Novinky v léčbě arytmií

Dan Wichterle

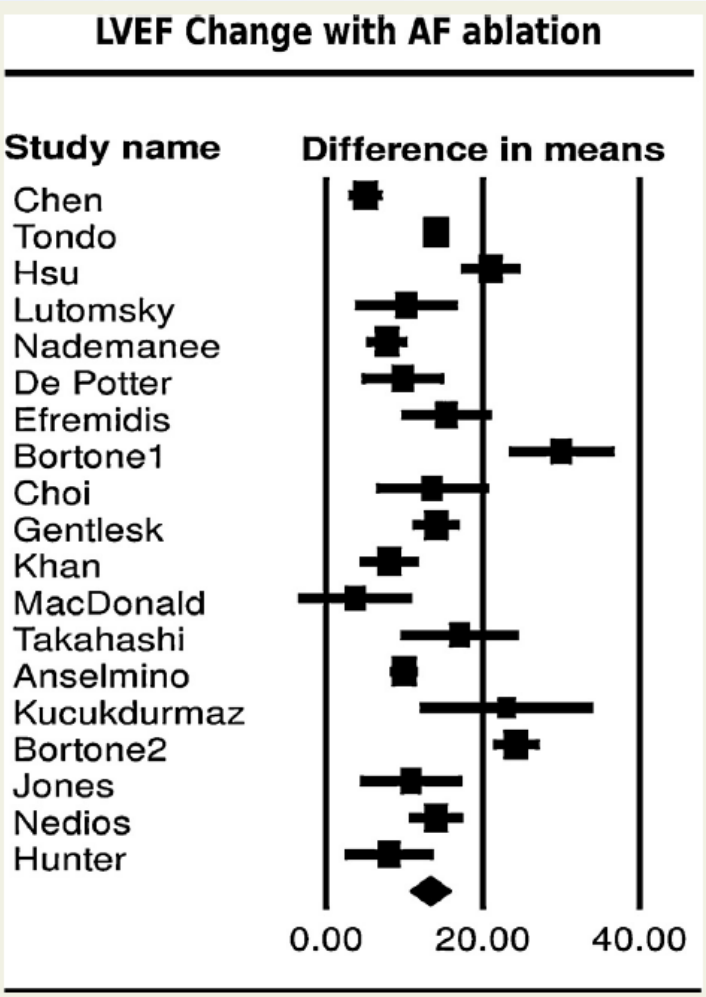
Klinika kardiologie IKEM, Praha

INSTITUT KLINICKÉ A EXPERIMENTÁLNÍ MEDICÍNY
KLINIKA KARDIOLOGIE
IK+E M

Ablační léčba
fibrilace síní
u pacientů se srdečním selháním

INSTITUT KLINICKÉ A EXPERIMENTÁLNÍ MEDICÍNY
KLINIKA KARDIOLOGIE
IKEM

Metaanalýza všech studií (N = 19)



Celkem 914 pacientů

Úspěch jedné procedury:
56.5% (95% CI: 48 - 64%)

Celkový úspěch včetně AAD:
81.8% (95% CI: 75 - 87%)

Vzestup EF LK:
13.3% (95% CI: 11 - 16%)

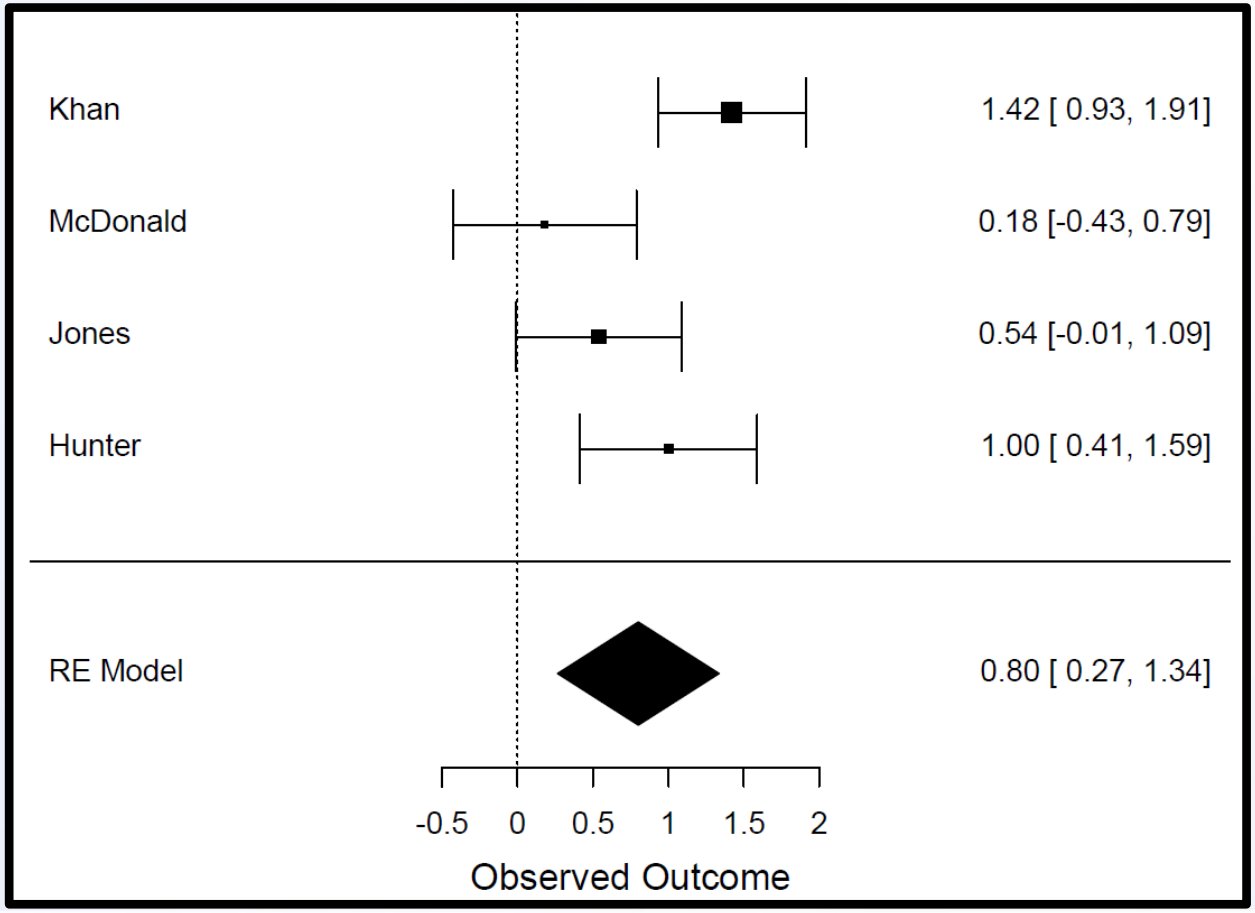
Ganesan et al. Heart Lung Circ 2015;24:270-280

