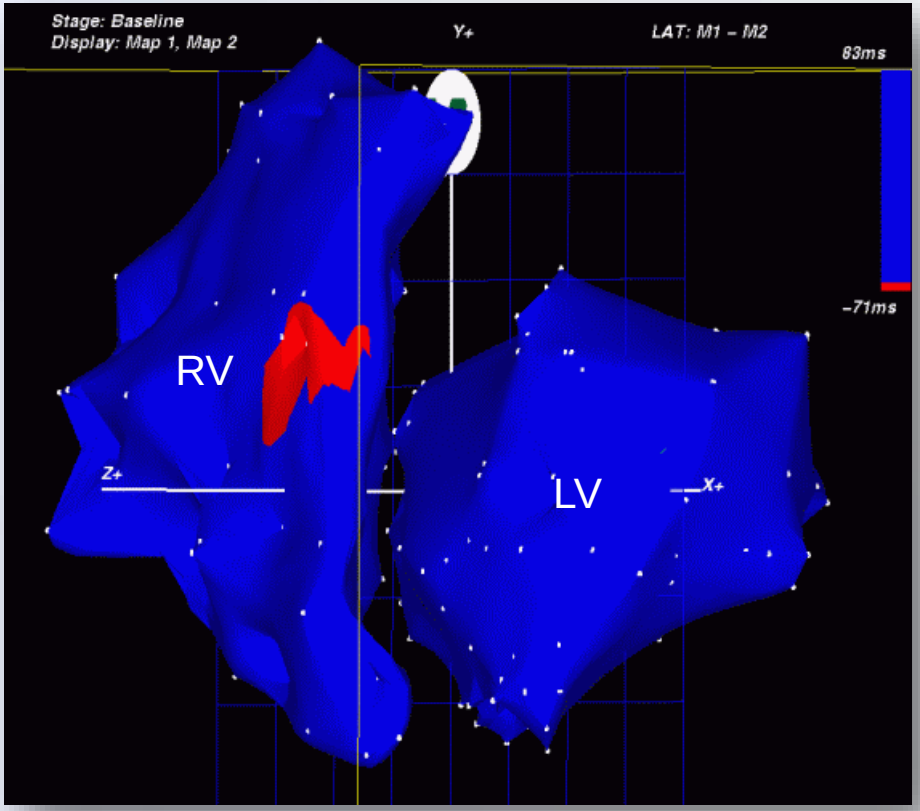
Nefarmakologická léčba srdečního selhání

