

Novas possibilidades no tratamento da insuficiência cardíaca
New possibilities in heart failure treatment

Da ressincronização à modulação da contractilidade cardíaca: realidades e mitos/ From resynchronization to modulation of cardiac contractility: realities and myths

Pedro Marques

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23 Fevereiro 2019

O que é?

A modulação da contractilidade cardíaca consiste na aplicação de estímulos elétricos em período refratário absoluto ventricular sem o objetivo de estimular.

Qual é o objetivo?

Melhorar a contractilidade do músculo cardíaco sem aumentar o consumo de O₂.

É novo?

 Heart Failure Reviews, 6, 55–60, 2001

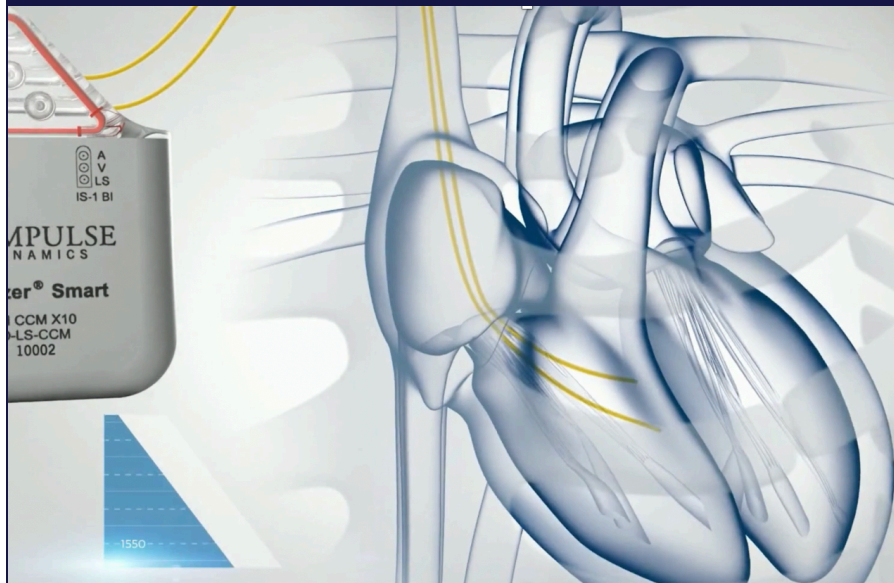
© 2001 Kluwer Academic Publishers. Manufactured in The Netherlands

Electrical Modulation of Cardiac Contractility: Clinical Aspects in Congestive Heart Failure

Carlo Pappone, MD¹, Gabriele Vicedomini, MD¹,

Como se aplica ?