Randomizované studie (N = 4)

Studie	Acronym	Kontrolní léčba	Počet pacientů	Follow up	Změna EFLK po ablaci	Změna EFLK u kontrol	P
Khan 2008	PABA-CHF	CRT RFA AVJ	41+40	6	**8 ± 8**	-1 ± 4	<0.001
McDonald 2011	-	AAD rate control	22+19	6	**4.5 ± 11.1**	2.8 ± 6.7	0.60
Jones 2013	ARC-HF	AAD rate control	26+26	12	**10.9 ± 11.5**	5.4 ± 8.5	0.055
Hunter 2014	CAMTAF	AAD rate control	26+24	6	**8.1 ± 13.0**	-3.6 ± 10.2	<0.001

Meta-analýza randomizovaných studií

standardizovaný efekt na EF LK



AATAC (multicentrická randomizovaná studie)

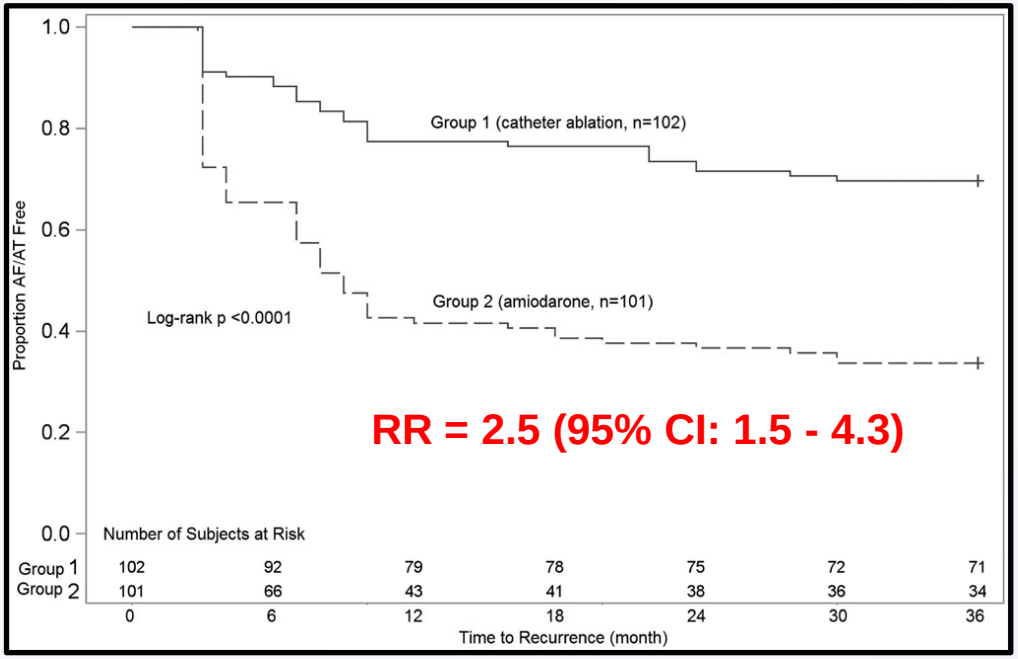
Populace
- Perzistující FS
- NYHA II-III
- EF LK <40%
- Impl. ICD / CRT-D

Randomizace 1:1
- Kontrola rytmu - ablace
- Kontrola rytmu - amiodaron

Zařazeno: 102+101 pacientů

Follow up: min. 2 roky

Primární endpoint:
Rekurence FS
Sekundární endpointy:
… změna EF LK ….



	Ablace	Amiodaron	P
Změna EF LK	+8.3 %	+5.0 %	0.02

Di Biase et al. Circulation 2016;133:1637-1644

CAMERA-MRI (multicentrická randomizovaná studie)

Populace:
- Perzistující FS … 73% >1 rok
- NYHA ≥ II
- EFLK ≤ 45% (MRI)
- LGE 36%
- Vyloučena ICHS
- Vyloučena valvulopatie

Randomizace 1:1
- Kontrola rytmu - ablace
- Kontrola frekvence - léky

Zařazeno: 33 + 33 pacientů

Follow up: 6 měsíců

Primární endpoint: Změna EF LK (MRI)

