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PLÁNOVANIE ABLÁCIE AV UZLA U PACIENTOV S PERMANENTNOU FIBRILÁCIOU PREDSIENÍ PO IMPLANTÁCII CRT

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Úvod

U pacientov s CRT a permanentnou fibriláciou predsiení je otázne kedy indikovať a časovať abláciu AV uzla:

- Včasná ablácia AV uzla po implantácii CRT má zvýšené riziko dislokácie nedávno implantovaných elektród a tiež problémov s maturáciou elektród u dependentného pacienta.
- Stratégia najprv realizovať abláciu AV uzla a následne implantovať CRT prináša ďalšie riziká dočasnej kardiostimulácie.
- Odložená ablácia AV uzla po implantácii CRT môže znižovať potenciálny benefit CRT.

ANACONDA Trial

Atrioventricular Node Ablation – Early versus Delayed Timing in Patients with Cardiac Resynchronization Therapy and Permanent Atrial Fibrillation

Cieľ: Prospektívna randomizovaná štúdia pacientov (p) s permanentnou FP indikovaných na CRT s cieľom zistiť klinický efekt včasnej ablácie AV uzla oproti odloženej ablácii AV uzla.

inklúzne kritériá:

- úspešne implantovaný CRT systém
- u pacientov s permanentnou fibriláciou predsiení a srdcovou frekvenciou nad 80/min
- so súčasne prítomným srdcovým zlyhávaním so zvýšenými plazmatickými koncentráciami nátriuretických peptidov adjustovanými na vek*

Sledovanie 6 mes.

Primárne ciele: hospitalizácie pre SZ, klinická potreba ablácie AV uzla v ramene odloženej ablácie

Sekundárne ciele: podieľ BiV stimulácie, intervencie ICD, klinická trieda SZ, kvalita života, NTproBNP, ECHO odpoveď, celková mortalita

* Januzzi JL, van Kimmenade R, Laichbury J et al. NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients. Eur Heart J 2006;27:330-37.

Súbor a metodika

- 37p so srdcovým zlyhávaním (SZ)
- CRT-P 62%

- Priemerný vek v čase zaradenia do štúdie: 72.4 ± 6.6 rokov
- Muži: 73% (27p)
- Ischemická etiológia SZ: 24% (9p)
- Klinická trieda NYHA III: 59% (22p)
- Priemerná EFLK: $30 \pm 7\%$
- Priemerná šírka QRS: 129 ± 32 ms
- BĽTR: 35% (13p)

Randomizácia
-
v rámci
elektronického CRF

- včasná ablácia AV uzla- 18p (zrealizovaná počas iniciálnej hospitalizácie)
- odložená ablácia AV uzla - 19p (podľa klinickej potreby počas poimplantačného sledovania)
- Štatisticky základne parametre bez signifikantného rozdielu v ramenách
 - okrem etiológie- významne viac ischemickej etiológie SZ v ramene včasnej ablácie

	Arm	N (%)	P
Ischemic	EARLY (N=18)	7 (38.9%)	P<0.001
	DELAYED (N=19)	2 (10.5%)	
Non-ischemic	EARLY (N=18)	11 (61.1%)	
	DELAYED (N=19)	16 (84.2%)	
Valvular	EARLY (N=18)	0 (0.0%)	
	DELAYED (N=19)	1 (5.2%)	

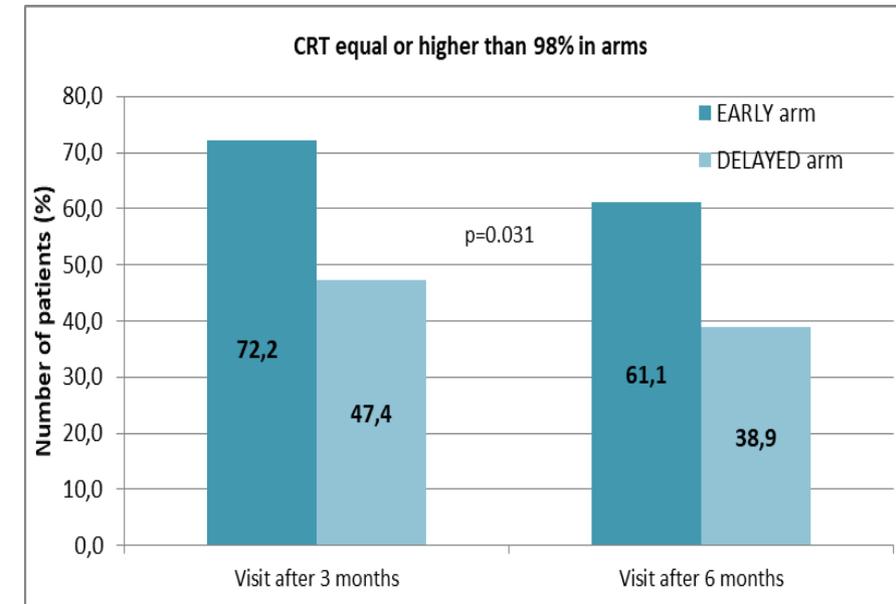
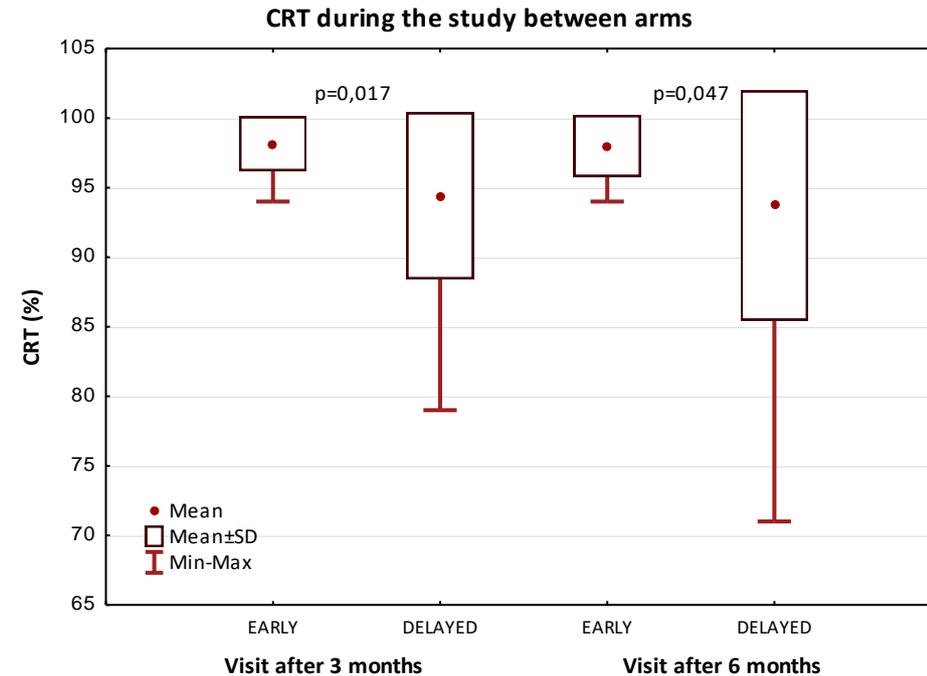
Výsledky:
Primárne ciele