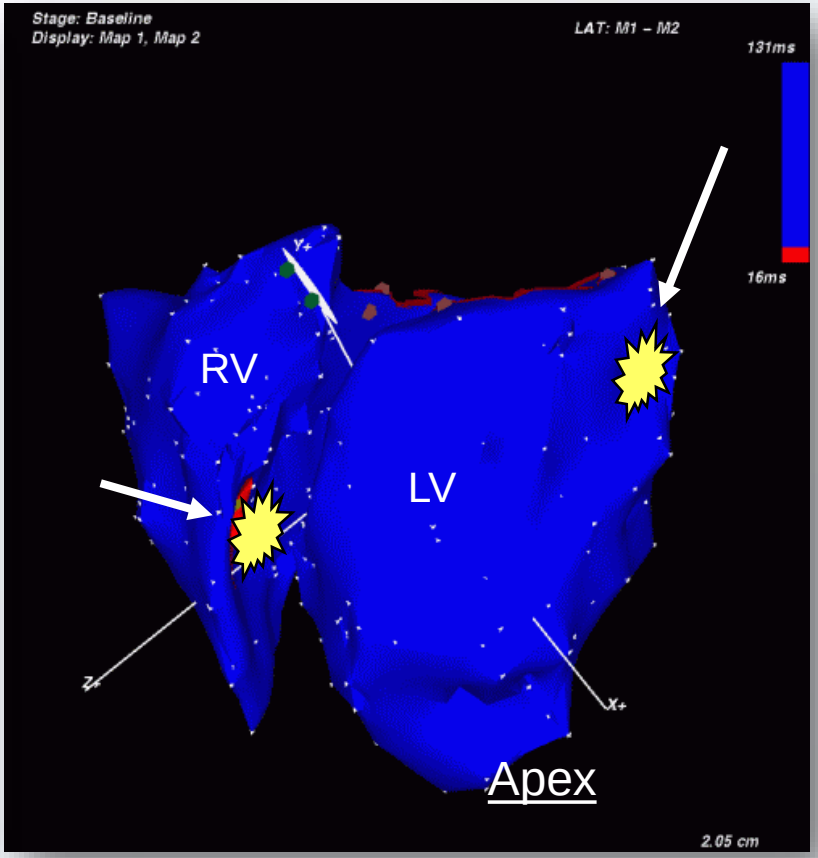
Kamil Sedláček

Klinika kardiologie IKEM
Praha

Princip CRT



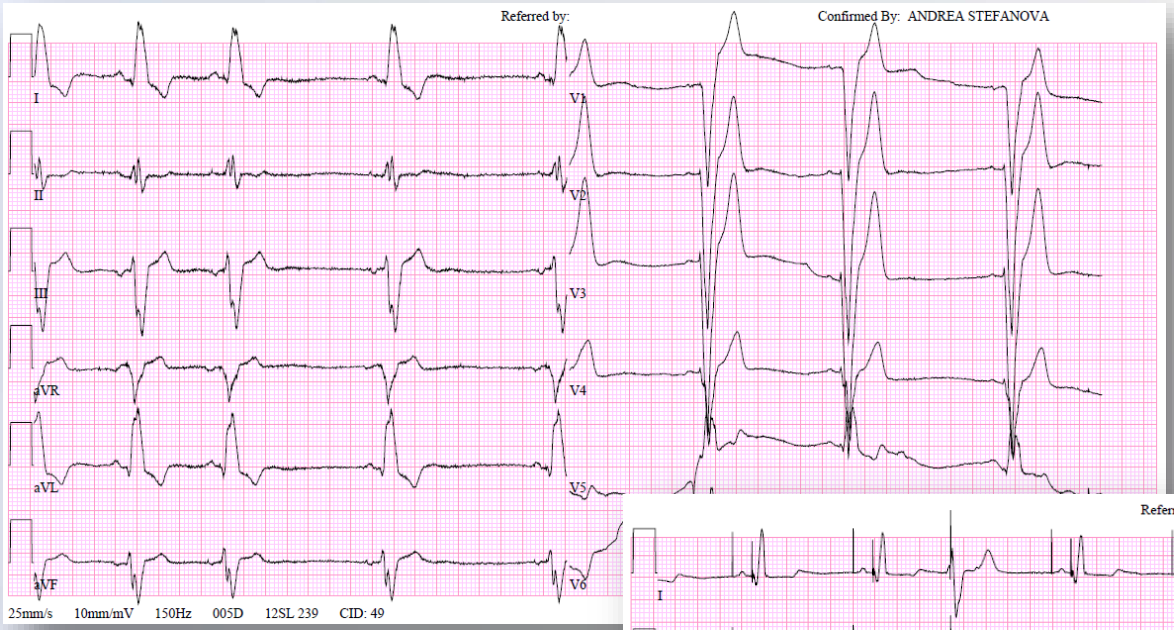
Electric activation in LBBB

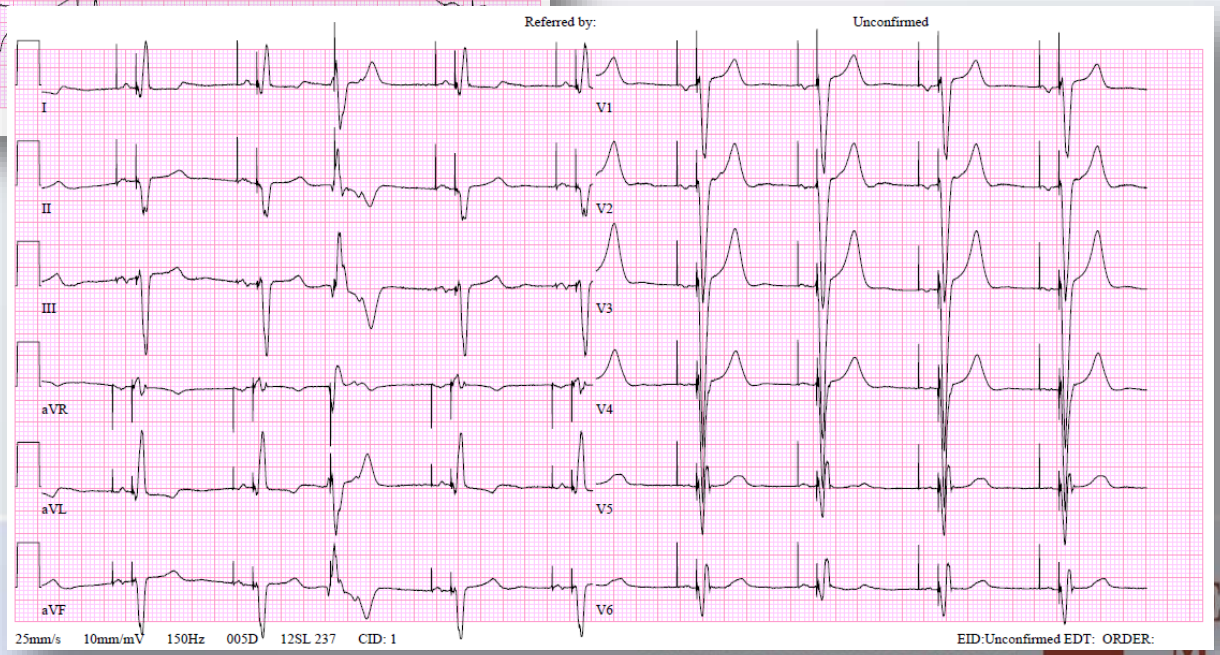


Biventricular pacing

Peichl P, Kautzner J, 2006

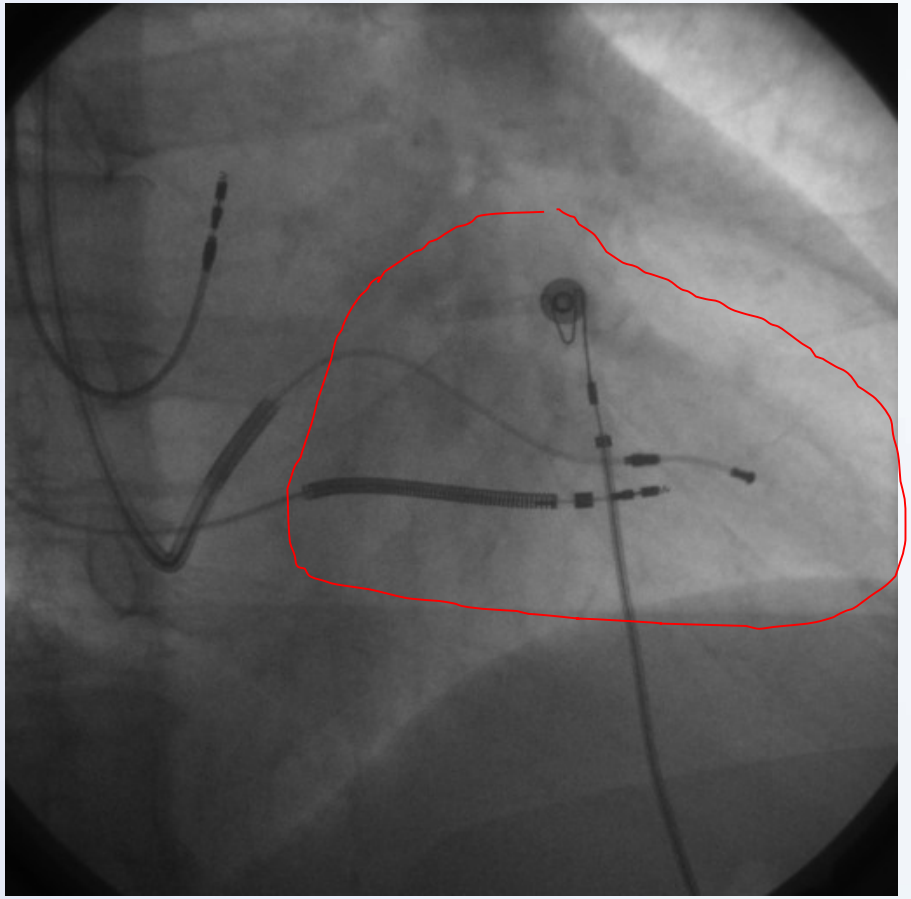
CRT je elektrická terapie



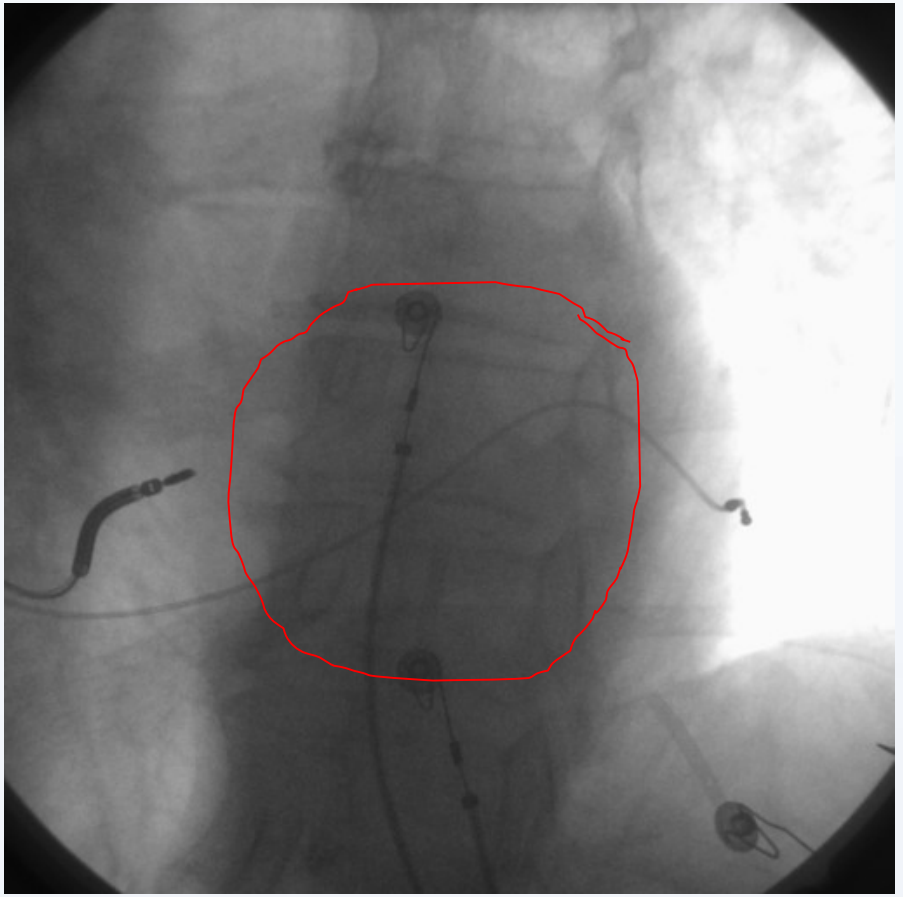


Elektrodový systém

RAO



LAO



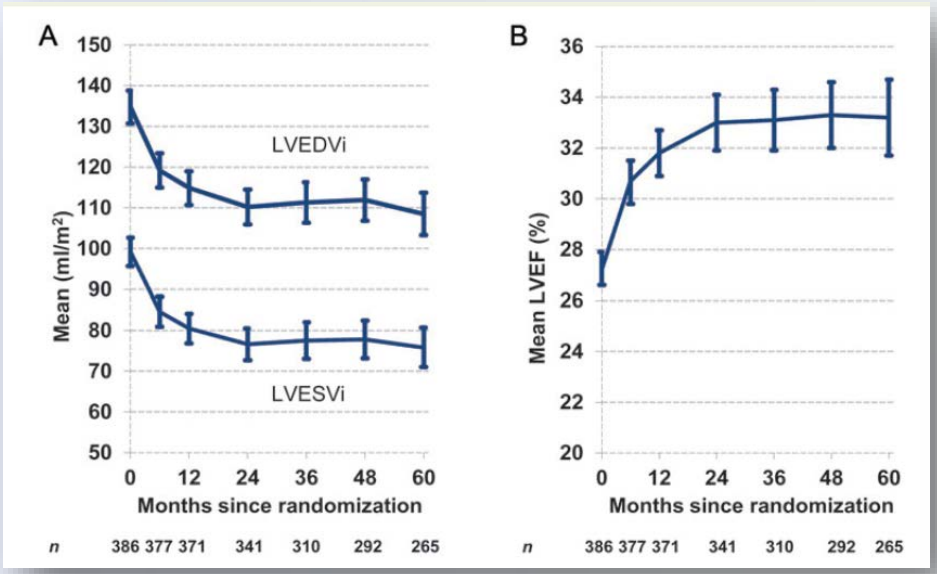
EBM - CRT

Trial (ref)	No.	Design	NYHA	LVEF	QRS	Primary endpoints	Secondary endpoints	Main Findings
MUSTIC-SR[52]	58	Single-blinded, crossover, randomized CRT vs. OMT, 6 months	III	<35%	≥150	6MWD	NYHA class, QoL, peak VO_2 LV volumes, MR hospitalizations, mortality	CRT-P improved 6MWD, NYHA class, QoL, peak VO_2, reduced LV volumes and MR and reduced hospitalizations
PATH-CHF[51]	41	Single-blinded, crossover,	III–IV	NA	≥150	Peak VO_2, 6MWD	NYHA class, QoL hospitalizations	CRT-P improved NYHA class, QoL and 6MWD and reduced
COMPANION[55]	1520	Double-blinded randomized OMT vs. CRT-P / or vs. CRT-D, 15 months	III–IV	≤35%	≥120	All-cause mortality or hospitalization	All-cause mortality, cardiac mortality	CRT-P and CRT-D reduced all-cause mortality or hospitalization
CARE-HF[56]	813	Double-blinded randomized OMT vs. CRT-P 29.4 months	III–IV	≤35%	≥120	All-cause mortality or hospitalization	All-cause mortality, NYHA class, QoL	CRT-P reduced all-cause mortality and hospitalization and improved NYHA class and QoL
REVERSE[61]	610	Double-blinded, randomized CRT-ON vs. CRT-OFF, 12 months	I–II	≤40%	≥120	% worsened by clinical composite endpoint	LVESV index, heart failure hospitalizations and all-cause mortality	CRT-P/CRT-D did not change the primary endpoint and did not reduce all-cause mortality but reduced LVESV index and heart failure hospitalizations.
MADIT-CRT[50]	1820	Single-blinded, randomized CRT-D vs. ICD, 12 months	I–II	≤30%	≥130	All-cause mortality or heart failure hospitalizations	All-cause mortality and LVESV	CRT-D reduced the endpoint heart failure hospitalizations or all-cause mortality and LVESV. CRT-D did not reduced all-cause mortality
RAFT[62]	1798	Double-blinded, randomized CRT-D vs. ICD 40 months	II–III	≤30%	≥120	All-cause mortality or heart failure hospitalizations	All-cause mortality and cardiovascular death	CRT-D reduced the endpoint all-cause mortality or heart failure hospitalizations. In NYHA III, CRT-D only reduced significantly all-cause mortality

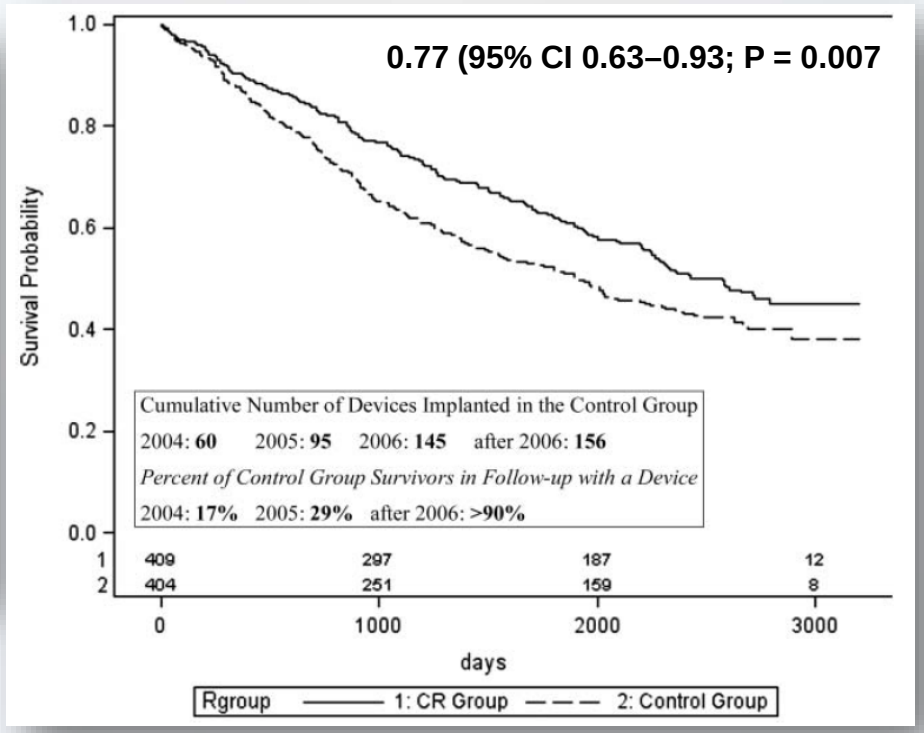
Brignole M et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. *Eur Heart J. 2013;34:2281-329.*

Dlouhodobý efekt CRT

REVERSE (5 yrs)



