZORNOST!

Kontakt: david.zemanek@vfn.cz



II. Interní klinika kardiologie a angiologie VFN a 1. LF UK
U nemocnice 2
128 00 Praha
Tel: + 420 224962634