Ablační větev

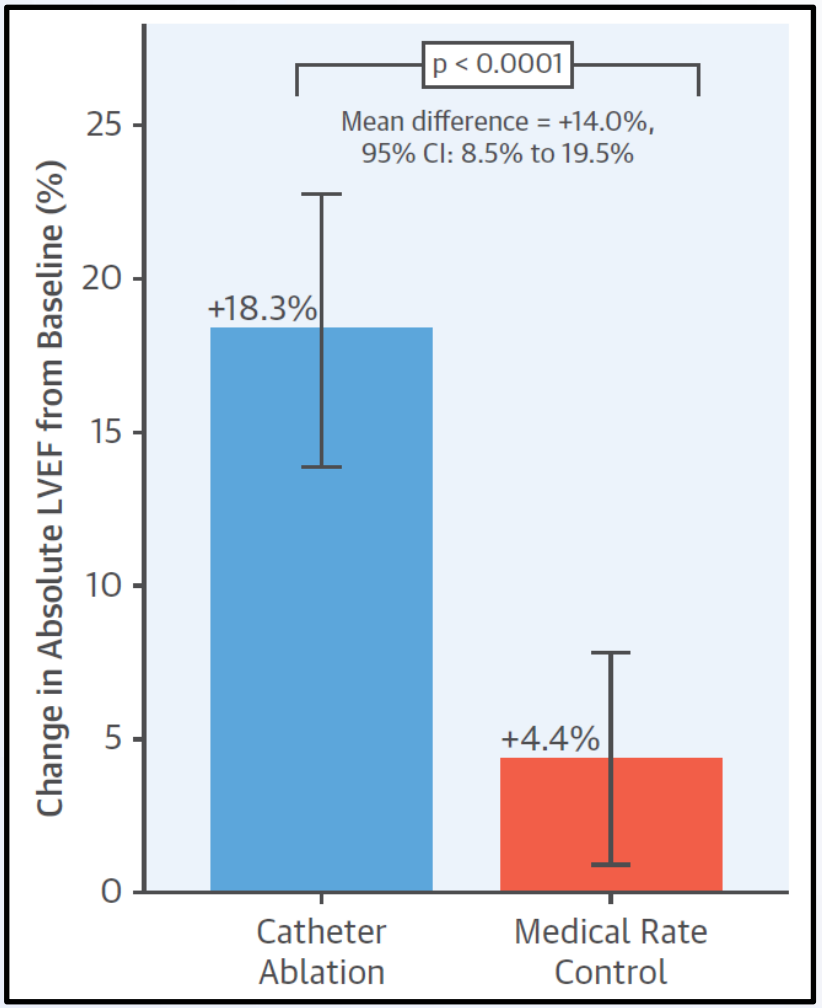
IPŽ + box
AF-free off AADs: 56%
AF-free on AADs: 75%
AF-burden (ILR): 1.6 ± 5%

Léková větev

Vstupní SF: 85 ± 17/min
Cílová SF <100/min
Výsledná SF 80 ± 10/min
(P = 0.10 pro pokles)