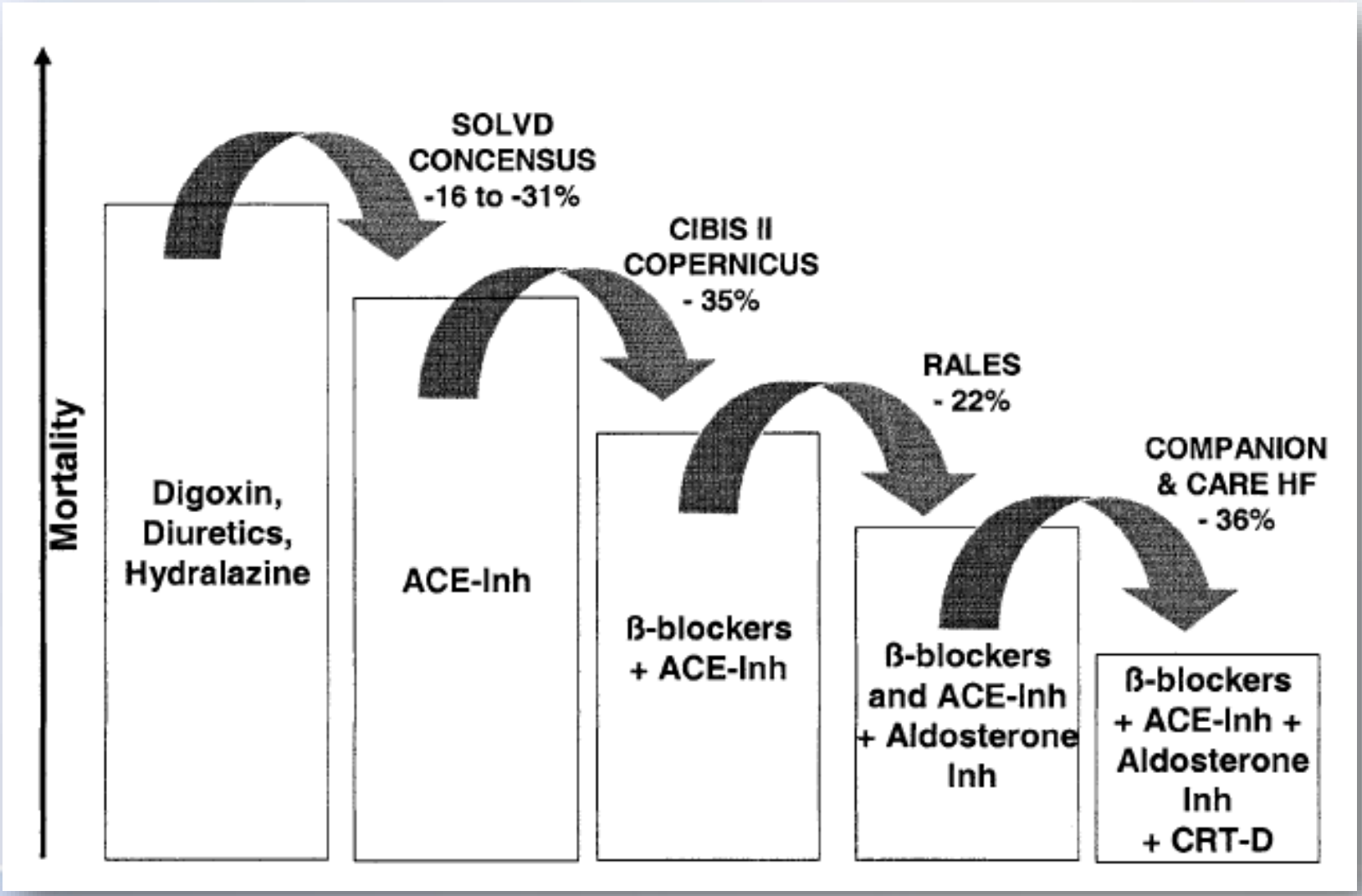
CARE-HF (9 yrs - mortality)



Linde C et al. Long-term impact of cardiac resynchronization therapy in mild heart failure: 5-year results from the REVERSE study. *European heart journal. 2013;34:2592-9.*

Cleland JG et al. Long-term mortality in the CARE-HF trial. *European journal of heart failure. 2012;14:628-34.*

EB terapie srdečního selhání



HF Guidelines ESC 2016

Recommendations	Class [a]	Level [b]	Ref [c]
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CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B	261–272
CRT is recommended for symptomatic pat…BB QRS morphology and with LVEF ≤35% despite …	I	B	266, 273
CRT may be considered for symptomatic p…on-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B	266, 273
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	274–277
CRT should be considered for patients with LVEF ≤35% in NYHA Class III–IV[d] despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

LBBB > 150 ms

European Heart Journal (2016) 37, 2129–2200

HF Guidelines ESC 2016

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CRT is recommended for [illegible] morphology and with LVE		B	266, 273
CRT may be considered f[illegible] QRS morphology and wit		B	266, 273
CRT rather than RV pacing[illegible] pacing and high degree AV		A	274–277
CRT should be considere[illegible] reduce morbidity and mo[illegible] capture is in place or the		B	275, 278–281
Patients with HFrEF who h[illegible] and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
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Non-LBBB > 150 ms

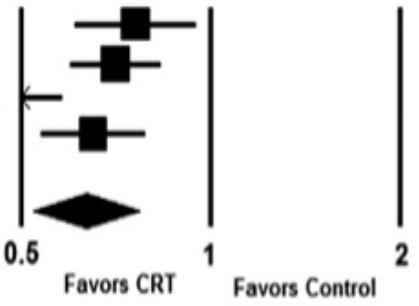
???????

European Heart Journal (2016) 37, 2129–2200

Analýzy u pacientů s non-LBBB

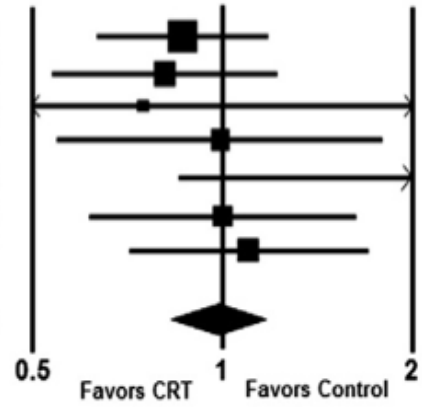
LBBB

Study name	Risk Ratio	Lower Limit	Upper limit	Z-Value	p-Value
COMPANION[10] - LBBB	0.76	0.61	0.95	-2.43	0.016
CARE-HF[11,32] - LBBB	0.70	0.60	0.83	-4.21	<0.0001
MADIT-CRT[12,13,15] - LBBB	0.45	0.35	0.58	-6.20	<0.00001
RAFT[14] - LBBB	0.65	0.54	0.79	-4.44	0.00001
Meta Analysis	**0.64**	**0.52**	**0.77**	**-4.55**	**0.00001**



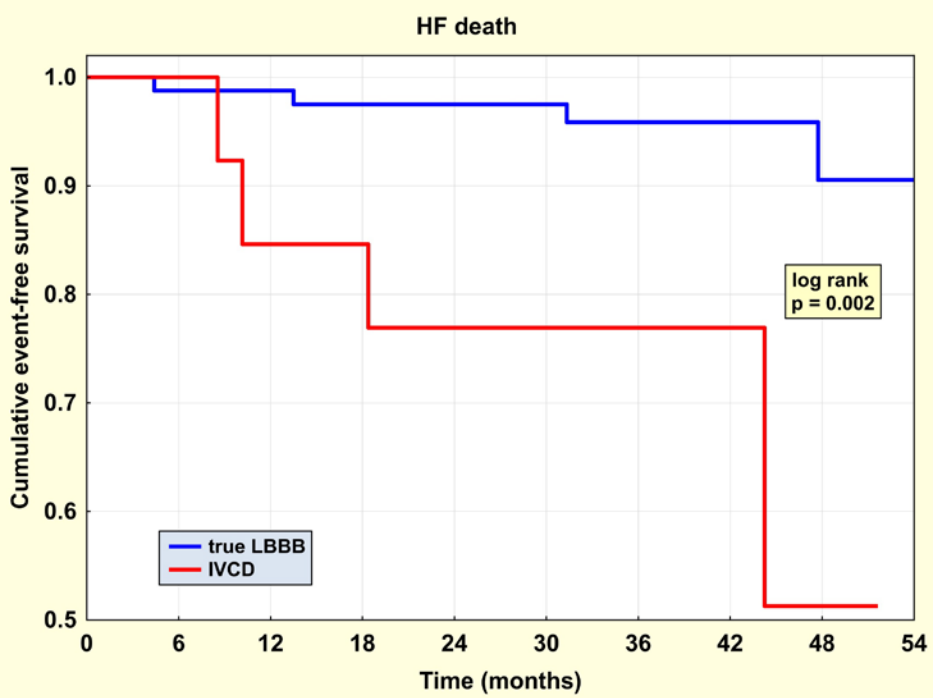
Non-LBBB

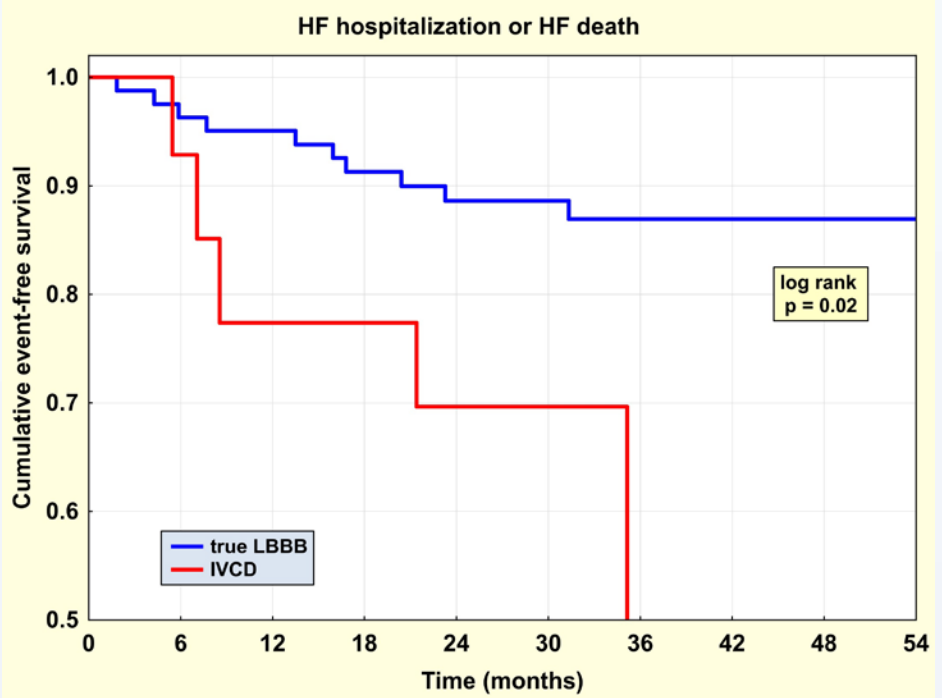
Study name	Risk Ratio	Lower Limit	Upper Limit	Z-Value	p-Value
COMPANION[10] - Non-LBBB	0.86	0.63	1.17	-0.96	0.34
CARE-HF[11,32] - RBBB	0.81	0.54	1.22	-0.99	0.32
CARE-HF[11,32] - IVCD	0.75	0.24	2.33	-0.50	0.62
MADIT-CRT[12,13,15] - RBBB	0.99	0.55	1.79	-0.03	0.97
MADIT-CRT[12,13,15] - IVCD	1.44	0.88	2.36	1.45	0.15
RAFT[14] - RBBB	1.00	0.62	1.62	0.00	1.00
RAFT[14] – IVCD	1.10	0.71	1.69	0.43	0.67
Meta Analysis	**0.97**	**0.82**	**1.15**	**-0.32**	**0.75**



Sipahi I, et al. *Am Heart J* 2012;163:260-267.e3.)