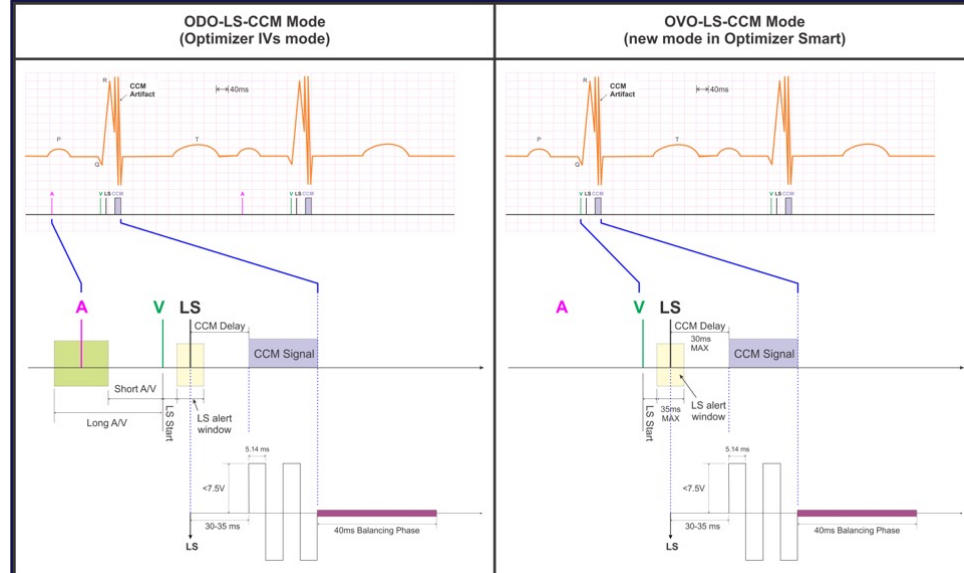
Sistema MCC



Gerador de Impulsos

2 Electrocateteres

Algoritmo de estimulação



2 estímulos bifásicos no período refratário

Amplitude 7.5V

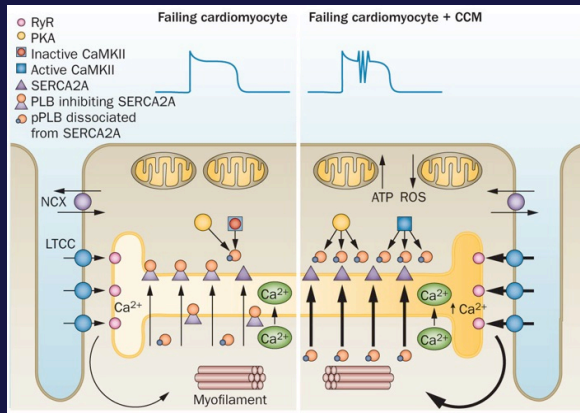
Largura 20 ms

Carregador do Optimizer – Carregamento semanal – Vida estimada 6 anos

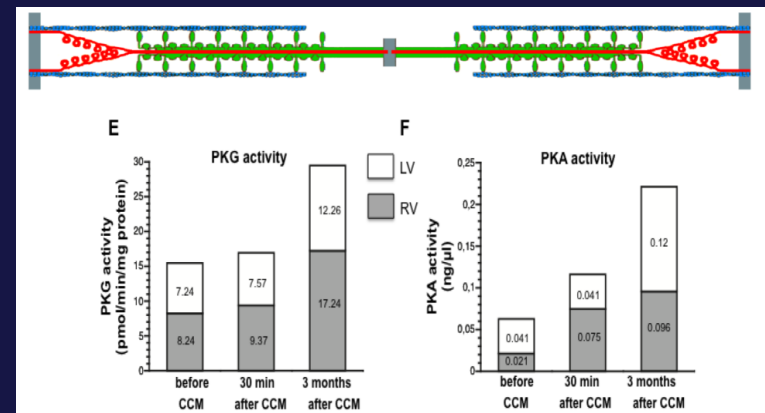


Como atua a Modulação da Contractilidade Cardíaca?