Prabhu et al. JACC 2017;70:1949-63

CAMERA-MRI

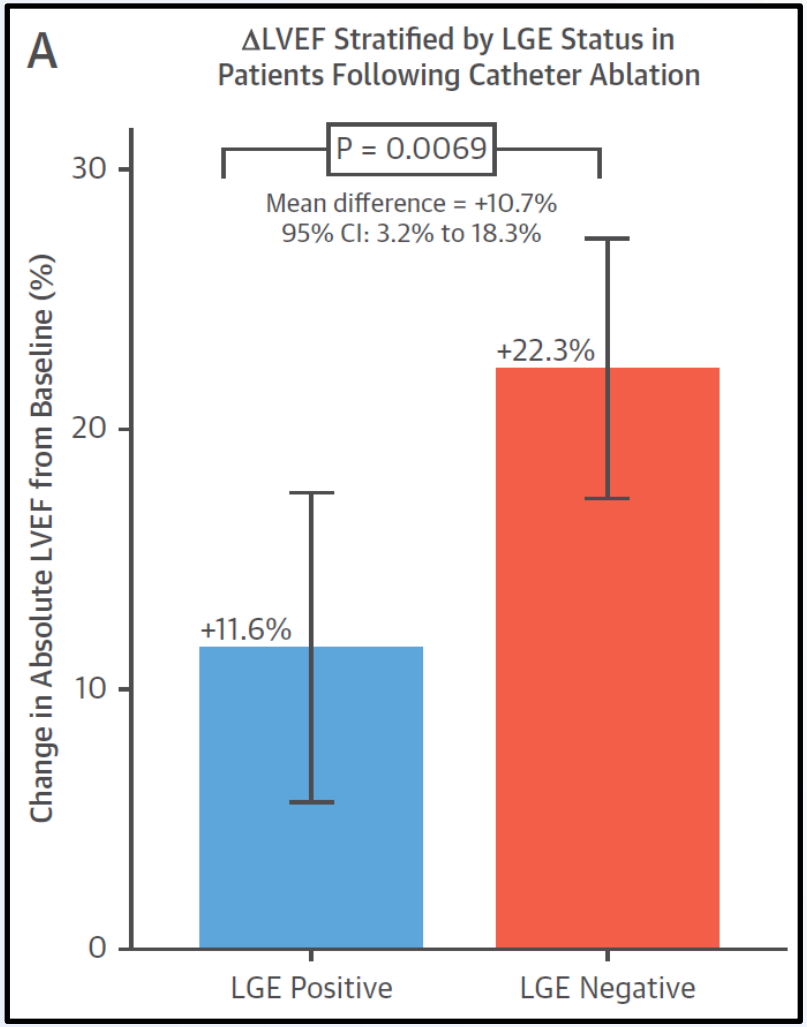


Normalizace EF LK (>50%)
58% vs. 9%

Těžká dysfunkce (EF LK <35%)
9% vs. 36%

Prabhu et al. JACC 2017;70:1949-63

CAMERA-MRI



Normalizace EF LK (>50%)
73% vs. 21%

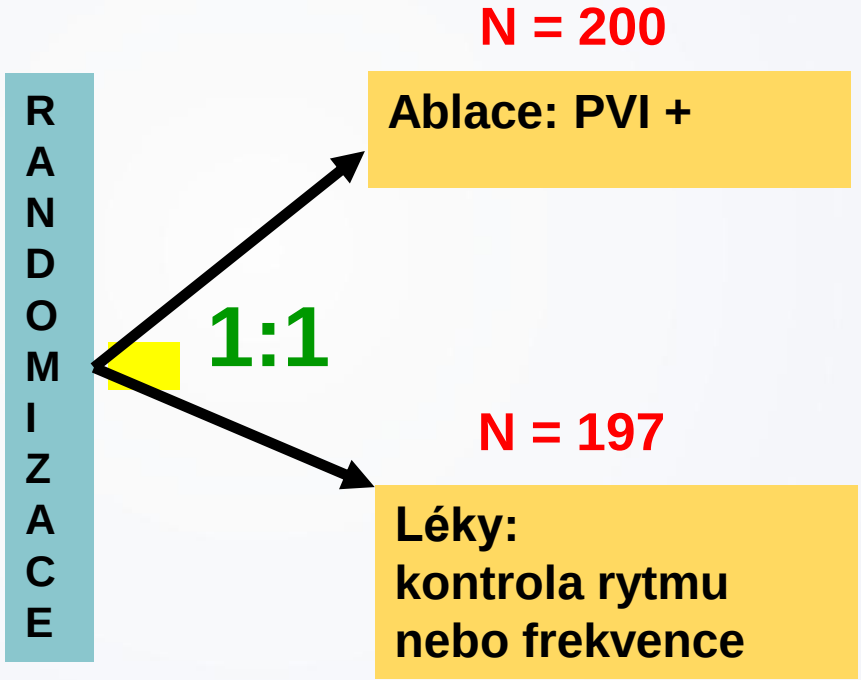
Těžká dysfunkce (EF LK <35%):
0% vs 21%

Absence LGE
jediný multivariační prediktor normalizace LVEF

Prabhu et al. JACC 2017;70:1949-63

CASTLE-AF design

Paroxysmální nebo perzistující FS
&
- EF LK ≤ 35%
- NYHA ≥ II
- ICD / CRT-D



POROVNÁNÍ

- Celková mortalita
- Hospitalizace pro srdeční selhání

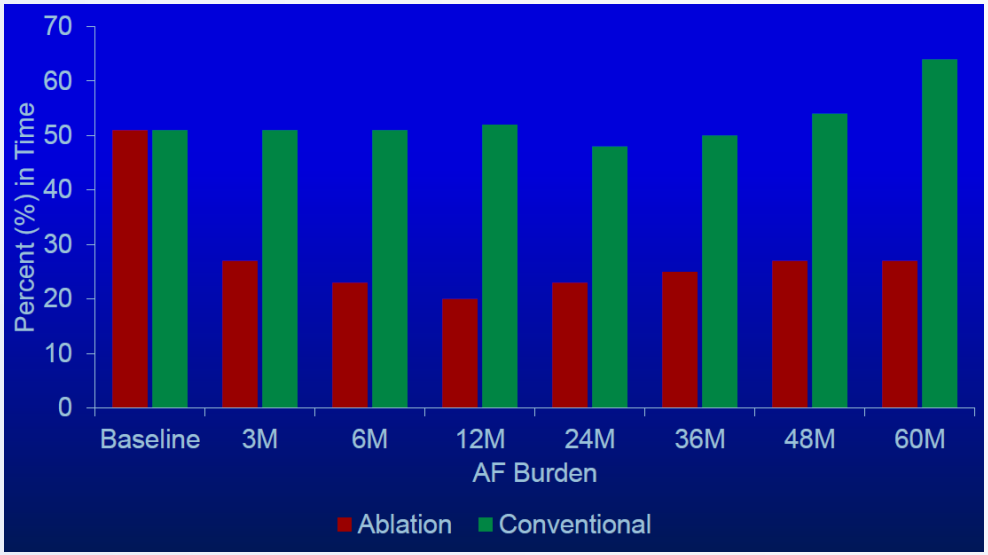
} **Primární kompozitní endpoint**

- EF LK
- … a mnoho dalších

Marrouche NF et al.
NEJM 2018; 378: 417-27

CASTLE-AF

Arytmická zátěž



Změna EF LK

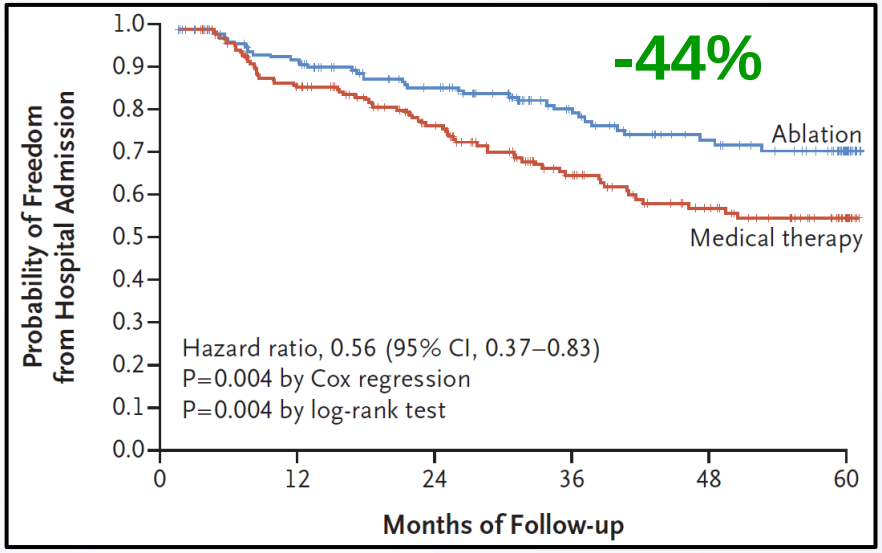
Skupina	Změna EF LK (%)	95% CI
Ablace	**8.0**	2.2 - 19.1
Léky	**0.2**	-3.0 - 16.1

P = 0.005

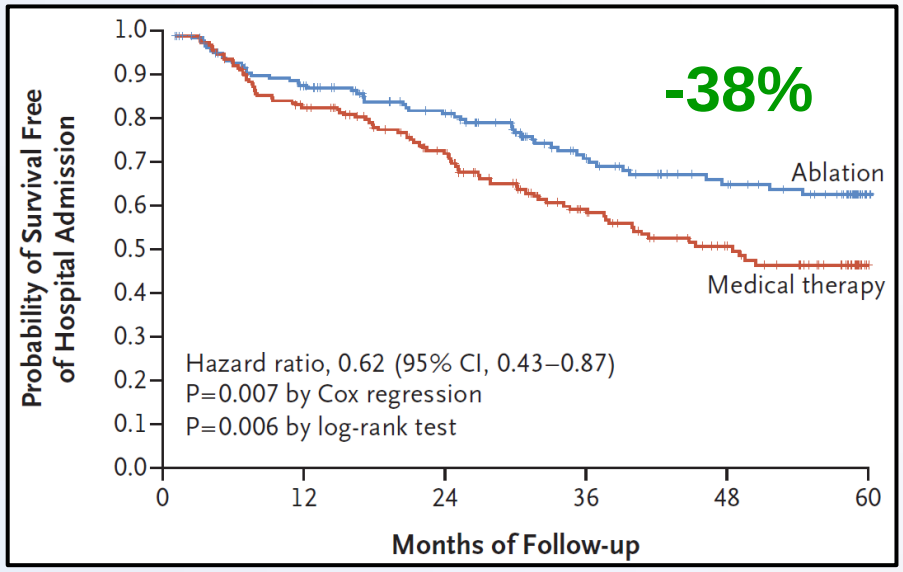
Marrouche NF et al.
NEJM 2018; 378: 417-27