CMR guided LV in non-LBBB





Kockova R, Sedlacek K, Wichterle D, ESC 2016

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CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

AV blokáda, dysfunkce LK

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CRT may be considered for symptoma QRS morphology and with LVEF ≤35%			66, 273
CRT rather than RV pacing is recomme pacing and high degree AV block in ord			74–277
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Srdeční selhání při PK stimulaci

European Heart Journal (2016) 37, 2129–2200

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Štíhlý komplex QRS

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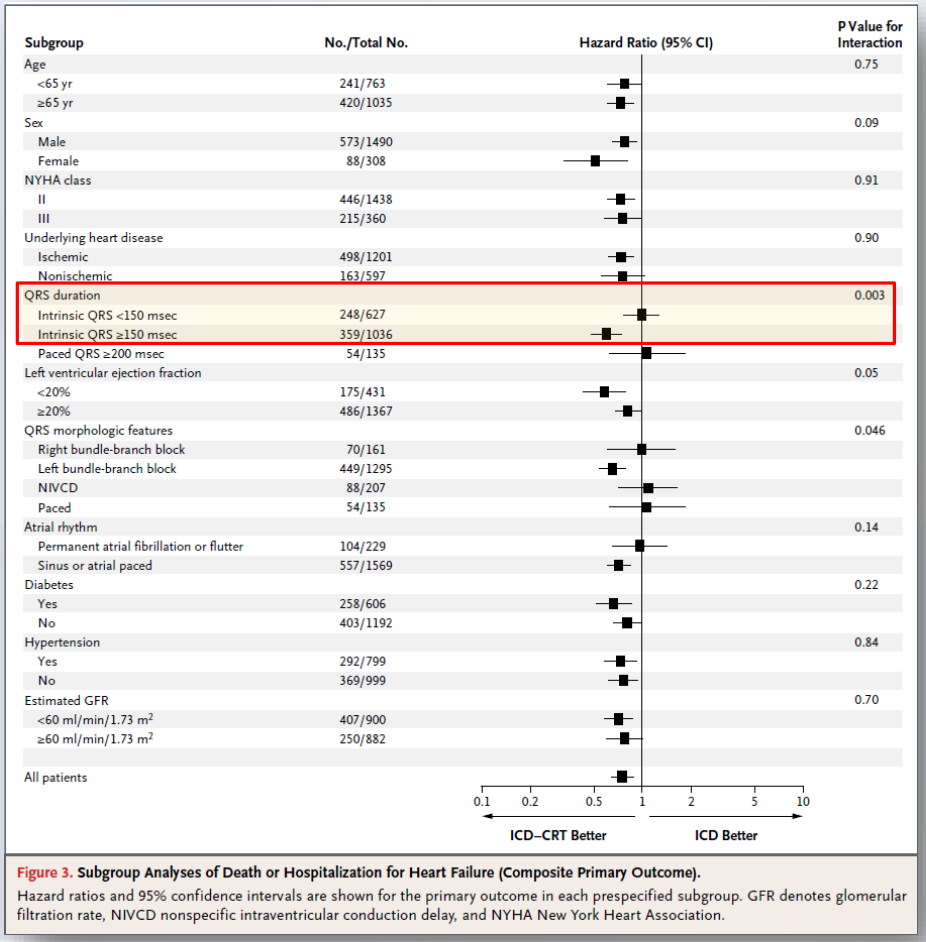
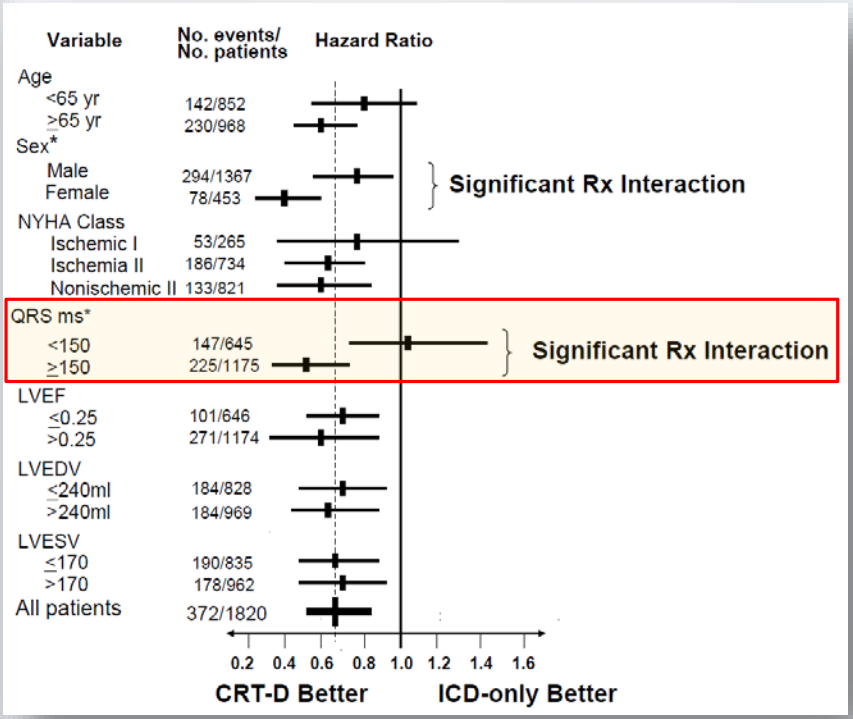
CRT Trials: Effect of QRS Duration



Subgroup	No./Total No.	P Value for Interaction
Age		0.75
<65 yr	241/763	
≥65 yr	420/1035	
Sex		0.09
Male	573/1490	
Female	88/308	
NYHA class		0.91
II	446/1438	
III	215/360	
Underlying heart disease		0.90
Ischemic	498/1201	
Nonischemic	163/597	
QRS duration		0.003
Intrinsic QRS <150 msec	248/627	
Intrinsic QRS ≥150 msec	359/1036	
Paced QRS ≥200 msec	54/135	
Left ventricular ejection fraction		0.05
<20%	175/431	
≥20%	486/1367	
QRS morphologic features		0.046
Right bundle-branch block	70/161	
Left bundle-branch block	449/1295	
NIVCD	88/207	
Paced	54/135	
Atrial rhythm		0.14
Permanent atrial fibrillation or flutter	104/229	
Sinus or atrial paced	557/1569	
Diabetes		0.22
Yes	258/606	
No	403/1192	
Hypertension		0.84
Yes	292/799	
No	369/999	
Estimated GFR		0.70
<60 ml/min/1.73 m²	407/900	
≥60 ml/min/1.73 m²	250/882	
All patients		

Figure 3. Subgroup Analyses of Death or Hospitalization for Heart Failure (Composite Primary Outcome).
Hazard ratios and 95% confidence intervals are shown for the primary outcome in each prespecified subgroup. GFR denotes glomerular filtration rate, NIVCD nonspecific intraventricular conduction delay, and NYHA New York Heart Association.

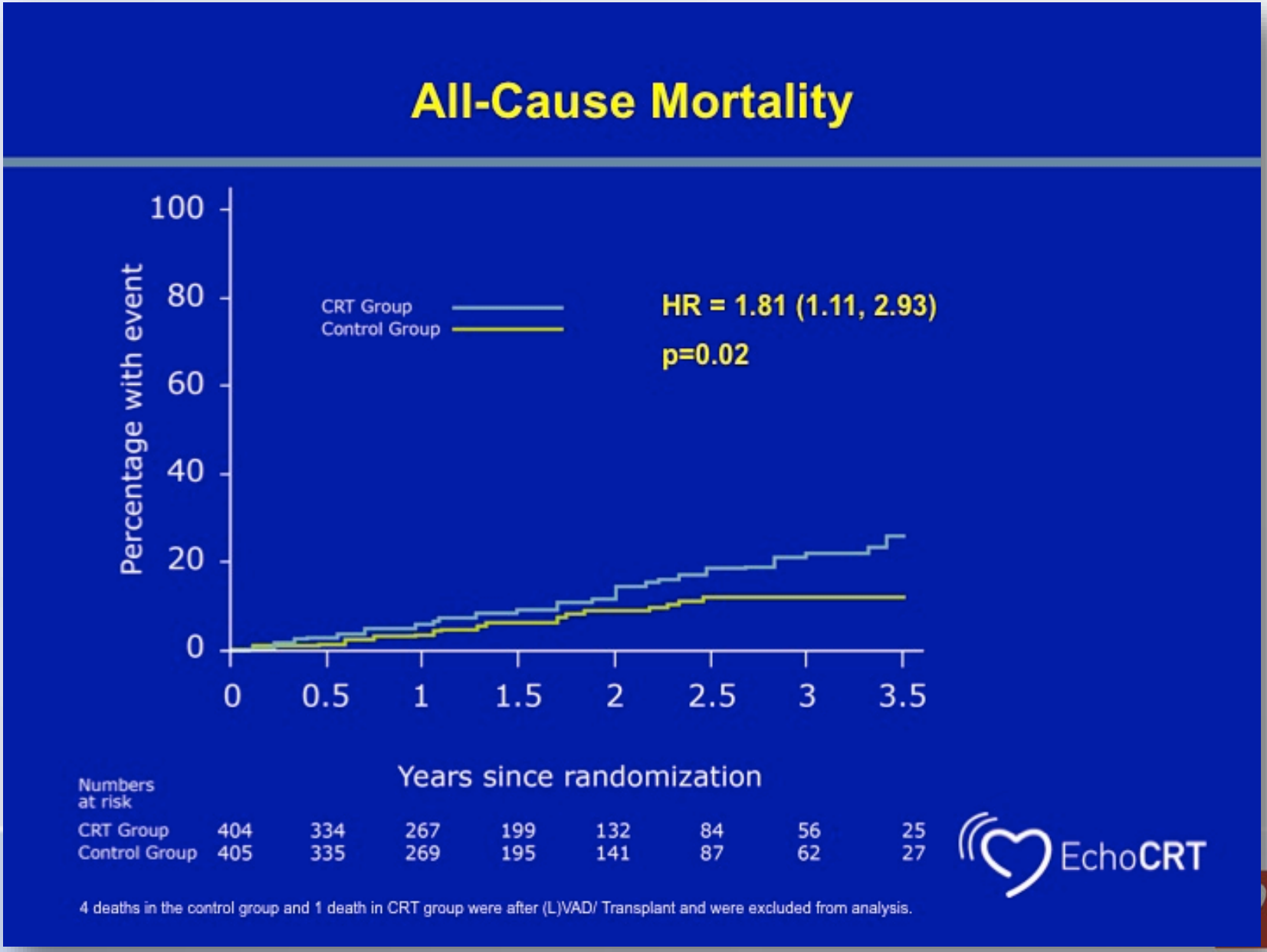
Tang et al. RAFT Trial. NEJM 2010



Variable	No. events/ No. patients	Hazard Ratio
Age		
<65 yr	142/852	
≥65 yr	230/968	
Sex*		
Male	294/1367	Significant Rx Interaction
Female	78/453	
NYHA Class		
Ischemic I	53/265	
Ischemia II	186/734	
Nonischemic II	133/821	
QRS ms*		
<150	147/645	Significant Rx Interaction
≥150	225/1175	
LVEF		
≤0.25	101/646	
>0.25	271/1174	
LVEDV		
≤240ml	184/828	
>240ml	184/969	
LVESV		
≤170	190/835	
>170	178/962	
All patients	372/1820	

Moss et al. MADIT-CRT Trial. NEJM 2009

Echo-CRT


All-Cause Mortality
Percentage with event
100
80
60
40
20
0
CRT Group
Control Group
HR = 1.81 (1.11, 2.93)
p=0.02
0
0.5
1
1.5
2
2.5
3
3.5
Years since randomization
Numbers at risk
CRT Group 404 334 267 199 132 84 56 25
Control Group 405 335 269 195 141 87 62 27
EchoCRT
4 deaths in the control group and 1 death in CRT group were after (L)VAD/ Transplant and were excluded from analysis.