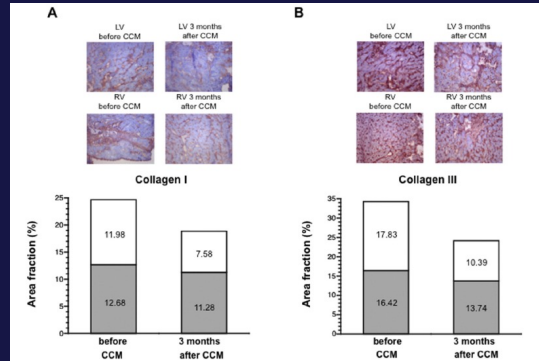
Regulação do Metabolismo do Cálcio



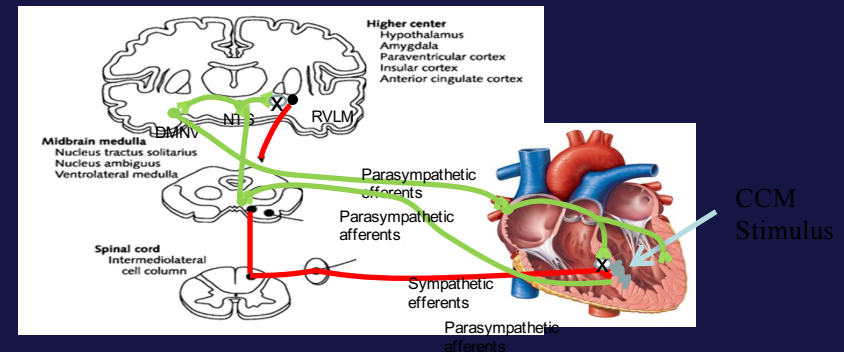
Fosforilação dos Miofilamentos



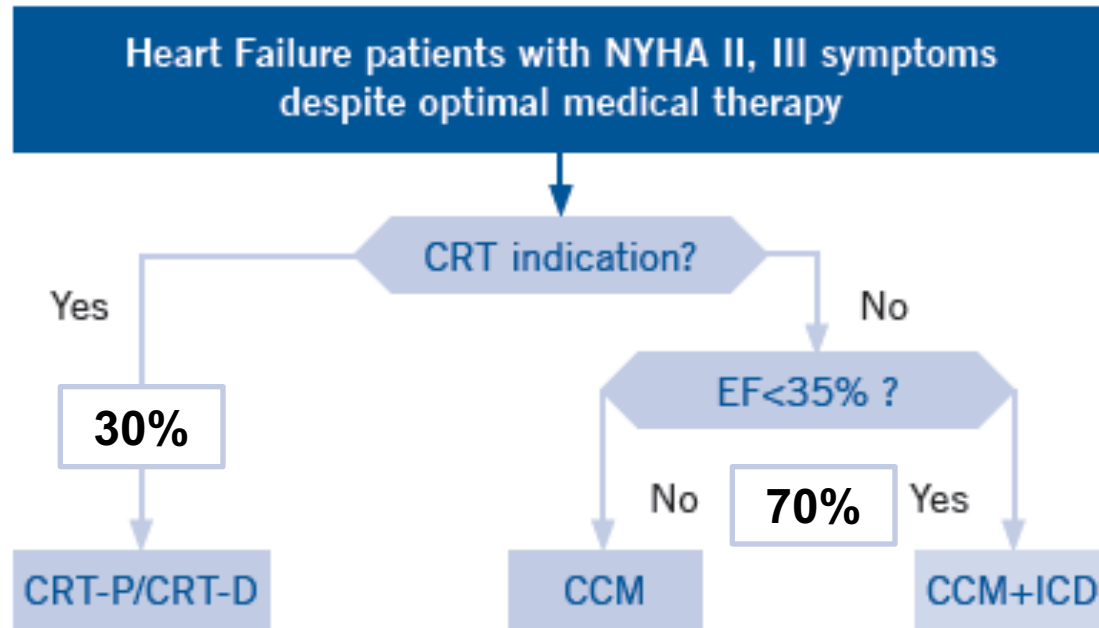
Redução da Fibrose Cardíaca



Balanceamento do S. Nervoso Autônomo



Indicações:



A modulação da Contractilidade Cardíaca estaria indicada em doentes com insuficiência cardíaca sintomática compromisso de função e QRS<130ms.