CASTLE-AF

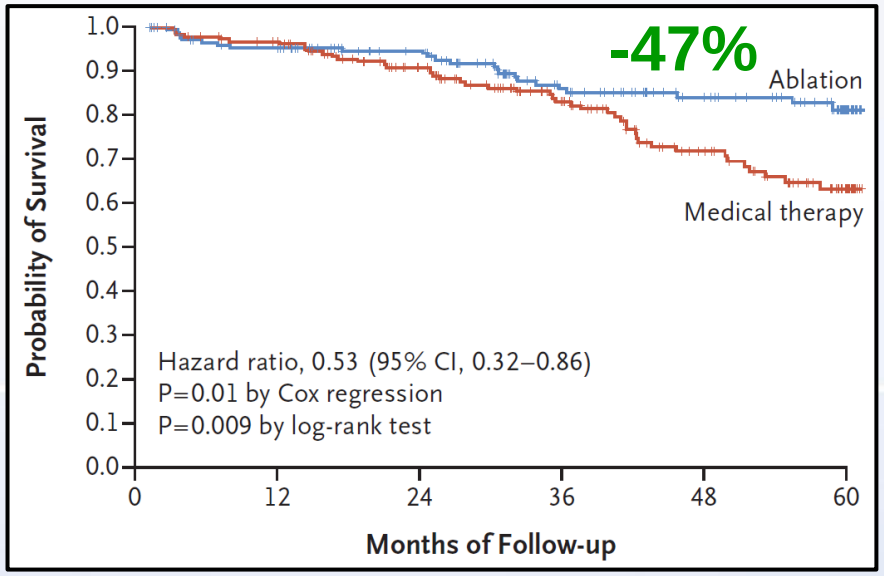
Hospitalizace pro srdeční selhání



Kompozitní primární endpoint



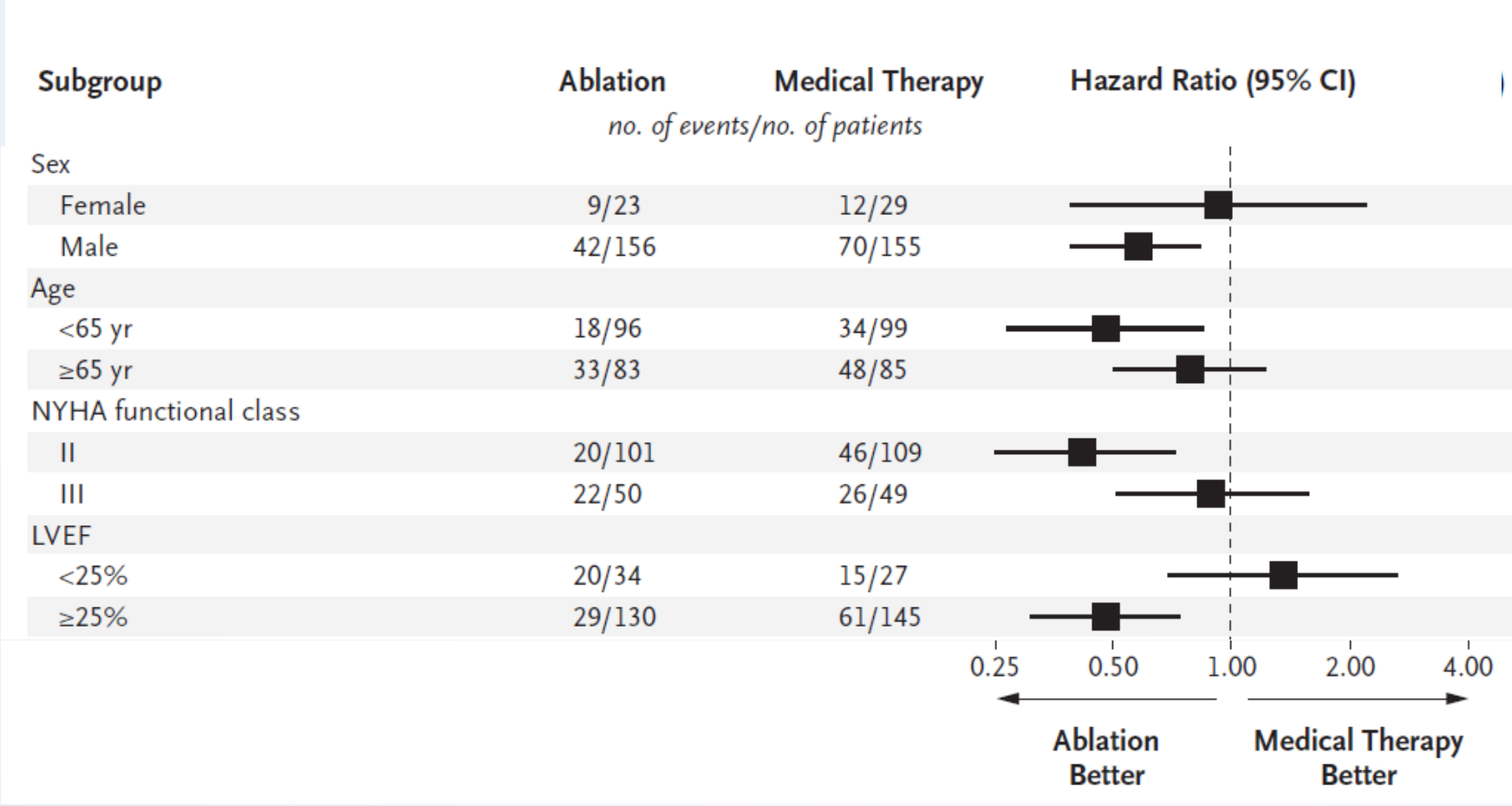
Celková mortalita



Marrouche NF et al.
NEJM 2018; 378: 417-27

CASTLE-AF

Podskupinové analýzy



Marrouche NF et al.
NEJM 2018; 378: 417-27

CABANA design

Nově zachycená nebo nedostatečně léčená FS jakéhokoli typu
&
alespoň jeden faktor CHA_2DS_2