Kazuistika

62-letý pacient s end-stage NIDCM

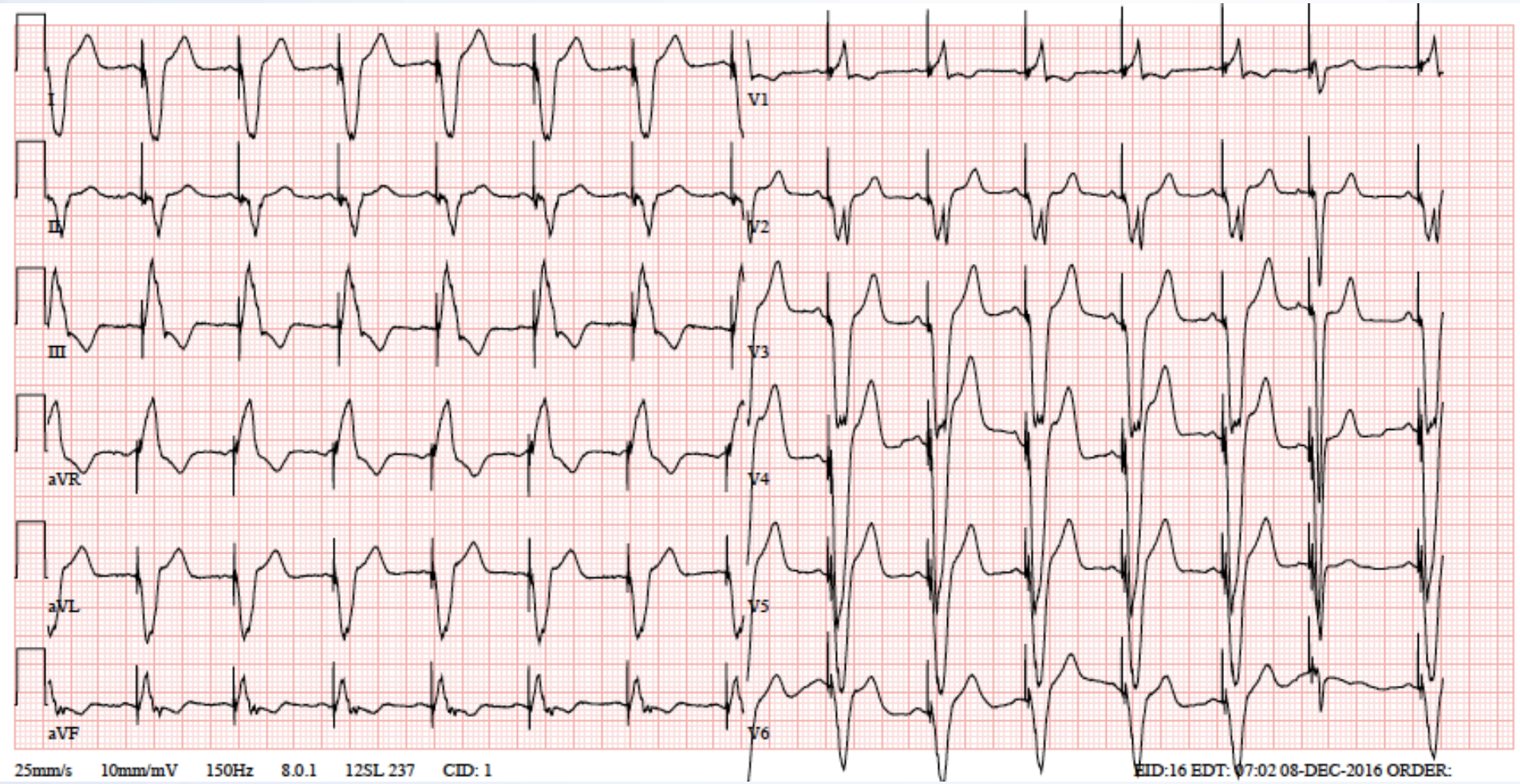
Farmakologická terapie optimalizována

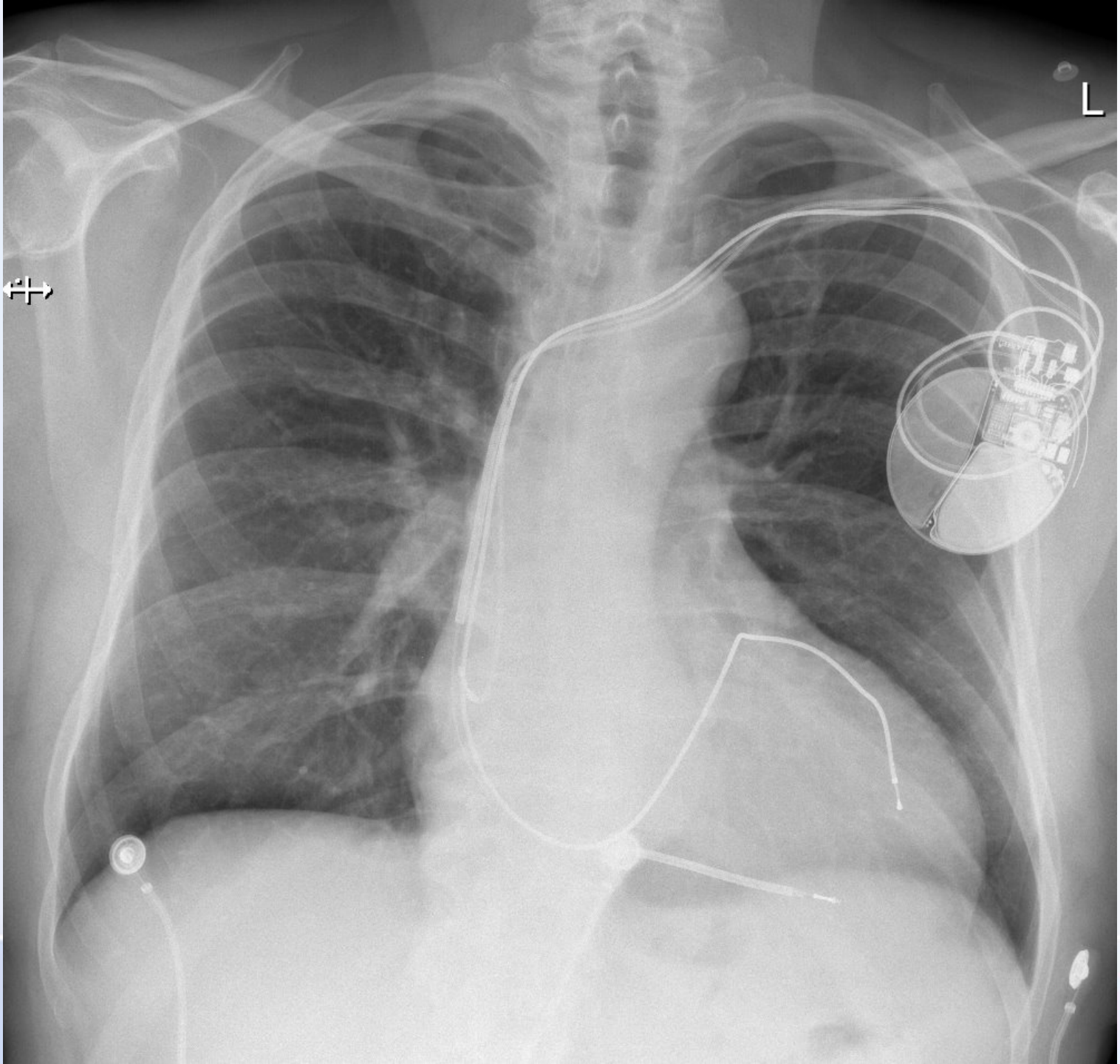
CRT „non-responder“, implantace 2014

Nedávno hospitalizován pro zhoršení srdečního selhání, EF 20%, LVEDD 75mm, těžká plicní hypertenze

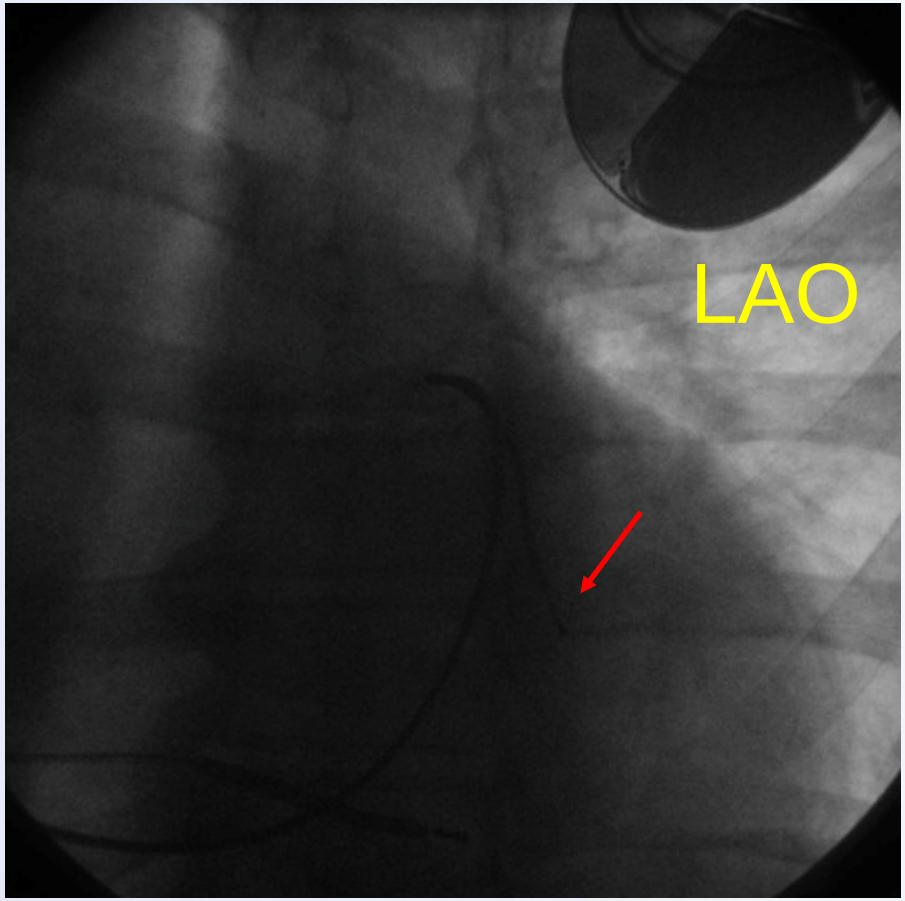
Doporučen ke zvážení transplantace nebo LVAD