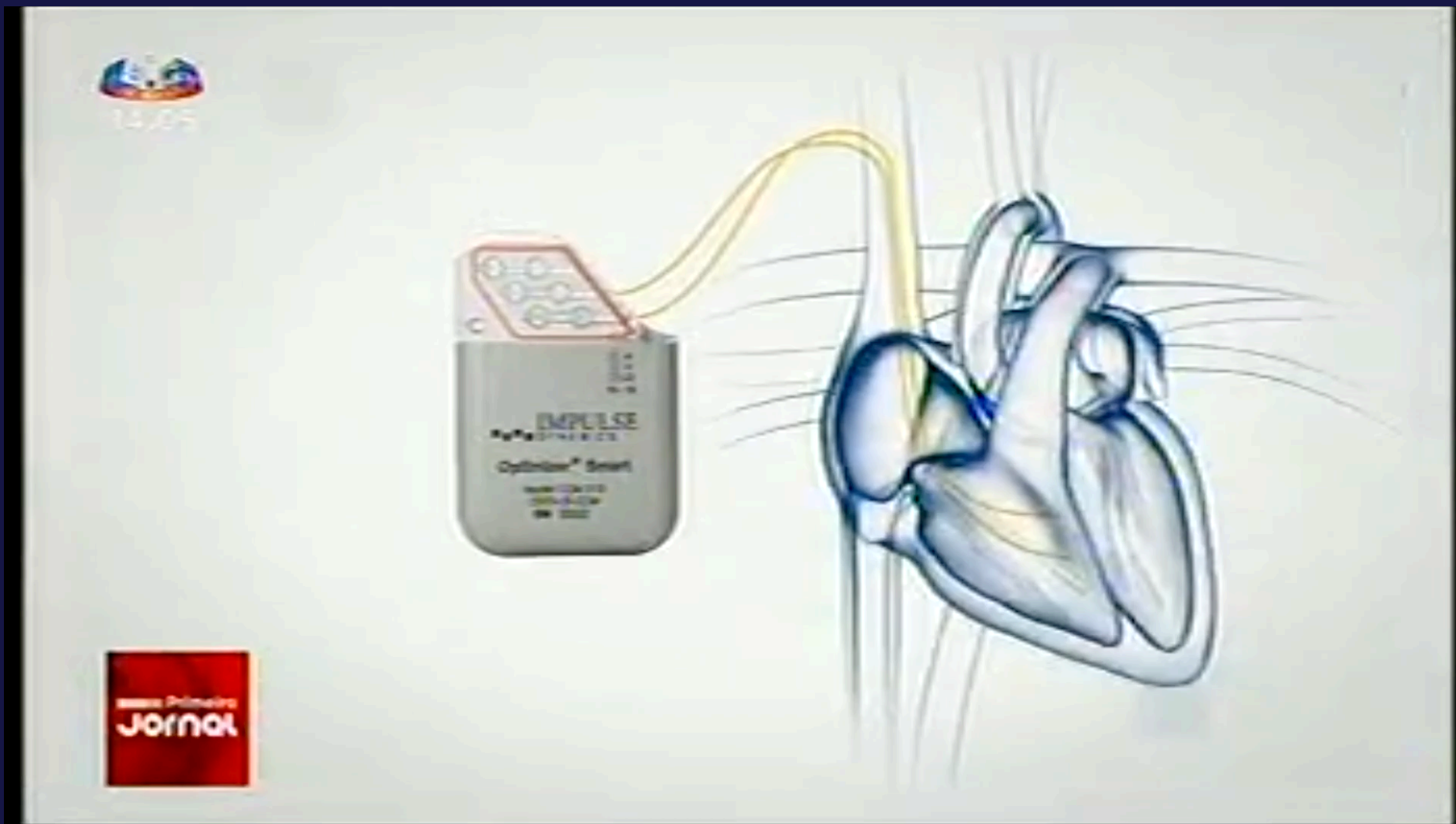
Quais os resultados dos estudos clínicos randomizados?

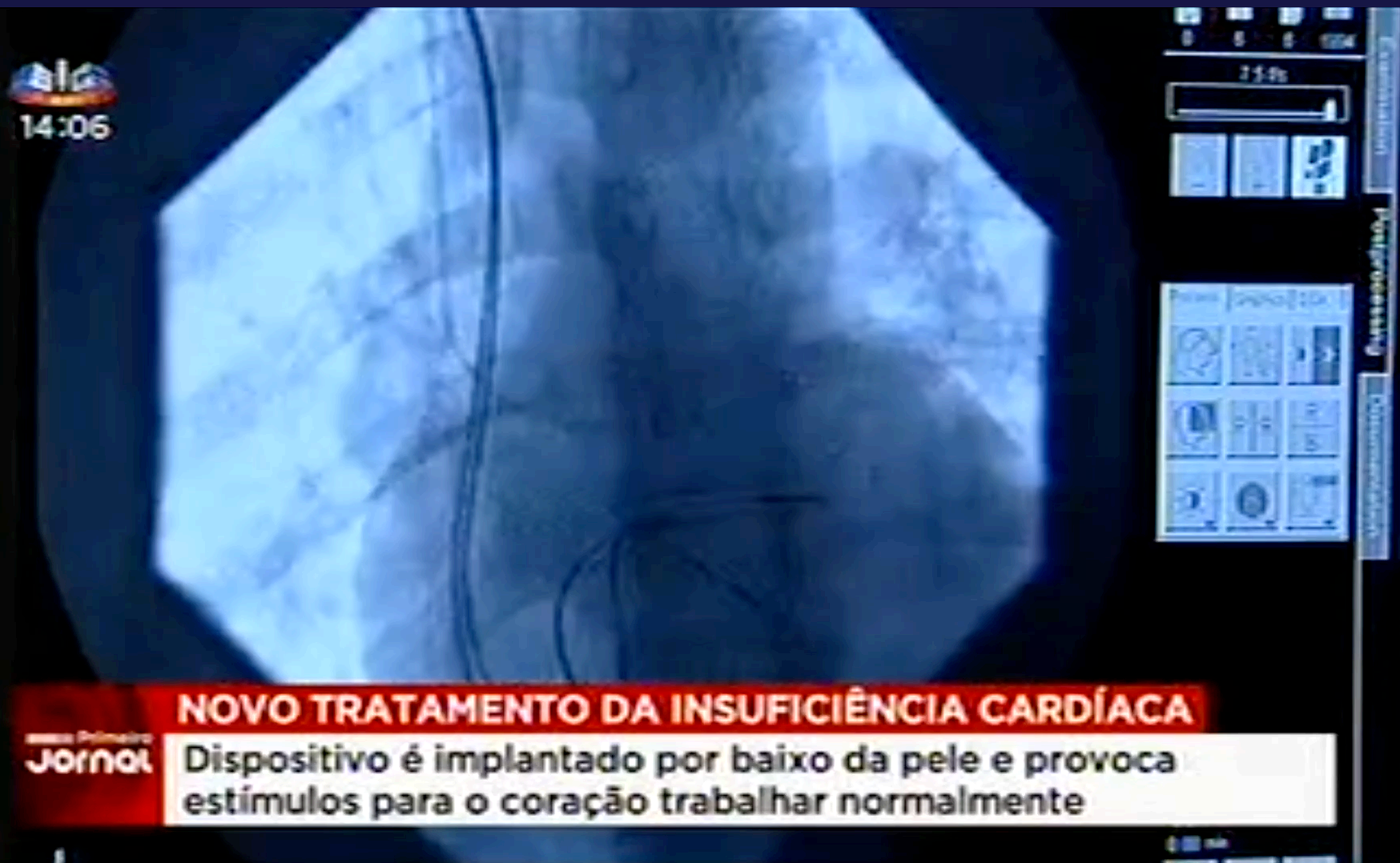
Redução da Mortalidade e das Hospitalizações?