V celom súbore:

- **Hospitalizácie pre dekompenzáciu SZ- 2 pacienti (5%)**
- bez rozdielu v ramenách
 - Celkovo hospitalizácie - 7p (19%)- spravidla elektívne hospitalizácie (RFA AVU v ramene odloženej ablácie, indikácia HTx, TAVI, MitraClip), 1 p rekurentná sepsa
- **47% (9/19p) v ramene odloženej ablácie malo indikovanú abláciu AV uzla** počas 6 mesiacov sledovania, výkon bol realizovaný väčšinou po ukončení štúdie.

Výsledky: Sekundárne ciele

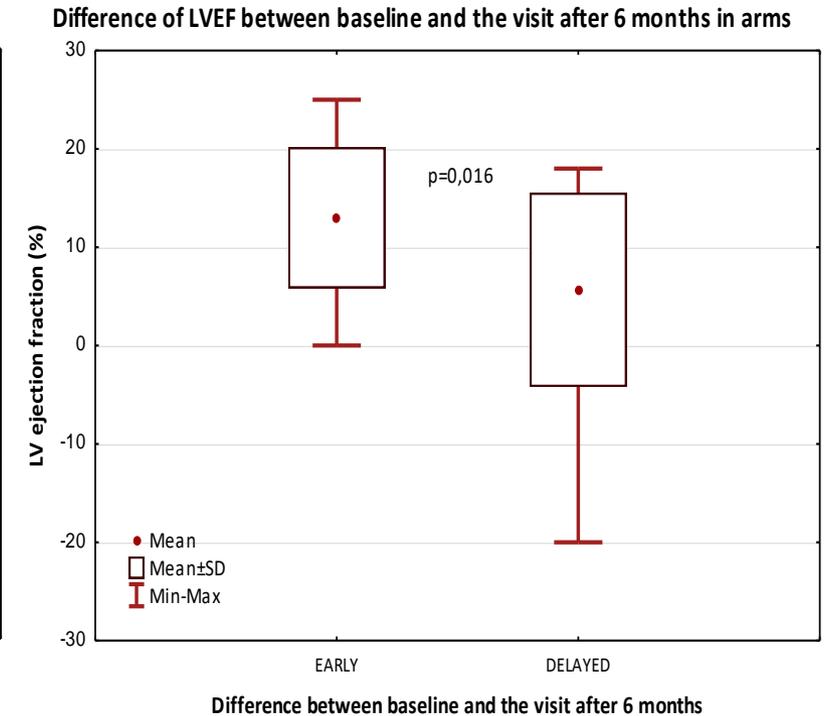
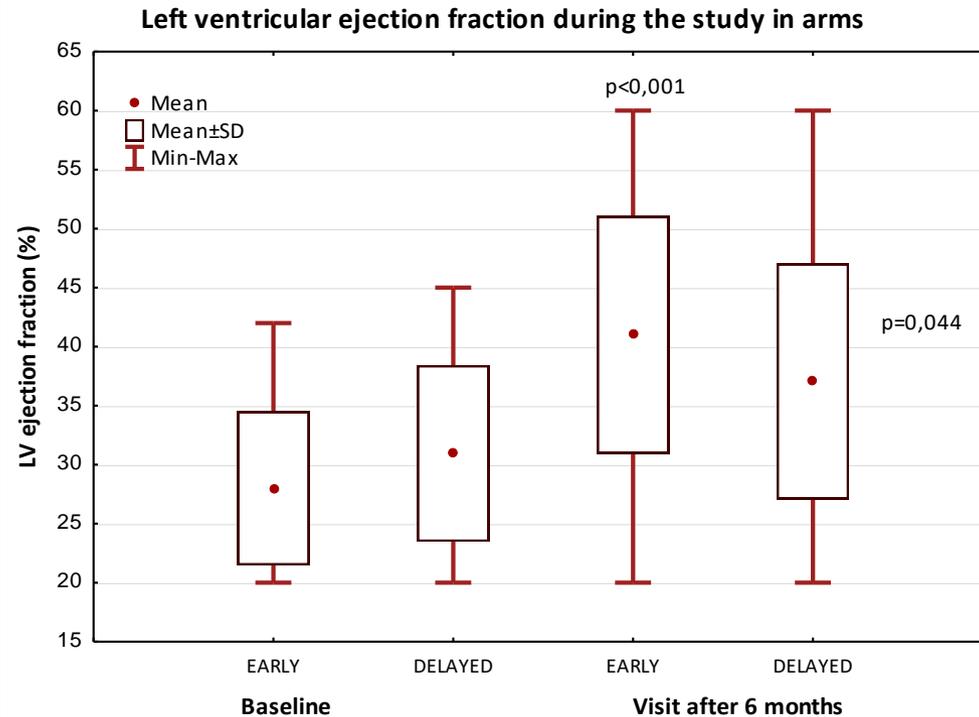
BiV stim



- Podiel biventrikulárnej stimulácie bol **signifikantne vyšší v ramene včasnej ablácie** (98% verus 94%, $p=0,017-0,047$)
- Podiel BiV stim $\geq 98\%$ významne vyšší v ramene včasnej ablácie ($p=0.031$)