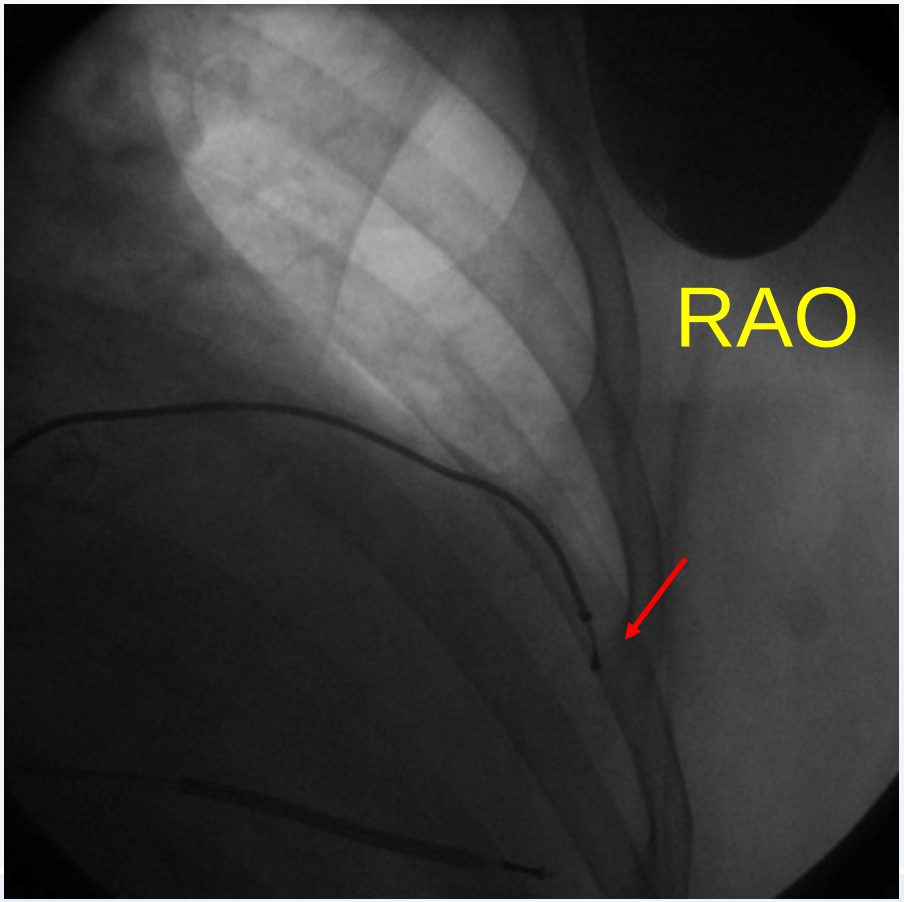
Kazuistika


I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
25mm/s 10mm/mV 150Hz 8.0.1 12SL 237 CID: 1
EID:16 EDT: 07:02 08-DEC-2016 ORDER:

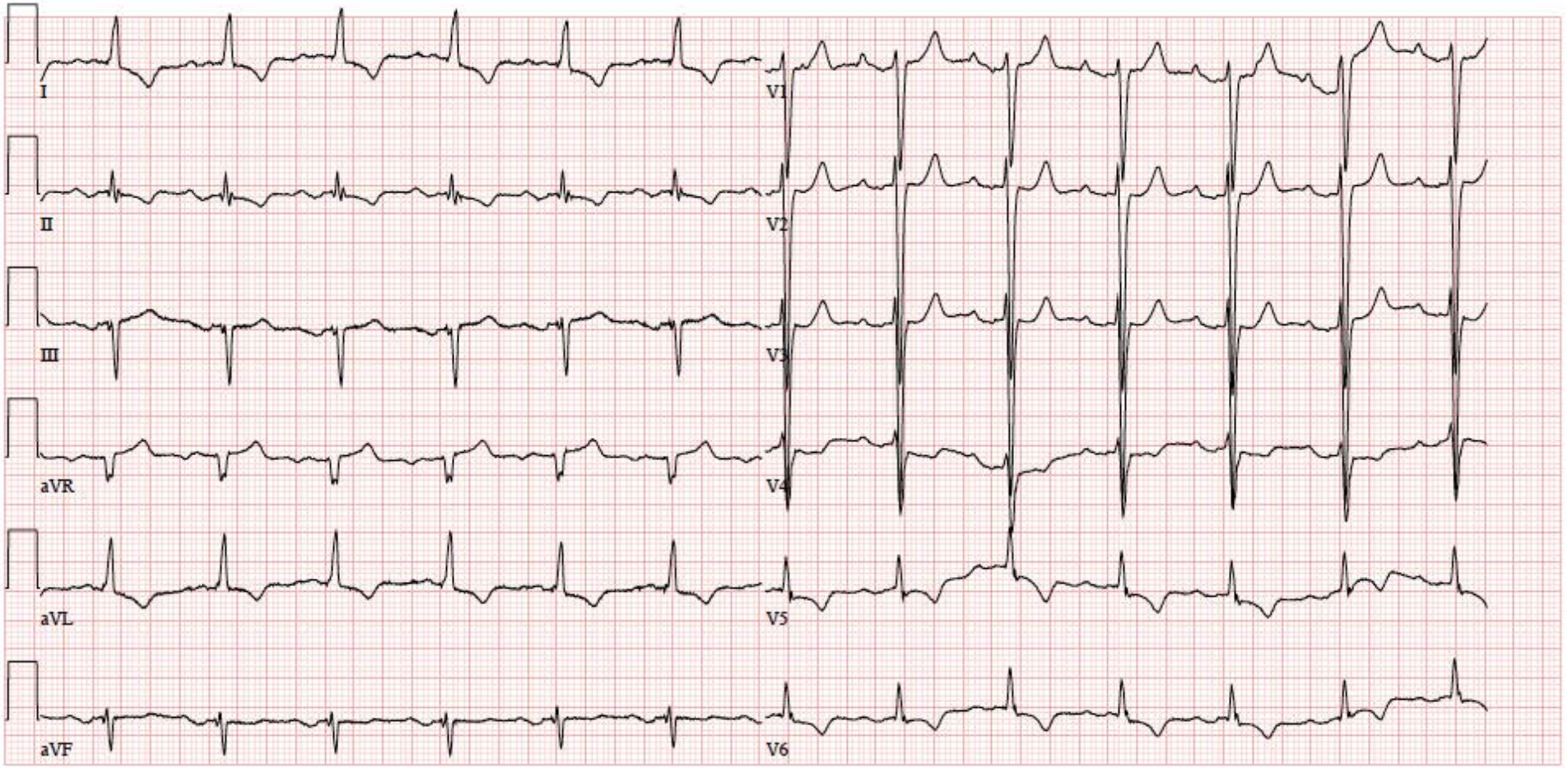

L

Kazuistika





Kazuistika



Komponenty prospěchu ze CRT (integrativní přístup)

Předimplantační– selekce pacientů

- LBBB (true-LBBB) a šíře QRS
- Absence fibrózy, jizev a dilatace
- Absence renální insuficience
- Absence významné MR

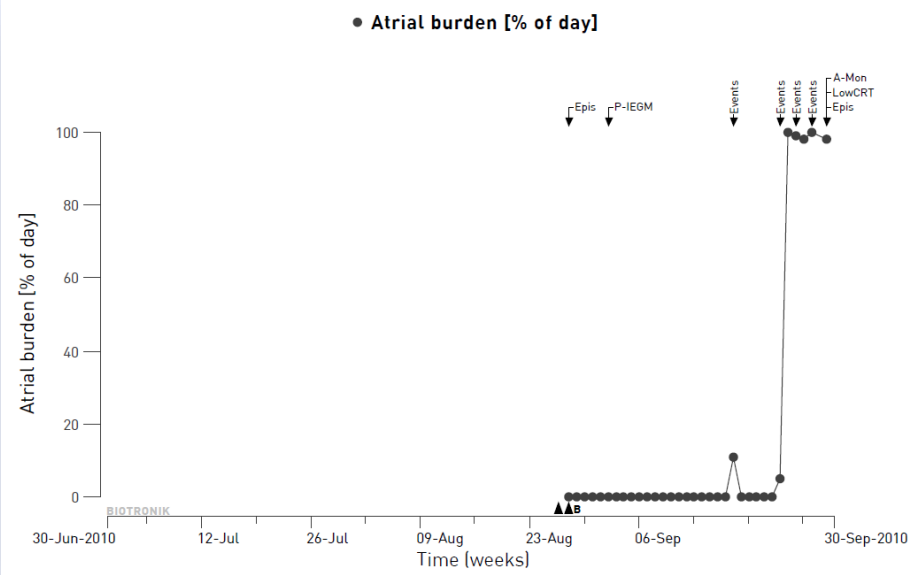
Implantační

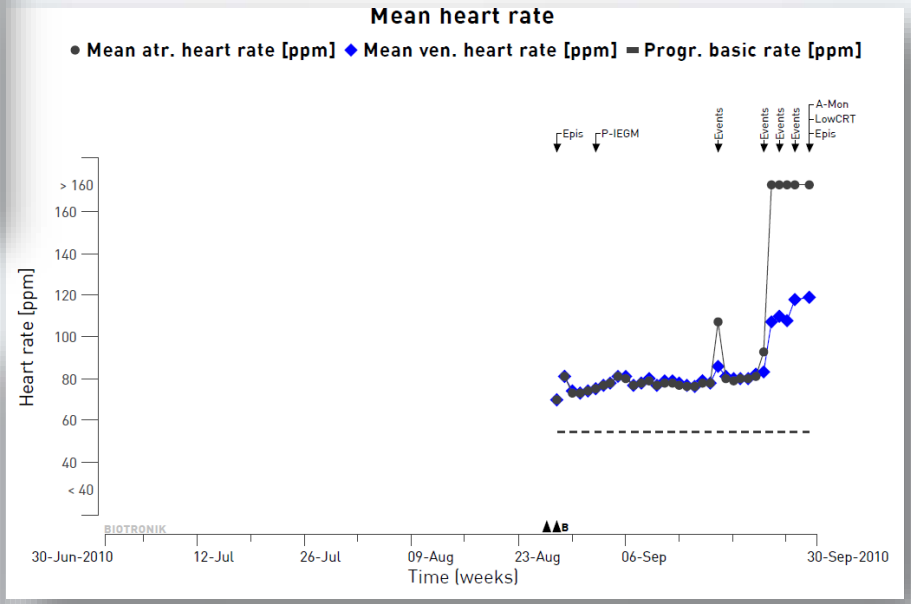
- Pozice Lk elektrody (konfigurace všech elektrod)
- Správná programace
- Minimalizace komplikací (infekcí)