Melhoria da capacidade funcional avaliada por peak VO2

Melhoria da Qualidade de vida avaliada MLHFQ

Reverse Remodeling avaliada por ecocardiograma?







European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Cardiac contractility modulation (CCM) is similar in its mode of insertion to CRT, but it involves non-excitatory electrical stimulation of the ventricle during the absolute refractory period to enhance contractile performance without activating extra systolic contractions. CCM has been evaluated in patients with HFrEF in NYHA Classes II–III with normal QRS duration (<120 ms).^{221,222} An individual patient data meta-analysis demonstrated an improvement in exercise tolerance (peak VO_2) and quality of life (Minnesota Living with Heart Failure questionnaire). Thus CCM may be considered in selected patients with HF. The effect of CCM on HF morbidity and mortality remains to be established.

Cardiac contractility modulation improves long-term survival and hospitalizations in heart failure with reduced ejection fraction



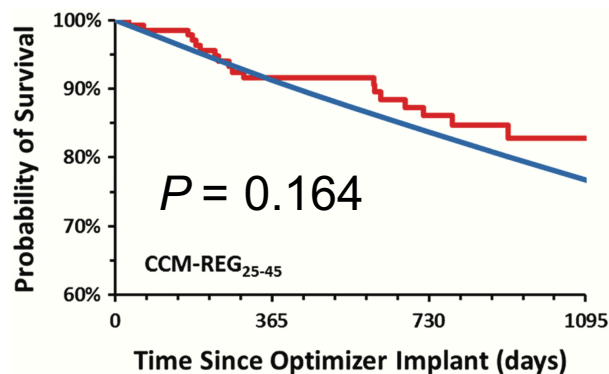
ESC
European Society
of Cardiology

European Journal of Heart Failure (2019)
doi:10.1002/ehf.1374

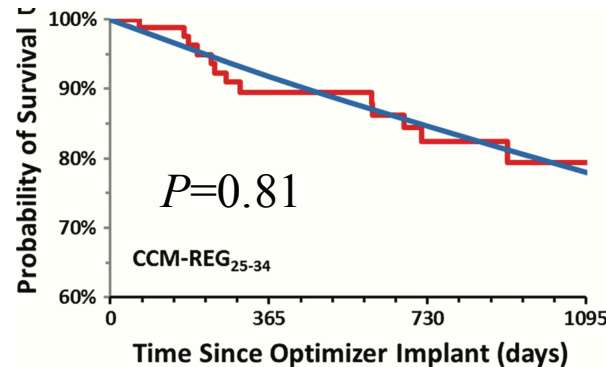
Registo Prospetivo Multicentrico 140 doentes