Výsledky: Sekundárne ciele

EFLK



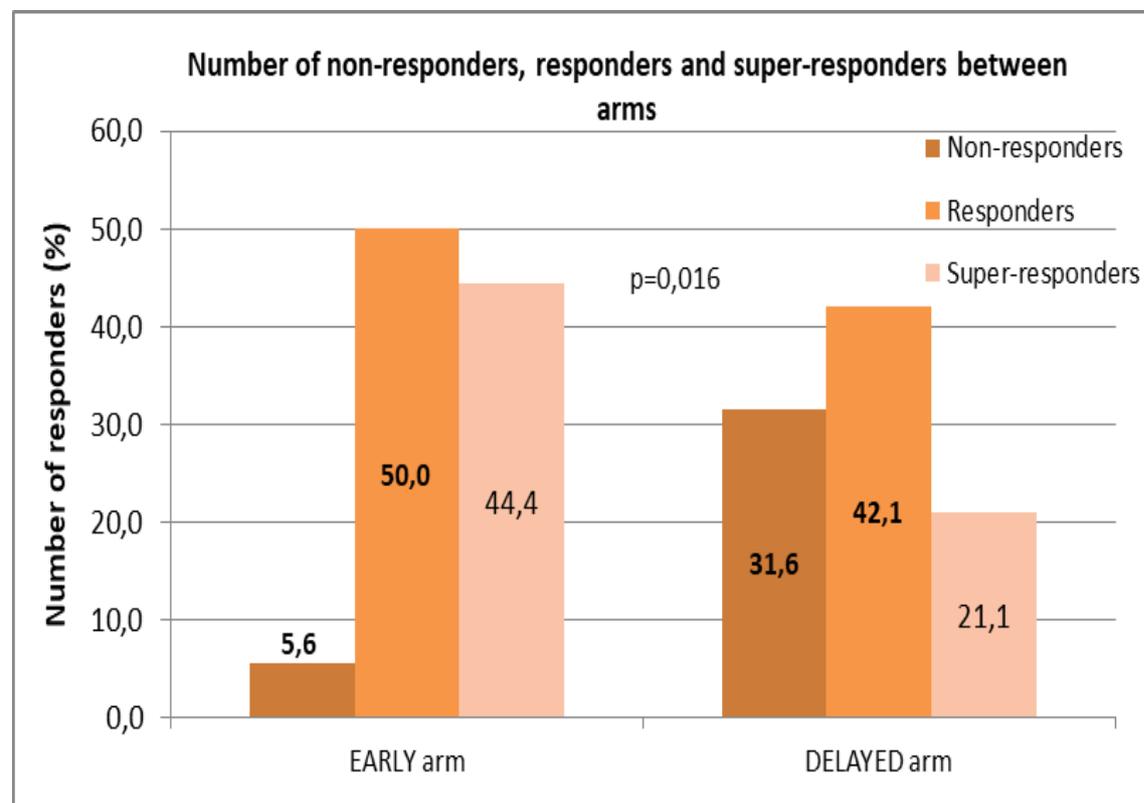
- V celom súbore významne stúpla EFLK (+9.5%, $p < 0,001$)
- Signifikantné zlepšenie EFLK v oboch ramenách
- **Signifikantne vyšší nárast EFLK v ramene včasnej ablácie oproti ramenu odloženej ablácie (13% verzus 5.7%, $p = 0.016$)**



Výsledky: Sekundárne ciele

ECHO responding

	EARLY AVN ablation (N=18)		DELAYED AVN ablation (N=19)	
	N (%)	Average change of LVEF	N (%)	Average change of LVEF
Non-responders (%)	1 (5.6%)	0.0%	6 (31.6%)	-6.3%
ECHO responders (%)	9 (50.0%)	8.6%	8 (42.1%)	8.5%
Super-responders (%)	8 (44.4%)	18.4%	4 (21.1%)	16.0%
Unclassified (%)	0 (0.0%)		1 (5.3%)	



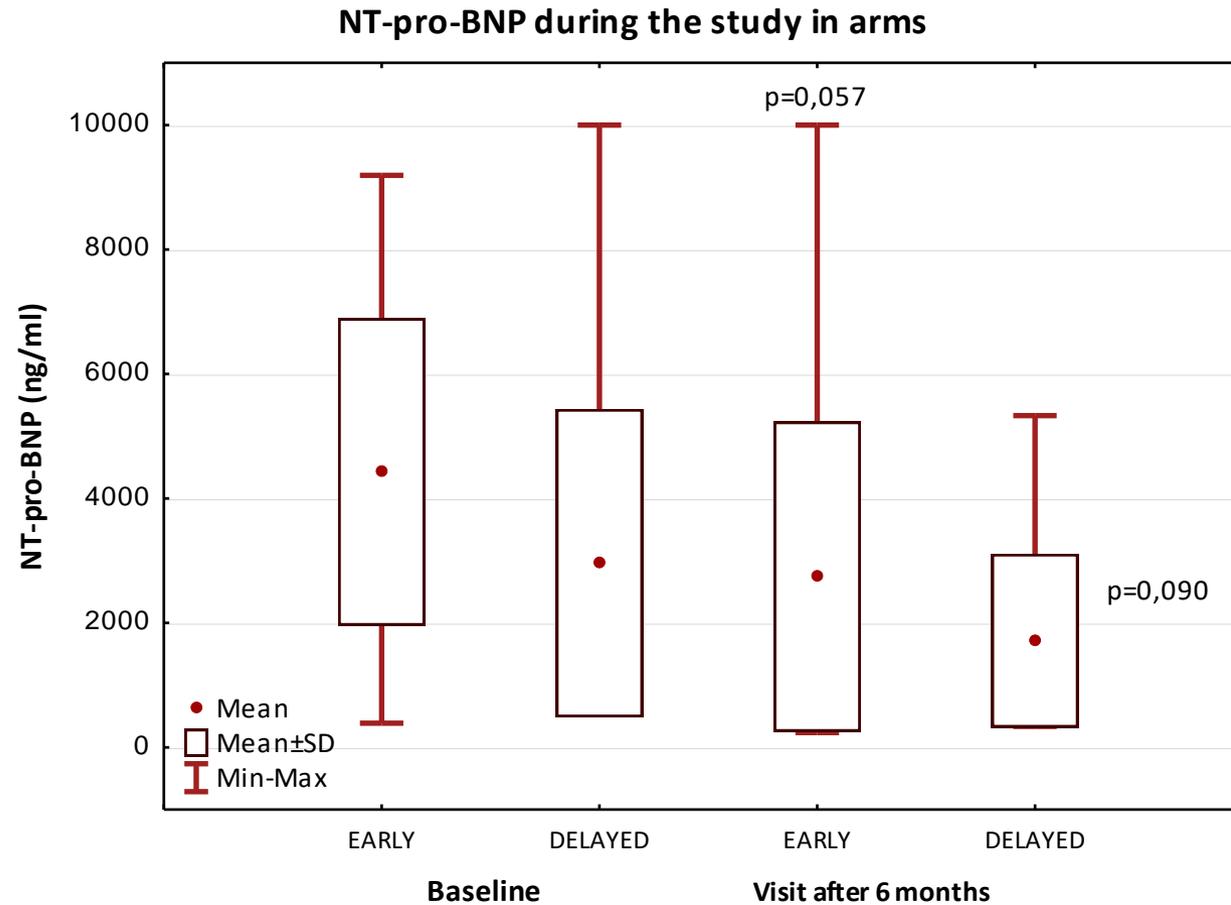
V celom súbore echo- non-respondéri:
7p (19%)

**ECHO responding bol signifikantne lepší
v ramene včasnej ablácie (p=0.016)**

- vyšší podiel echo- super-respondérov (44% verzus 21%),
- nižší podiel echo- non-respondérov (6% verzus 32%).