- Srdeční selhání
- Hypertenze s HLK
- Věk >65 let
- Diabetes
- CMP /TIA
- LAd >50mm nebo LAVi >40 ml/m^2

RANDOMIZACE **1:1**

N = 1108

Ablace: PVI +

N = 1096

Léky: kontrola rytmu nebo frekvence

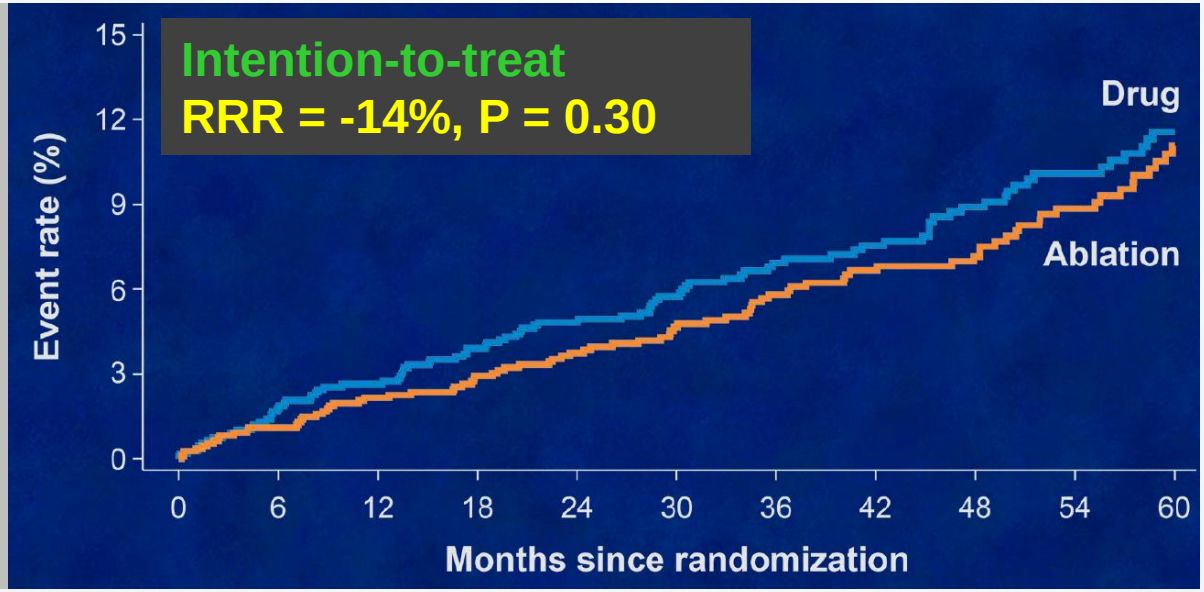
POROVNÁNÍ	• Klinické endpointy včetně komplikací léčby • Výskyt arytmií • Symptomy • Kvalita života

Packer DL et al.
American Heart Journal 2018; 199: 192-9

CABANA – primary endpoint

Composite endpoint

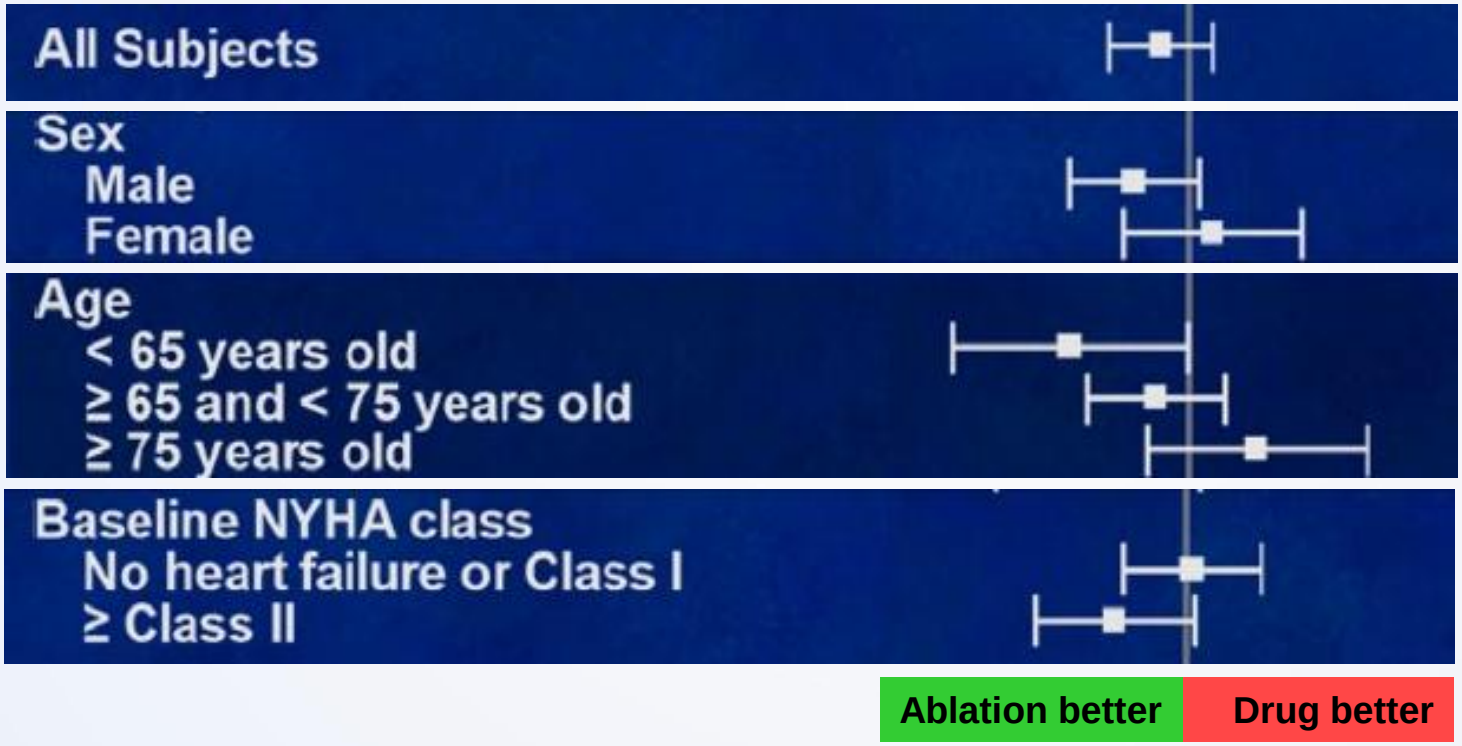
- **death**
- **disabling stroke**
- **serious bleeding**
- **cardiac arrest**