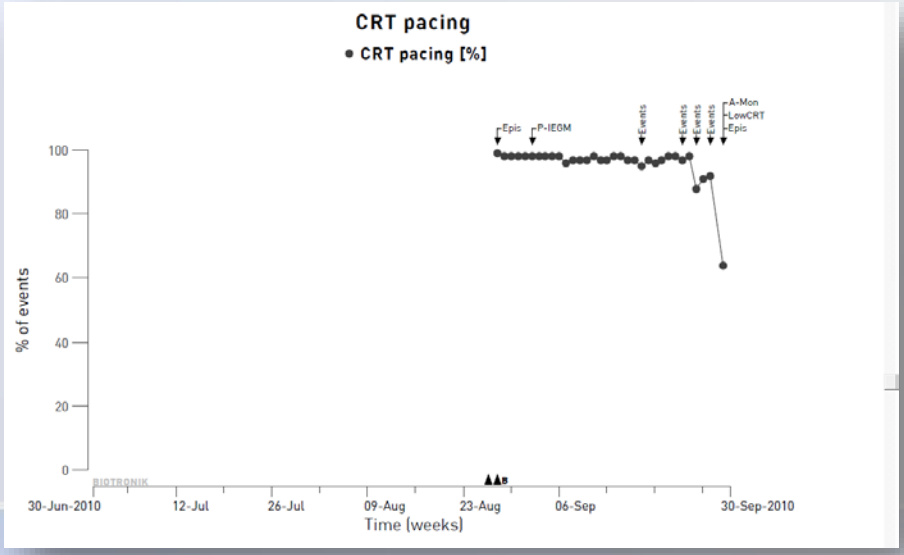
Postimplantační

- Optimalizace farmakoterapie
- % biventrikulární stimulace
- Ablace AV uzlu u pacientů s fibrilací síní
- Reprogramace
- Remote monitoring
- Optimalizace CRT přístrojovými algoritmy

Remote monitoring







Aktuální témata v CRT

Multisite pacing

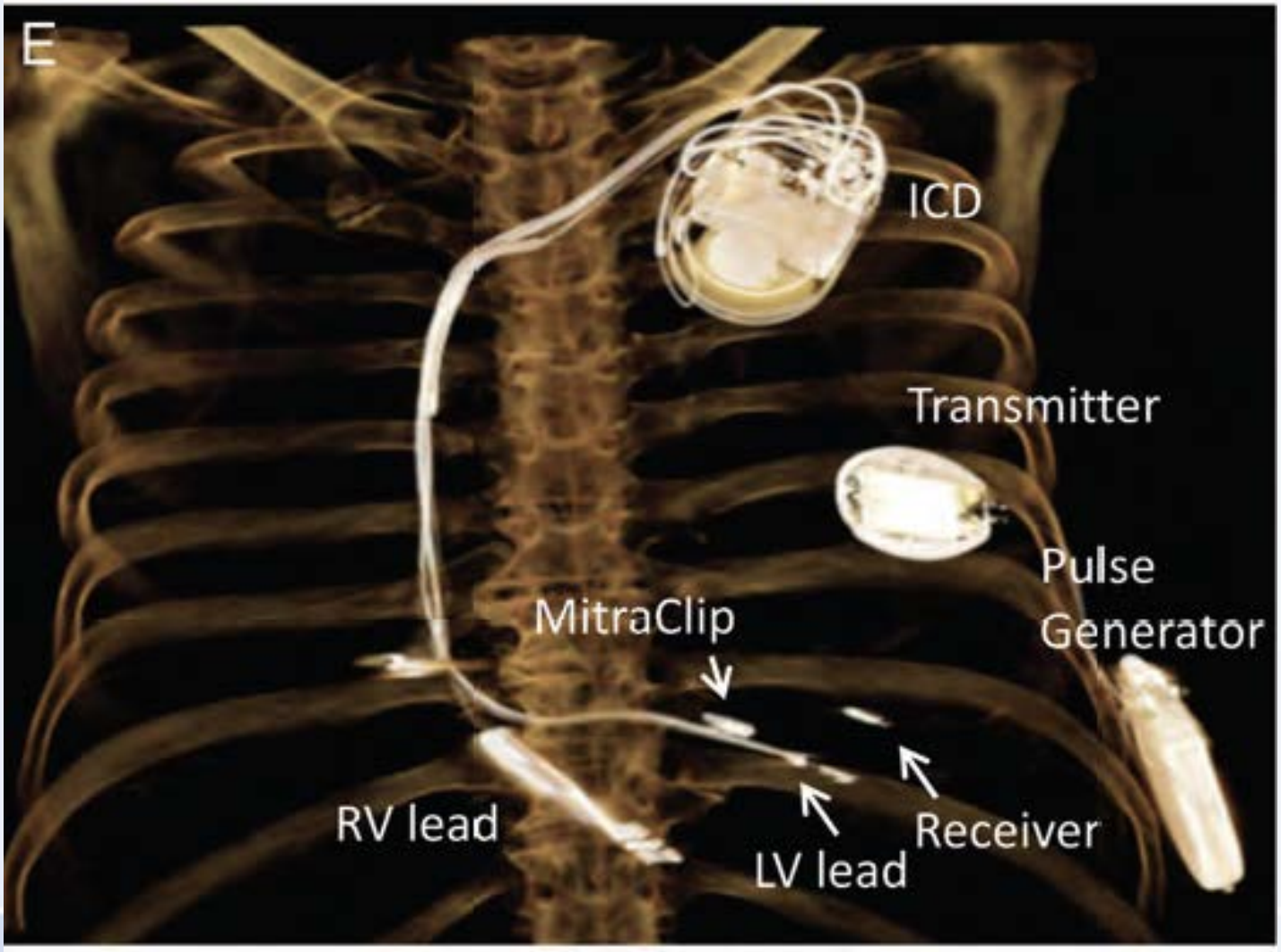
LV endokardiální stimulace – Select LV

Automatizovaná optimalizace přístrojem

Kombinované postupy k uplatnění CRT a zlepšení mitrální regurgitace

- Chirurgie
- Mitraclip
- CRT
- Terapie využívající CS

MitraClip kombinovaný s WiCS-LV



ICD

Doporučení

DANISH

Redukce neadekvátní terapie

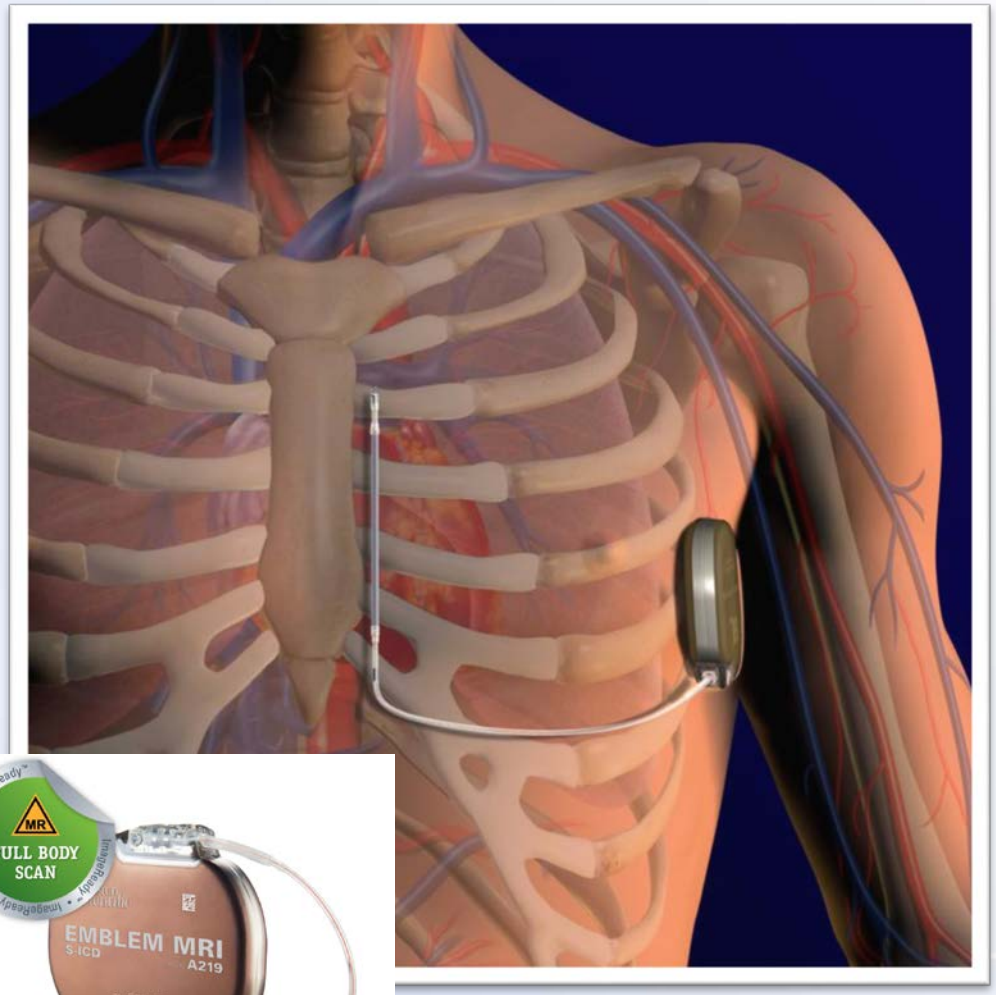
SJM alert – možné předčasné vybití baterie