Výsledky:
Sekundárne ciele

NT pro BNP

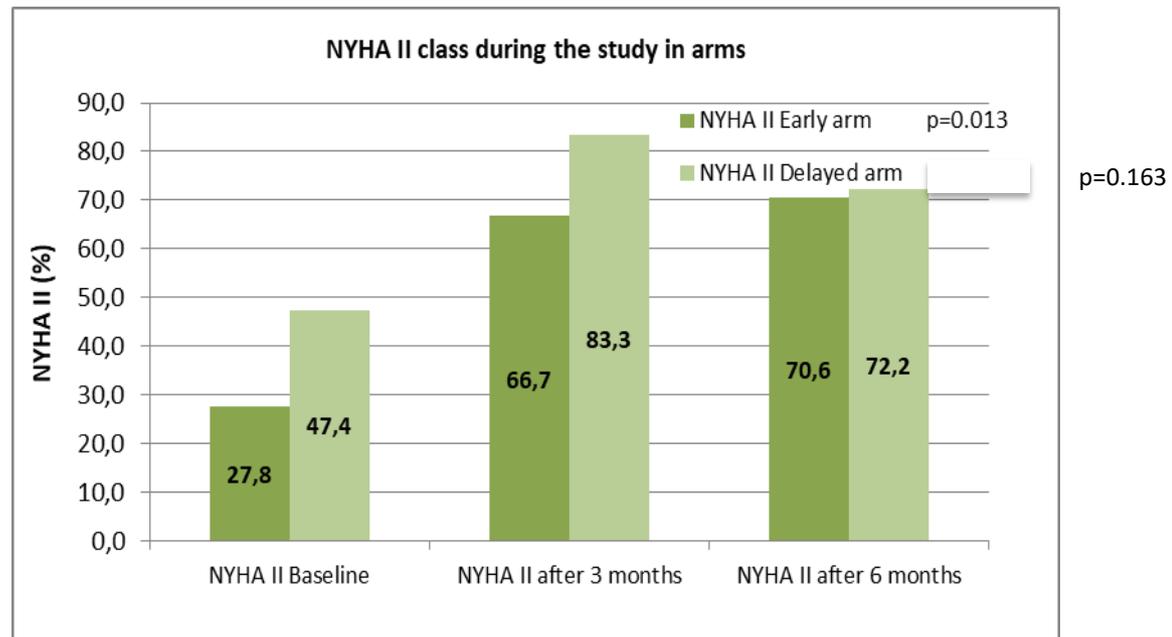


- V celom súbore sa významne znížilo sa NTproBNP (-40%, $p=0,011$)
- NT-pro-BNP kleslo v oboch ramenách (viac v ramene včasnej ablácie) - nesignifikantne

Výsledky:
Sekundárne ciele

NYHA

- V celom súbore sa signifikantne zlepšila klinická trieda SZ – nárast NYHA II ($p=0,002$)
- **Zlepšenie do NYHA II signifikantné ($p=0,013$) len v ramene včasnej AVN ablácie**

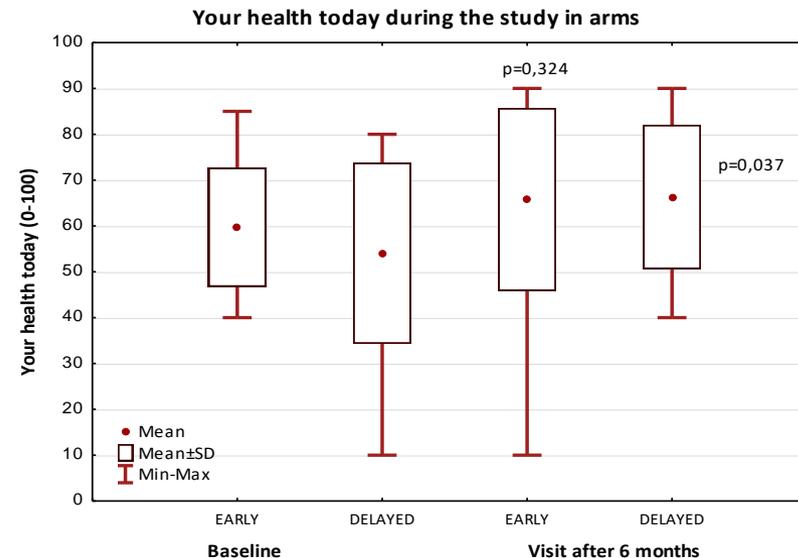
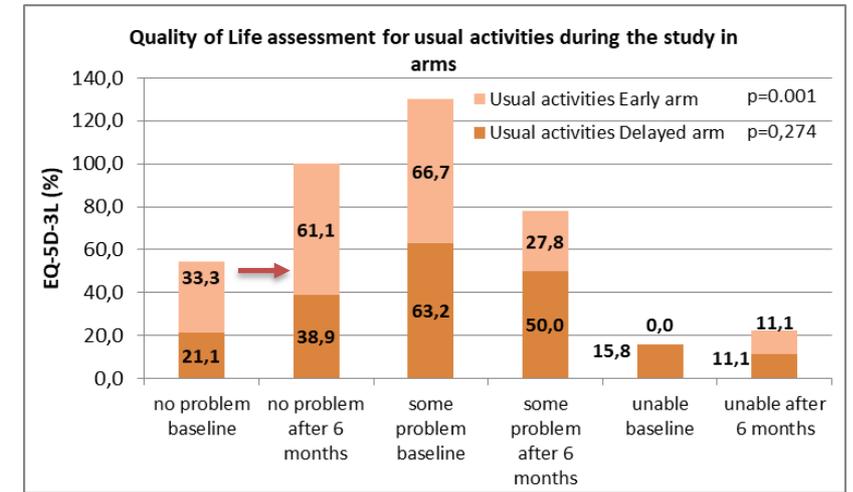
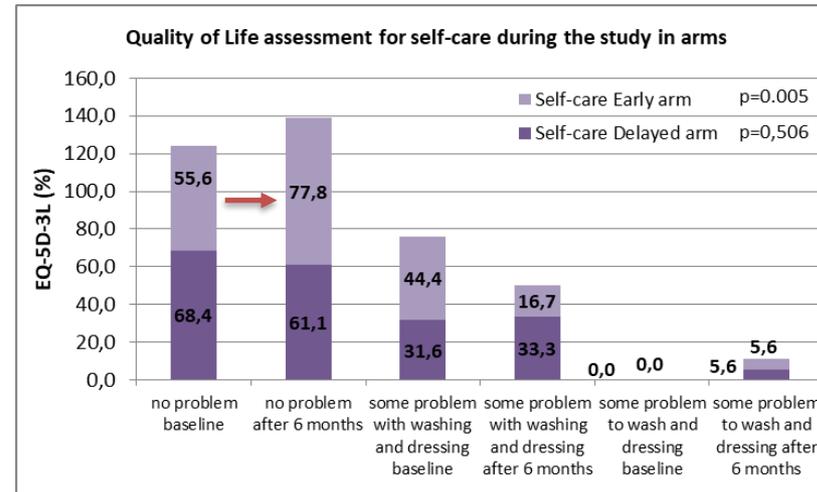