Packer DL et al.
HRS Congress, 9-12 May 2018

CABANA

Podskupinové analýzy

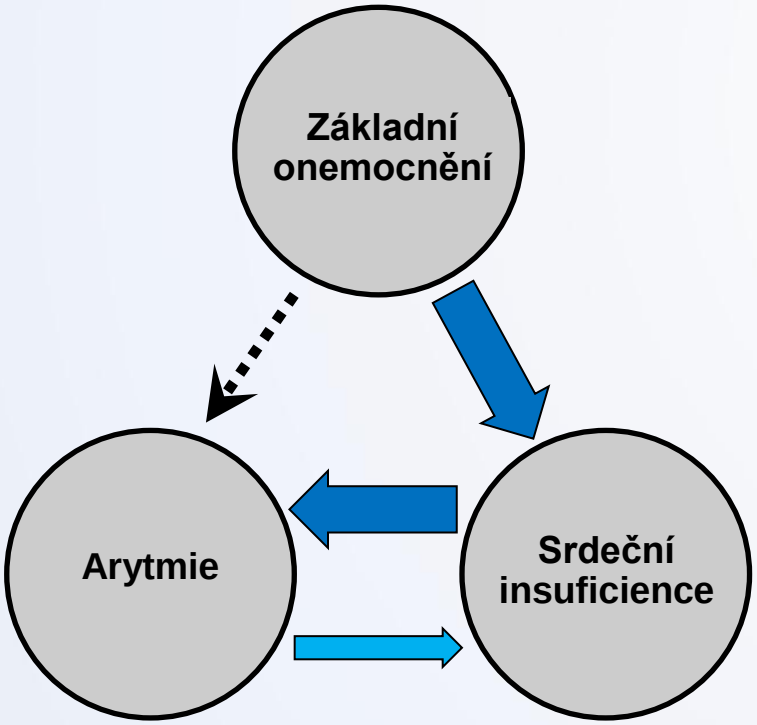


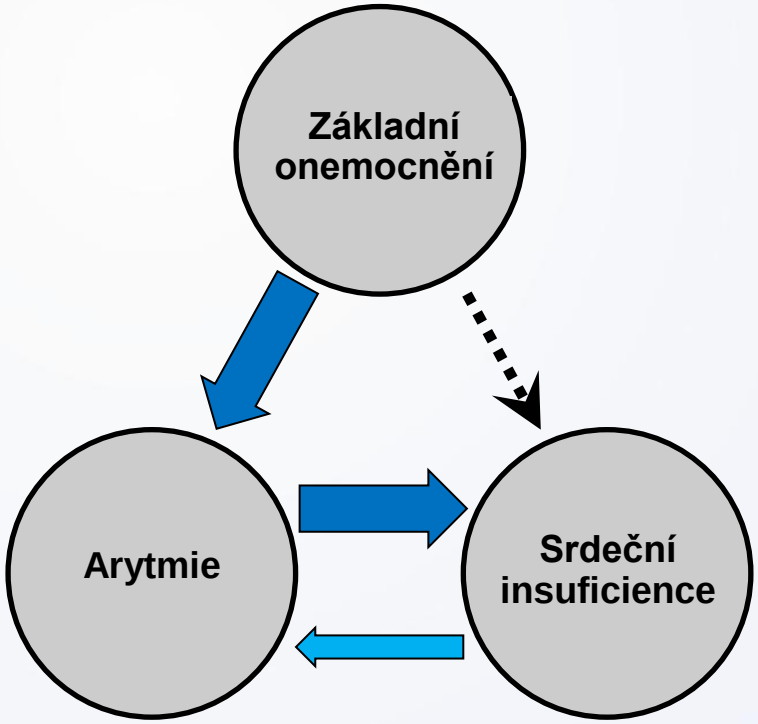
Packer DL et al.
HRS Congress, 9-12 May 2018

Závěry

- **Selektovaní pacienti se srdečním selháním mají signifikantní „mortalitní“ benefit z katetrizační ablace fibrilace síní.**

- **Výběr vhodných kandidátů:**
  - Muži
  - Věk < 65-70 let
  - EF LK ≥ 25%
  - NYHA II
  - **Suspektní arytmií-indukovaná KMP**
    - Dynamická korelace mezi přítomností arytmie a aktuální systolickou funkcí levé komory
    - Nepříliš dilatovaná levá komora
    - Žádné nebo nevýrazné jizvení myokardu


Základní onemocnění
Arytmie
Srdeční insuficience


Základní onemocnění
Arytmie
Srdeční insuficience

Pulmonary Artery Denervation to Treat Pulmonary Arterial Hypertension

The Single-Center, Prospective, First-in-Man PADN-1 Study (First-in-Man Pulmonary Artery Denervation for Treatment of Pulmonary Artery Hypertension)