Mortalidade vs Mortalidade prevista Seattle Heart Failure Model (SHFM)

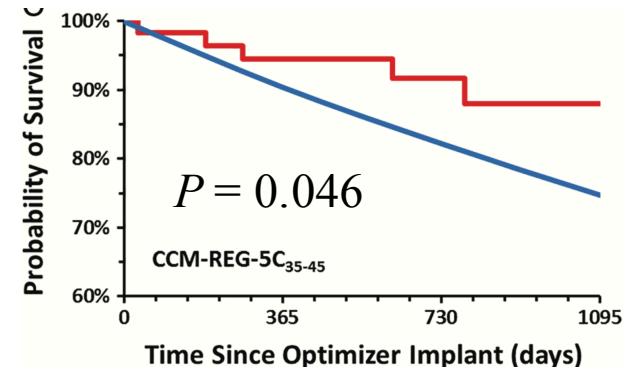
Doentes Fej basal 25-45%



Doentes Fej basal 25-34%



Doentes Fej basal 35-45%



Cardiac contractility modulation improves long-term survival and hospitalizations in heart failure with reduced ejection fraction

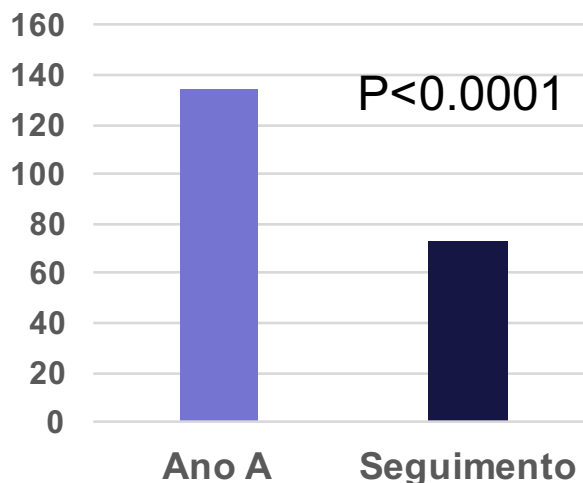


European Journal of Heart Failure (2019)
doi:10.1002/ehf.1374

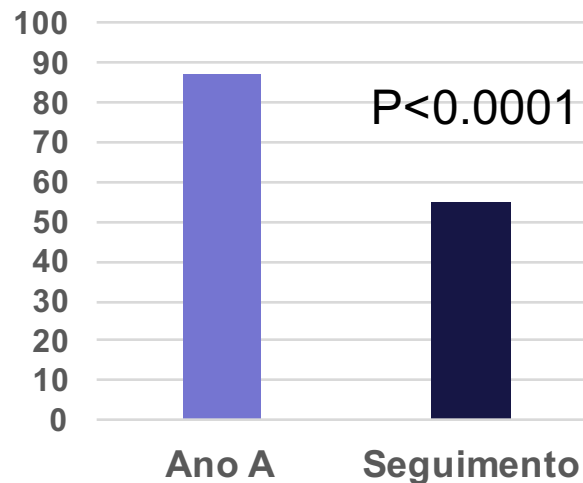
Registo Prospetivo Multicentrico 140 doentes