Zlepšenie kvality života (sebestačnosť, obvyklé činnosti) signifikantné len v ramene včasnej AVN ablácie

- Mobilita, bolesti/nepohoda, úzkosť/depresia bez štatisticky významnej zmeny

Výsledky:
Sekundárne ciele

Kvalita života
EQ-5D-3L



Len v ramene odloženej ablácie významné zlepšenie subjektívneho aktuálneho hodnotenia zdravia



Výsledky:
Sekundárne ciele

- **Mortalita 6- mesačná- 2p (5%)**
 - NKS u p s CRT-P v ramene odloženej ablácie
 - rekurentná sepsa u p s CRT-P v ramene včasnej ablácie (superresponder CRT)
- **Intervencie ICD- žiadne**
- **Komplikácie ablácie AVU:**
 - 1p- dislokácia elektródy pri včasnej ablácii
 - 1p- obnovenie vedenia AV uzlom po RFA AVU u pacient v ramene odloženej ablácie

- Odporúčanie pre CRT u pacientov so srdcovým zlyhávaním (SZ) a permanentnou AF má podstatne nižšiu dôkazovú silu ako u pac v sínusovom rytme.

Z literatúry:

CRT u pacientov s permanentnou fibriláciou predsiení

Vždy zvážiť indikáciu katérovej ablácie FP!:

Katérová ablácia FP - je odporúčaná u pac. s vysokou pravdepodobnosťou tachykardiou indukovanej KMP

- sa má zvážiť u selektovaných pacientov s FP a SZ s redukovanou EFLk

AF catheter ablation is recommended in patients with AF and HFrEF with high probability of tachycardia-induced cardiomyopathy to reverse left ventricular dysfunction.^{604,611}

I

B

AF catheter ablation should be considered in selected AF patients with HFrEF to reduce HF hospitalization and prolong survival.^{4,513,514,604,610,612}

IIa

B



European Journal of Heart Failure (2018) 20, 1039–1051
doi:10.1002/ejhf.1142

RESEARCH ARTICLE

CRT Survey II: a European Society of Cardiology survey of cardiac resynchronisation therapy in 11 088 patients—who is doing what to whom and how?

Kenneth Dickstein^{1,2*}, Camilla Normand^{1,2}, Angelo Auricchio³, Nigussie Bogale¹,

Patient characteristics

The median (IQR) age at implantation was 70 (62–76) years, 32% of patients were aged ≥ 75 years and 24% were women. Half of the patients had ischaemic heart disease, 41% had a prior history of AF of which 42% of these were permanent AF, 31% had diabetes mellitus, and 47% had a HF hospitalisation during the previous year (Table 3).



Výskyt perm AF pri implantácii CRT bol 17%

Table 3 Patient demographics (n = 11 088)

Age (years), median (IQR)	70 (62–76)
Age ≥ 75 years	32% (3536/11 039)
Female gender	24% (2686/11 052)
Primary HF aetiology	
Ischaemic	45% (4875/10 953)
Non-ischaemic	55% (6078/10 953)
Past history and major co-morbidity	
Previous myocardial infarction	36% (3957/10 926)
Prior revascularisation (PCI/CABG)	39% (4245/10 924)
Hypertension	64% (6962/10 900)
Atrial fibrillation	41% (4459/10 920)
Valvular heart disease	27% (2968/10 920)
Obstructive lung disease	12% (1315/10 922)
Diabetes	31% (3428/10 921)
Anaemia	15% (1640/10 916)
Chronic kidney disease (eGFR < 60 mL/min/1.73 m ²)	31% (3395/10 907)
Previous device (PPM or ICD)	28% (3059/10 992)
HF hospitalisation during past year	47% (5078/10 917)
Currently enrolled in a clinical trial	8% (918/11 028)

In parenthesis, number of patients in each category compared to the total cohort for each data-point.

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; HF, heart failure; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; PCI, percutaneous coronary intervention; PPM, permanent pacemaker.

Benchmarking the top 10 recruiting countries

Data from the 10 countries that enrolled the most patients were compared. There were substantial differences amongst countries in the mean age of patients implanted (Figure 1A). Symptom severity

Table 4 Pre-implant clinical evaluation (n = 11 088)

NYHA class	
I	3% (370/10 848)
II	38% (4083/10 848)
III	55% (5909/10 848)
IV	5% (486/10 848)
BMI (kg/m ²), median (IQR)	27 (25–31)
Systolic blood pressure (mmHg), median (IQR)	122 (110–137)
Diastolic blood pressure (mmHg), median (IQR)	72 (66–80)
Laboratory measurement (most recent), median (IQR)	
BNP (ng/L)	422 (150–1115)
NT-proBNP (ng/L)	2400 (1049–5517)
Serum creatinine (μ mol/L)	100 (83–129)
Haemoglobin (g/dL)	13 (12–15)
Pre-implant ECG	
Heart rate (b.p.m.), median (IQR)	70 (60–80)
Atrial rhythm	
Sinus	69% (7496/10 836)
Atrial fibrillation	26% (2778/10 836)
Atrial paced	3% (303/10 836)
Other	2% (259/10 836)
PR interval (ms), median (IQR)	180 (160–210)
AV block II/III	19% (2026/10 700)
Pacemaker dependent	14% (1511/10 752)
Intrinsic QRS morphology	
LBBB	73% (7861/10 800)
Non-LBBB	27% (2939/10 800)
Intrinsic QRS duration (ms), median (IQR)	160 (140–174)
< 120	8% (711/9535)
120–129	5% (505/9535)
130–149	19% (1779/9535)
150–179	47% (4486/9535)
> 180	22% (2054/9535)