Shao-Liang Chen, MD,*† Feng-Fu Zhang, MD,* Jing Xu, MD,* Du-Jiang Xie, MD,* Ling Zhou, MD,* Thach Nguyen, MD,‡ Gregg W. Stone, MD§

Nanjing, China; Hobart, Indiana; and New York, New York

Hemodynamic, Functional, and Clinical Responses to Pulmonary Artery Denervation in Patients With Pulmonary Arterial Hypertension of Different Causes

Phase II Results From the Pulmonary Artery Denervation-1 Study

Shao-Liang Chen, MD; Hang Zhang, MD; Du-Jiang Xie, MD; Juan Zhang, MD; Ling Zhou, MD; Alexander M.K. Rothman, MD; Gregg W. Stone, MD

J Am Coll Cardiol 2013;62:1092–100

Circ Cardiovasc Interv. 2015;8:e002837

INSTITUT KLINICKÉ A EXPERIMENTÁLNÍ MEDICÍNY
KLINIKA KARDIOLOGIE

IKEM

Pulmonary Artery Denervation Significantly Increases 6-Min Walk Distance for Patients With Combined Pre- and Post-Capillary Pulmonary Hypertension Associated With Left Heart Failure

The PADN-5 Study

Hang Zhang, MD,[a,*] Juan Zhang, MD,[a,*] Mengxuan Chen, MD,[b,*] Du-Jiang Xie, MD,[c,*] Jing Kan, MBBS,[a] Wande Yu, MD,[c] Xiao-Bo Li, MD,[c] Tian Xu, MBBS,[c] Yue Gu, PHD,[a] Jianzeng Dong, MD,[d] Hong Gu, MD,[d] Yaling Han, MD,[e] Shao-Liang Chen, MD[a]

J Am Coll Cardiol Intv 2019;12:274–84

jaa
Just accepted article

EuroIntervention

Title: **Pulmonary Artery Denervation Using Catheter-based Ultrasonic Energy.**

Authors: Alexander Rothman, BMBCh, PhD; Michal Jonas, M.D; David Castel, M.D; Abraham Rami Tzafriri, PhD; Hannes Traxler, M.D; Dalit Shav, PhD; Martin Leon, M.D; Ori Ben-Yehuda, M.D; Lewis Rubin, M.D

Manuscript submission date: 14 November 2018

Revisions received: 19 March 2019

Accepted date: 03 May 2019

Online publication date: 07 May 2019

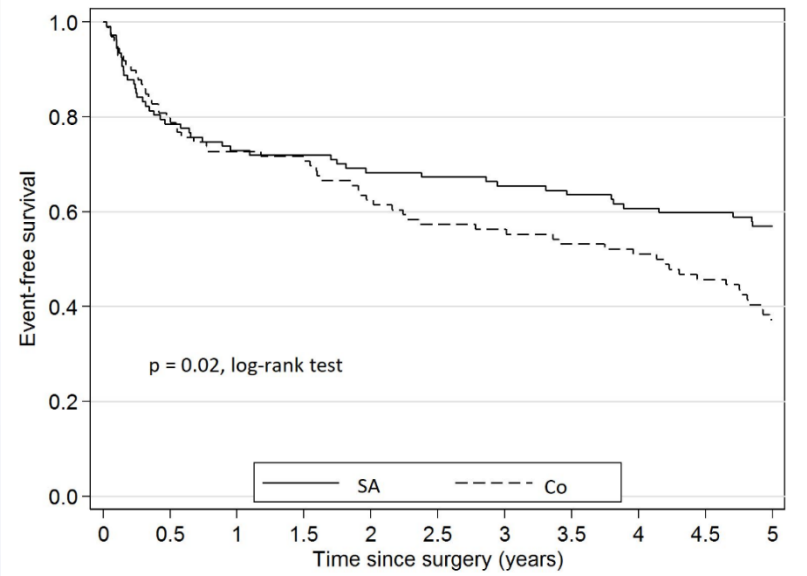
PRAGUE 12

Introduction: Previous randomized trials have shown the efficacy of the MAZE procedure in terms of maintaining sinus rhythm, but without an effect on clinical outcomes. However, most of these studies were small with short follow-ups, generally not exceeding 1 year. The aim of this study was to assess clinical outcomes of the MAZE procedure after 5 years of follow-up.

Methods: The PRAGUE-12 study was a prospective, randomized multicenter clinical trial assessing cardiac surgery with left atrial ablation for AF vs. cardiac surgery alone. Patients with AF who were also indicated for cardiac surgery (coronary artery disease (CAD), valve surgery) were enrolled and randomized to group SA (surgical ablation) or Co (control, no ablation). All patients were followed for 5 years. The primary endpoint was a composite of cardiovascular (CV) death, stroke, hospitalization for heart failure (HFH) or severe bleeding. Secondary endpoints included all parts of the primary endpoint and recurrence of AF.

Applications: Originally, 224 patients were enrolled, with 207 patients ultimately analyzed (group SA=108, group Co=99 patients). Both groups were similar relative to important clinical characteristics except for CAD, which was more common in the Co group (SA: 55 pts. (50.9%) vs. Co 64 pts.(64.6%), p<0.05). Kaplan-Meier survival curves showed a higher incidence of the primary endpoint in the Co group (p=0.02, Figure). However, in the Cox regression model and after adjusting for all covariables, the difference between groups was not significant (hazard ratio (HR) 0.69, [0.46-1.02], p=0.063). The incidence of CV death, bleeding or HFH was nonsignificantly reduced in the SA group. The incidence of stroke and AF recurrences were significantly reduced in the SA group, and remained significant even after adjustment for all covariables incl. CAD (stroke: HR 0.31, [0.12-0.92], p=0.019, AF recurrences: HR 0.44, [0.31-0.62], p<0.001).

Next Steps/Future: Concomitant SA of AF is associated with a greater likelihood of maintaining sinus rhythm and a decreased



INSTITUT KLINICKÉ A EXPERIMENTÁLNÍ MEDICÍNY
KLINIKA KARDIOLOGIE
IKEM