Internamentos por IC vs Internamentos no ano anterior

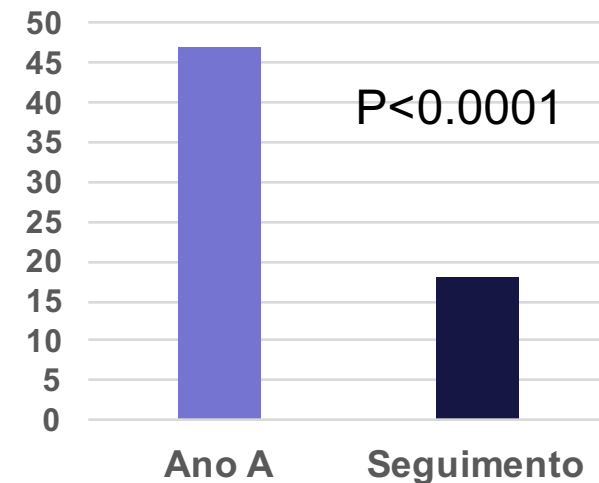
Doentes Fej basal 25-45%



Doentes Fej basal 25-34%



Doentes Fej basal 35-45%



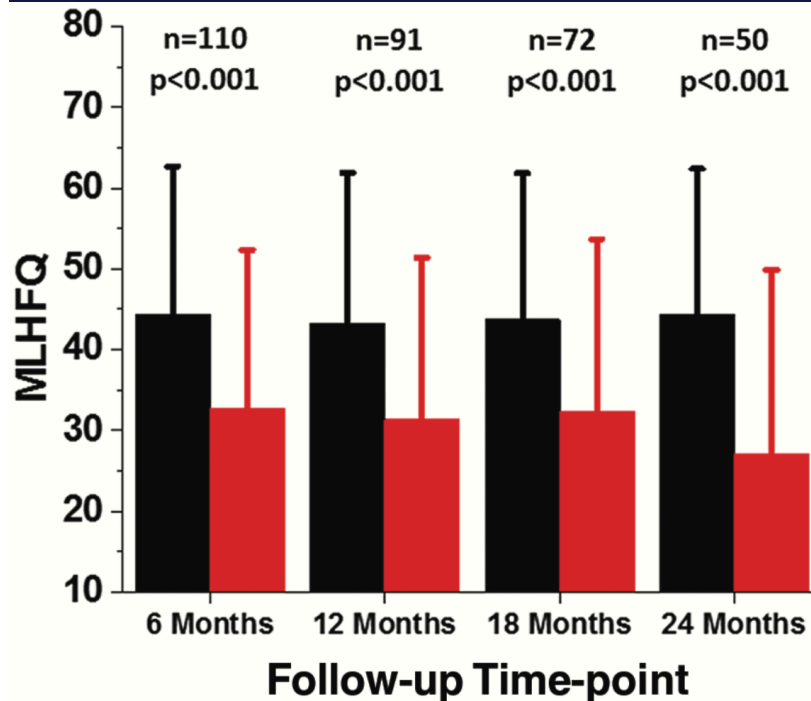
Cardiac contractility modulation improves long-term survival and hospitalizations in heart failure with reduced ejection fraction



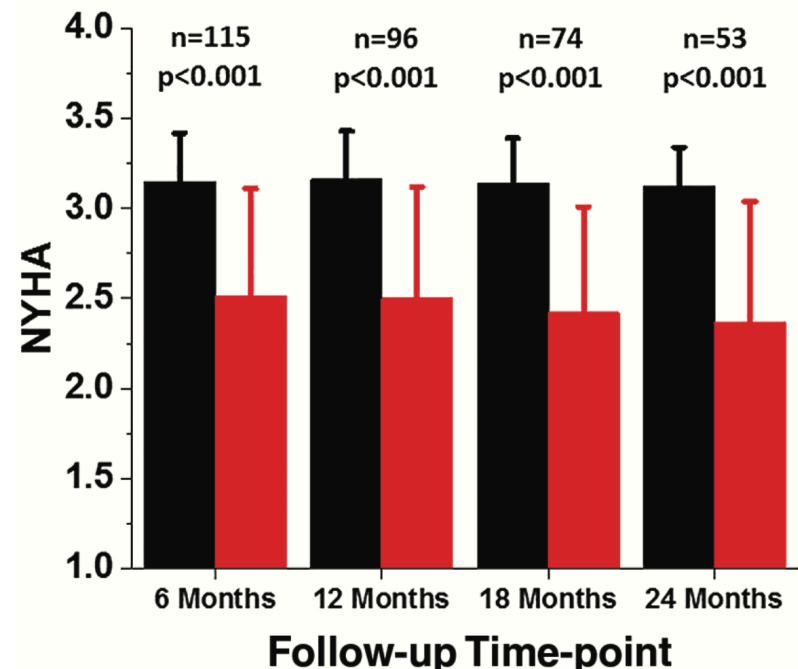
European Journal of Heart Failure (2019)
doi:10.1002/ehf.1374