Effects of Atrioventricular Nodal Ablation on Permanent Atrial Fibrillation Patients With Cardiac Resynchronization Therapy: A Systematic Review and Meta-analysis

Jie Yin, MD, ^{1,2} Hesheng Hu, MD, ¹ Ye Wang, MD, ¹ Mei Xue, MD, ¹ Xiaolu Li, MD, ¹ Wenjuan Cheng, MD, ¹ Xinran Li, MD, ^{1,2} and Suhua Yan, MD¹

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Abstract

Go to: 

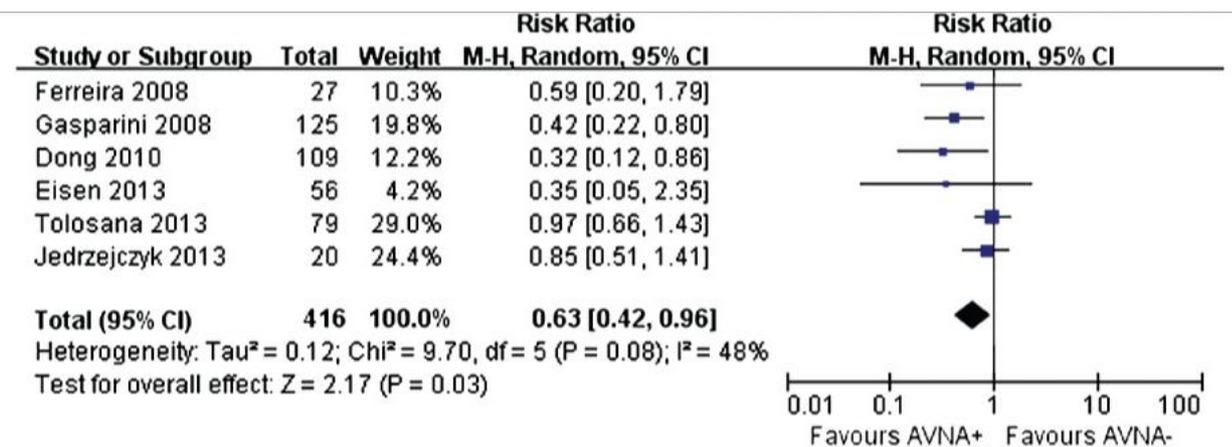
Cardiac resynchronization therapy (CRT) is a well-established therapy for patients with heart failure (HF) and wide QRS configuration, especially for those in sinus rhythm. However, for those with permanent AF, atrioventricular nodal (AVN) ablation use remains under debate. Our objective was to evaluate clinical outcomes and mortality of AVN ablation in HF patients with permanent AF receiving CRT. Electronic publication database and reference lists through October 1, 2013 were searched. Observational cohort studies comparing CRT patients with AF who received either AVN ablation or medical therapy were selected. Outcomes included mortality, CRT nonresponse, changes in left ventricular remodeling, and functional outcomes, such as New York Heart Association (NYHA) functional class, quality of life, and 6-minute hall walk distance. Of 1641 reports identified, 13 studies with 1256 patients were included. Among patients with permanent AF and insufficient biventricular pacing (<90%), those who had undergone AVN ablation compared to those who did not had numerically lower all-cause mortality (risk ratio [RR]: 0.63, 95% confidence interval [CI]: 0.42 to 0.96, P = 0.03) and significantly lower nonresponse to CRT (RR: 0.41, 95% CI: 0.31 to 0.54, P < 0.00001). Furthermore, AVN ablation was not associated with additional improvements on left ventricular ejection fraction, NYHA functional class, 6-minute hall walking distance, and quality of life. In patients with permanent AF undergoing CRT, AVN ablation tended to reduce mortality potentially and improved clinical response when it was applied to patients with inadequate biventricular pacing (<90%). Randomized controlled trials are needed to further address the efficacy of AVN ablation among this population.

A total of 1256 CRT-AF recipients was involved, of whom 644 underwent AVN ablation, and 798 were on pharmacological therapy for rate control.



V publikovaných štúdiách CRT s permanentnou **podstúpilo AF abláciu AV uzla 45% pacientov**

Porovnávanie celkovej mortality v 6 štúdiách:



Thirteen Studies and Patient Characteristics

Study Author, Year	Design	Inclusion Criteria	Sample Size	Mean Age, y			Permanent AF	Mean Follow-up	ICD	Ablation Criteria	Outcome
				y	Male						
Molhoek, 2004	+	Drug-refractory HF, NYHA III–IV, LVEF \leq 35%, QRS duration \geq 120 ms	SR	30	68 \pm 8	80	100% persistent AF	18 \pm 6 months	—	Not reported	Clinical outcome
			AVNA+	17	63 \pm 10 ^a	90 ^a					
			AVNA–	13							
Gasparini, 2006 ^b	+	Drug-refractory HF, NYHA \geq II, LVEF \leq 35%, QRS duration \geq 120 ms	SR	511	63 \pm 10	77.3	100% permanent AF	25.2 \pm 18 months	58.5	BiVP% <85%	Clinical outcome
			AVNA+	114	67 \pm 9	86.8					
			AVNA–	48	64 \pm 6	83.3					
Tolosana, 2008	0	Drug-refractory HF, NYHA III–IV, LVEF \leq 35%, QRS duration \geq 120 ms	SR	344	67 \pm 9	87 ^a	100% permanent AF	12 months	52	Poor rate control	Clinical outcome, mortality
			AVNA+	19	69 \pm 7						
			AVNA–	107	68 \pm 10						
Ferreira, 2008	0	Drug-refractory HF, NYHA \geq II, LVEF \leq 35%, QRS duration \geq 120 ms	SR	78	66 \pm 10	74	Contains all kinds of AF, not listed for each	6 months	76	Inadequate BiVP% or ICD shocks	Clinical outcome, mortality
			AVNA+	26	67 \pm 9	92					
			AVNA–	27	70 \pm 8	96					
Gasparini, 2008 ^b	+	–	SR	1042	63 \pm 9	75	100% permanent AF	Median follow-up of 34 months	57.8	BiVP% <85%	Mortality
			AVNA+	118	67 \pm 9	86					
			AVNA–	125	66 \pm 9	78					
Schutte, 2009	0	Drug-refractory HF, NYHA III–IV, LVEF \leq 35%, LBBB QRS duration \geq 120 ms	SR	64	70 ^a	86 ^a	100% permanent AF	11 \pm 0.34 months	—	BiVP% <90%	Clinical outcome
			AVNA+	27							
			AVNA–	9							
Dong, 2010	+	Drug-refractory HF, symptom, LVEF \leq 35%, QRS duration \geq 120 ms	AVNA+	45	72 \pm 9	84	88% permanent AF	274 days	100	Poor rate control	Clinical outcome, mortality
			AVNA–	109	68 \pm 11	87		222 days			
Tolosana, 2012	+	Drug-refractory HF, NYHA \geq III, LVEF \leq 35% QRS duration \geq 120 ms	SR	156	66 \pm 9	77	100% permanent AF	12 months	87	BiVP% <85%	Clinical outcome, mortality
			AVNA+	13	68 \pm 10	84					
			AVNA–	33	67 \pm 9	67					
Himmel, 2012	+	Drug-refractory HF, NYHA III–IV, LVEF \leq 35%, QRS duration \geq 120 ms	SR	230	69 \pm 9	—	100% permanent AF	12 \pm 3 months	—	BiVP% <80%	Clinical outcome
			AVNA+	15	70 \pm 7	—					
			AVNA–	31	69 \pm 9	—					
Tolosana, 2013	+	Drug-refractory HF, NYHA III–IV, LVEF \leq 35%, QRS duration \geq 120 ms	AVNA+	76	70 \pm 8	82	100% permanent AF	At	49	BiVP% <85%	Clinical outcome, mortality
			AVNA–	79	68 \pm 8	81		12, 24, 36, and 60 months			
Eisen, 2013	0	Not specifically reported, average NYHA III, LVEF \leq 35%, QRS duration >120 ms,	SR	109	68 \pm 11	78.8	47% permanent AF	At 12 and 24 months	64.2	—	Clinical outcome, mortality
			AVNA+	10	70 \pm 13	78.9					