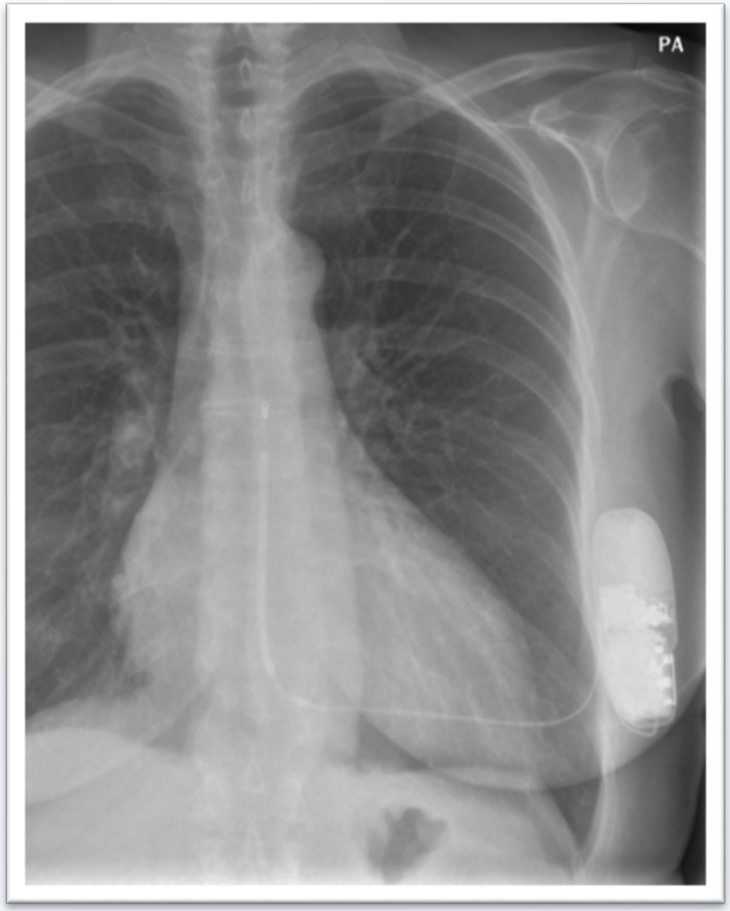
S-ICD

ICD – doporučení 2016

Recommendations	Class [a]	Level [b]
Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.	I	A
Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:		
• IHD (unless they have had an MI in the prior 40 days – see below).	I	A
• DCM.	I	B
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A
ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C

S-ICD – Emblem MRI (3. generace)





DANISH

DANISH

A DANish randomized, controlled, multicenter study to assess the efficacy of Implantable cardioverter defibrillator in patients with nonischemic Systolic Heart failure on mortality)

Lars Kober

Department of Cardiology

Rigshospitalet

University of Copenhagen

on behalf of the DANISH Study group

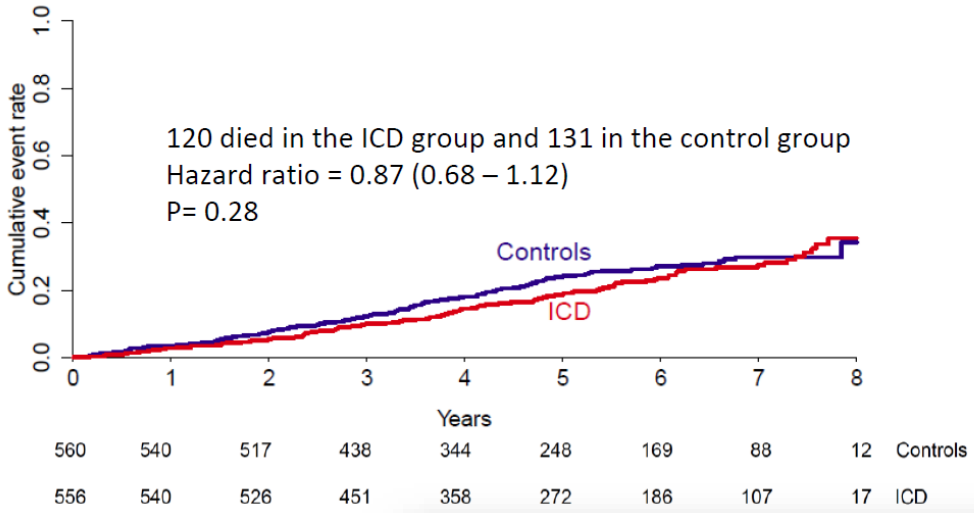
Baseline characteristics

DANISH

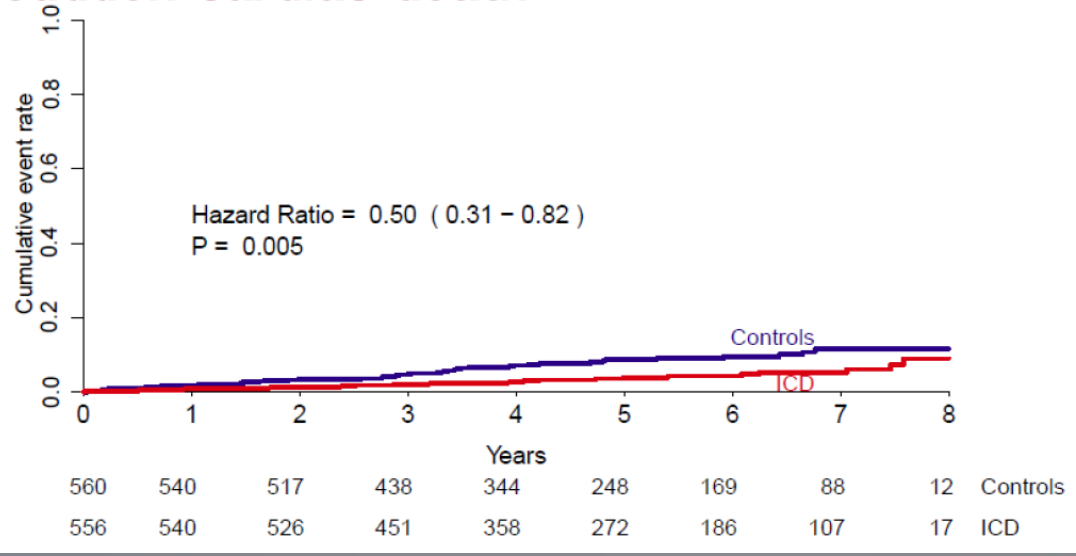
	ICD (N=556)	Control (N=560)
Age (years)	64 (56-72)	63 (56-70)
Female gender (%)	151 (27)	156 (28)
NT-proBNP (pg/ml)	1244 (616-2321)	1110 (547-2166)
LVEF (%)	25 (20-30)	25 (20-30)
eGFR (ml/min/1.73 m2)	74 (58-91)	73 (58-92)
NYHA II (%)	297 (53)	300 (54)
NYHA III (%)	252 (45)	253 (45)
NYHA IV (%)	7 (1)	7 (1)
Duration of HF (months)	20 (8-72)	18 (8-50)
BMI (kg/m2)	26.8 (23.9-30.5)	26.8 (23.8-30.1)
Hypertension (%)	181 (11)	167 (30)
Diabetes (%)	99 (18)	112 (20)
Perm. atrial fibr. (%)	135 (24)	113 (20)
Aetiology (%)		
Idiopathic	424 (76)	425 (76)
Hpt, valvular, other	132 (24)	135 (24)
Medications (%)		
ACEi/ARB	533 (96)	544 (97)
Beta-blocker	509 (92)	517 (92)
MRA	326 (59)	320 (57)
Planned CRT (%)	322 (58)	323 (58)

IK+E M

Primary outcome
– all-cause mortality



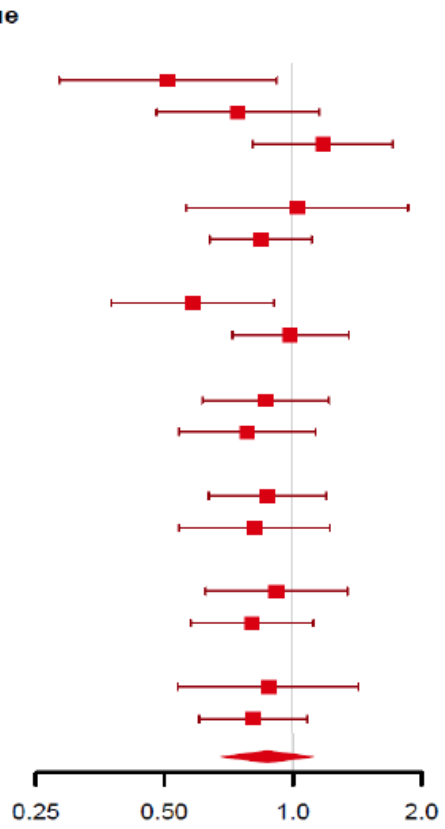
Secondary outcome
– sudden cardiac death



Subgroup analysis: all-cause mortality

DANISH

Subgroup	ICD	Control	HR	P value	P value
Age					**0.009**
<59 years	17/167	34/181	0.51 (0.29–0.92)	0.02	
≥59 – <68 years	36/173	50/202	0.75 (0.48–1.16)	0.19	
≥68 years	67/216	47/177	1.19 (0.81–1.72)	0.38	
Gender					**0.66**
Women	22/151	23/156	1.03 (0.57–1.87)	0.92	
Men	98/405	108/404	0.85 (0.64–1.12)	0.24	
NT-proBNP					**0.06**
<1177 pg/mL	32/266	74/268	0.59 (0.38–0.91)	0.02	
≥1177 pg/mL	57/292	88/290	0.99 (0.73–1.36)	0.96	
LV ejection fraction					**0.69**
<25%	70/264	65/242	0.87 (0.62–1.22)	0.42	
≥25%	50/292	66/318	0.79 (0.54–1.14)	0.21	
eGFR					**0.86**
<73 mL/min/1.73m²	75/272	80/278	0.88 (0.64–1.21)	0.42	
≥73 mL/min/1.73m²	45/283	50/280	0.82 (0.55–1.23)	0.33	
NYHA functional class					**0.71**
II	52/297	54/300	0.92 (0.63–1.35)	0.68	
III–IV	68/259	77/260	0.81 (0.58–1.13)	0.21	
Heart failure duration					**0.73**
<18 months	31/254	36/277	0.88 (0.54–1.43)	0.61	
≥18 months	89/301	95/283	0.81 (0.61–1.09)	0.17	
Overall			**0.87 (0.68–1.12)**	**0.28**	



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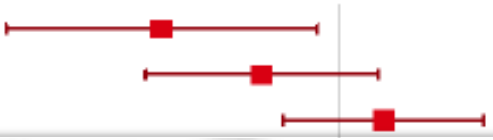

SJM riziko předčasného vybití baterie

Říjen 2016: SJM ICD family battery advisory alert (350 tis. celosvětově)
Příčina: interní zkrat v lithiové baterii
Vybití: v řádu týdnů (někdy i hodin?)

IKEM:

Identifikace všech postižených
Implantace: 528 pacientů 24.8. 2010 – 12.10 2016
81 pacientů již zemřelo (15,5 %)
28 pacientů po transplantaci srdce
38 pacientů je sledováno v jiném centru
414 žijících pacientů s rizikovým implantátem
170 pacientů vysoce rizikových (depence, KT)
1 pacient s vybitým přístrojem, 1 pacient s náhlým poklesem životnosti baterie

Řešení: informace pacientů, vibrační alert, Merlin, výměny

Závěr

CRT: indikace víceméně zůstávají stejné

Otazný benefit u non-LBBB, možnost zhoršení stavu u štíhlého QRS (do 150 ms)

Vývoj: multisite, kombinované techniky u pacientů s MR, endokardiální pacing

ICD: nositelný (wearable) ICD (zatím ne v ČR), S-ICD
Doporučení bez významných změn
SJM battery advisory – potenciálně velký problém

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Tel.: 728-199-382