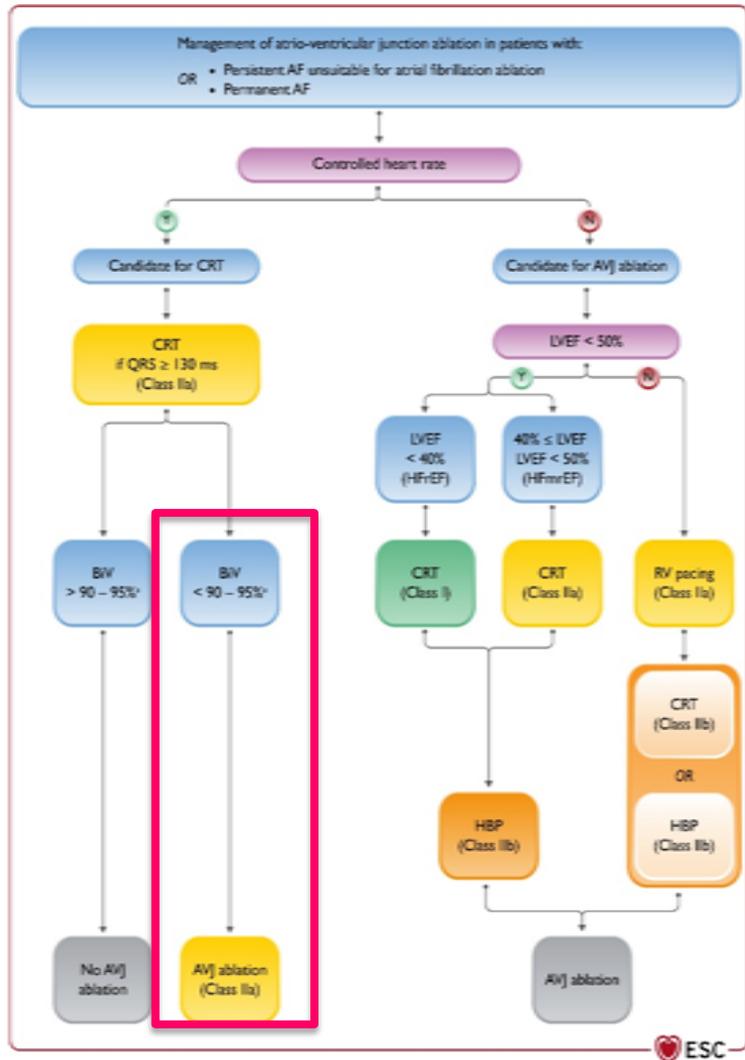
Abbreviations: AF, atrial fibrillation; AVN, atrioventricular nodal; AVNA+, patients who had undergone AVN ablation; AVNA–, patients who did not undergo AVN ablation; BiVP, biventricular pacing; HF, heart failure; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SR, sinus rhythm.

— indicates that information was not reported, + indicates prospective design, and 0 indicates retrospective design.

^aTrials did not report separate information for the AF subgroup.

^bThe 2 articles by Gasparini included duplicate patients but assessed different outcomes.

LVEF ≤ 35%
NYHA III-IVa



Indication for atrioventricular junction ablation in patients with symptomatic permanent atrial fibrillation or persistent atrial fibrillation unsuitable for atrial fibrillation ablation

AF = atrial fibrillation; AVJ = atrioventricular junction; BIV = biventricular; CRT = cardiac resynchronization therapy; ESC = European Society of Cardiology; HBP = His bundle pacing; HFmrEF = heart failure with mildly reduced ejection fraction; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; QRS = Q, R, and S waves; RV = right ventricular/right ventricle.

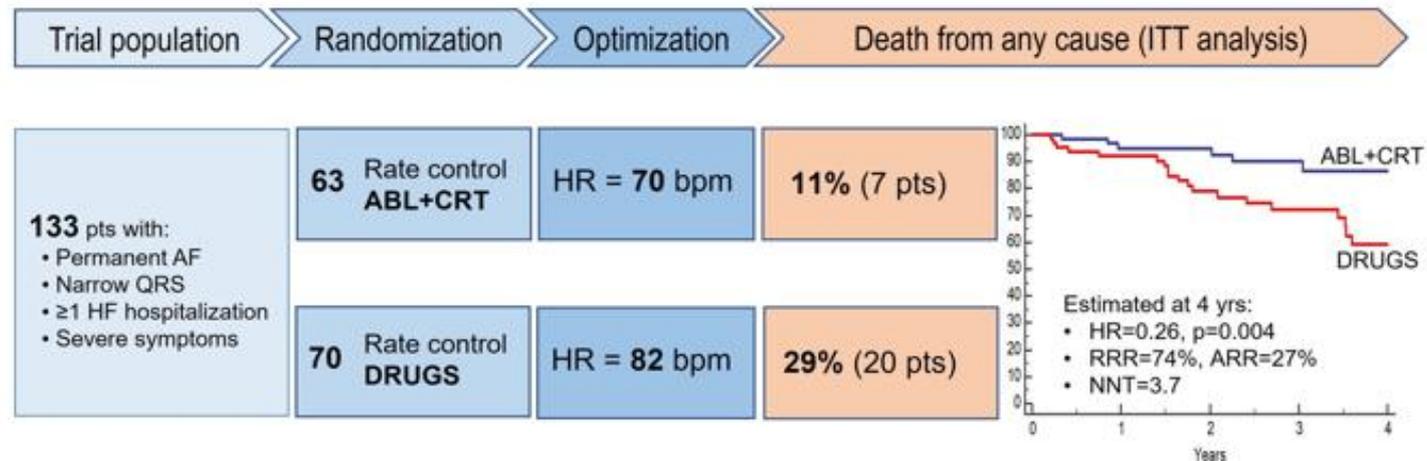
^a Due to a rapid ventricular response.

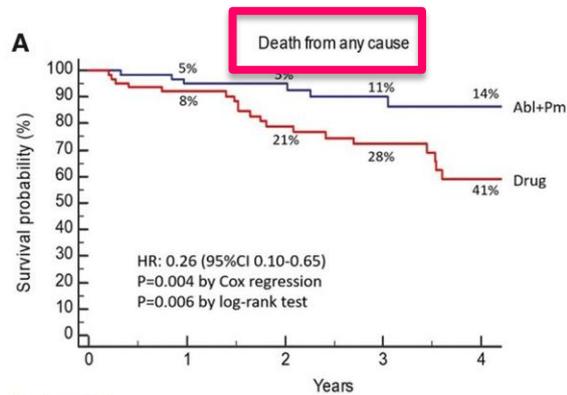
Note: Figure based on the recommendations in the ESC guidelines on AF.

APAF-CRT Mortality Trial

- randomizovaná štúdia u pacientov s permanentnou fibriláciou predsiení a **úzkym QRS**, ktorí boli hospitalizovaní pre srdcové zlyhávanie v poslednom roku (**bez ohľadu na EFLK a srdcovú frekvenciu**)
- 133 p, priem. vek 73 ± 10 r., 47% žien
- **Predčasne ukončená pre efektivitu po 29 mes.**

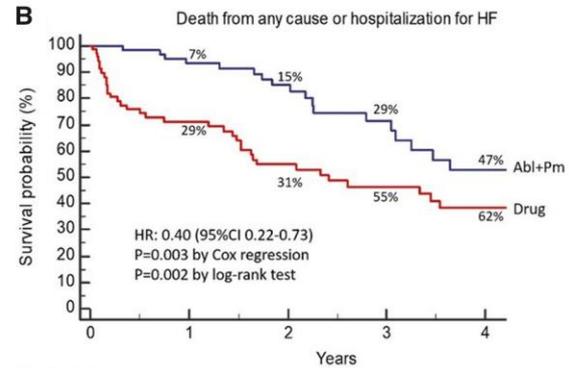
AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: The APAF-CRT Mortality Trial. *Brignole M et al.*





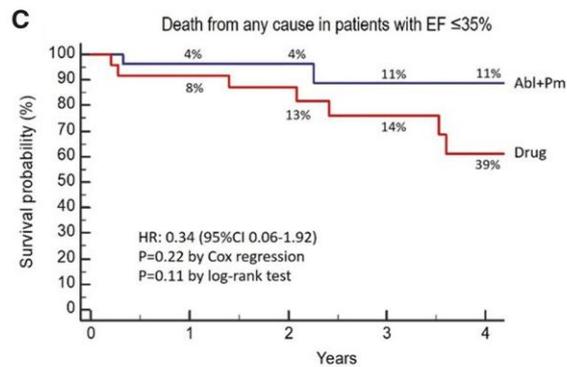
Number at risk

Abl+Pm	63	52	41	27	12
Drug	70	56	38	29	9



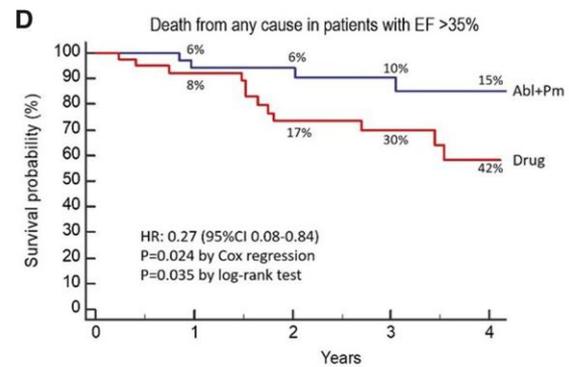
Number at risk

Abl+Pm	63	51	36	21	9
Drug	70	44	27	21	7



Number at risk

Abl+Pm	27	21	16	9	6
Drug	26	22	18	13	4



Number at risk

Abl+Pm	36	31	25	18	6
Drug	44	34	20	16	5

- **Mortalita 11% v skupine Abl + CRT versus 29% v skupine farmakoterapie, (HR) 0.26, P = 0.004**
- **Kombinovaný cieľ mortalita a hospitalizácia pre SZ- v skupine Abl + CRT 29% vs. farmakoterapie 51%; HR 0.40, P = 0.002**
- **Efektivita bola rovnaká v skupine EFĽK ≤35% a >35%.**

Záver: liečba abláciou AV uzla a resynchronizačnou liečbou významne redukovala mortalitu oproti farmakoterapii na kontrolu SF



CRT+ ablácia AVU verzus IPV

Ablácia AVU a CRT sa má zvážiť v skupine pac. s permanentou FP významne symptomatických hospitalizovaných pre SZ

Atrioventricular node ablation combined with cardiac resynchronization therapy should be considered in severely symptomatic patients with permanent AF and at least one hospitalization for HF to reduce symptoms, physical limitations, recurrent HF hospitalization, and mortality.

Ila

B

Van Gelder IC, 2024 ESC Guidelines for the management of atrial fibrillation, EHJ 2024

Záver:

Odpovede projektu ANACONDA:

- **U pacientov s CRT a permanentnou FP so SF nad 80/min** sme potvrdili klinický benefit včasnej ablácie AV uzla. Jej odloženie pri súčasnej optimalizácii farmakoterapie podobný benefit neprináša.
 - Významne vyšší podiel BiV stim
 - Významne lepší echokg responding
 - Významné zlepšenie triedy SZ, niektorých parametrov kvality života
 - Vysoký podiel následnej potreby ablácie AV uzla (49%)



Ďakujem za pozornosť