Registo Prospetivo Multicentrico 140 doentes

Qualidade de Vida



Classe Funcional



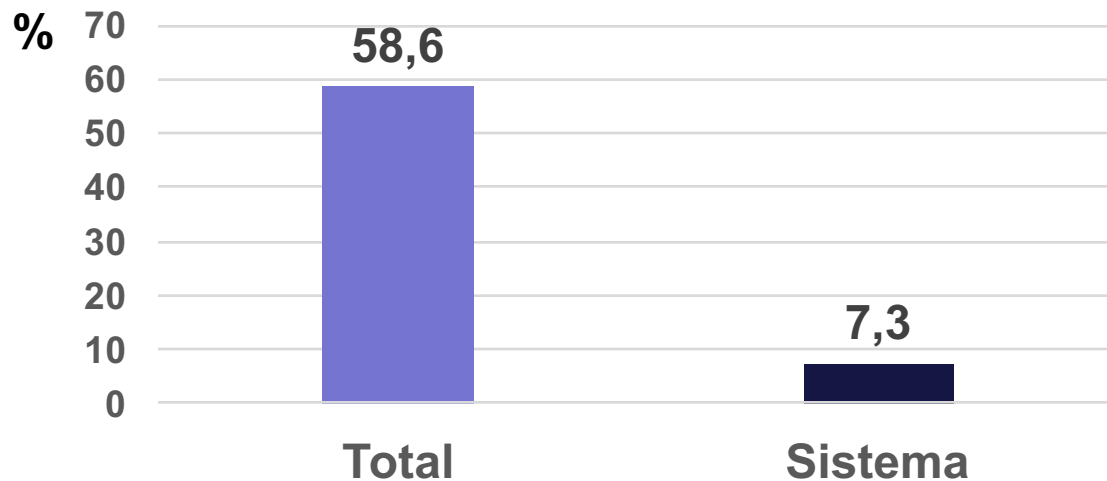
Cardiac contractility modulation improves long-term survival and hospitalizations in heart failure with reduced ejection fraction



European Journal of Heart Failure (2019)
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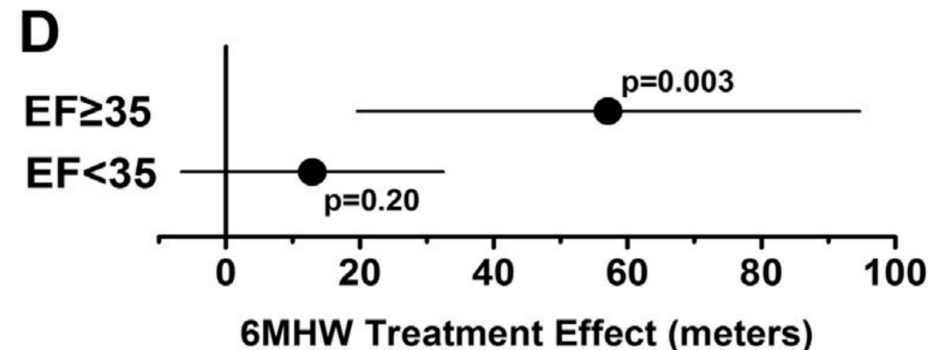
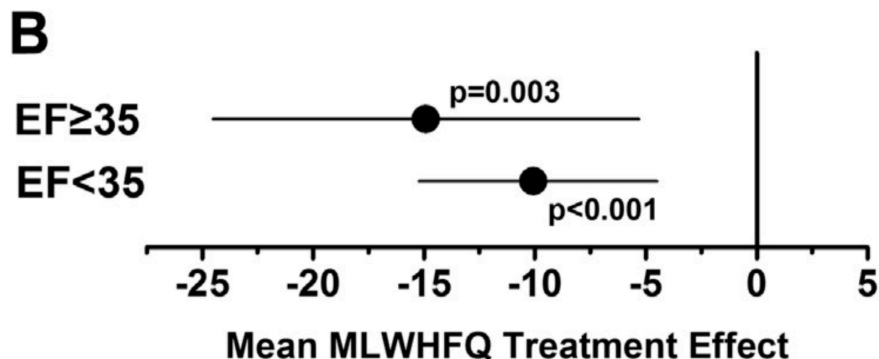
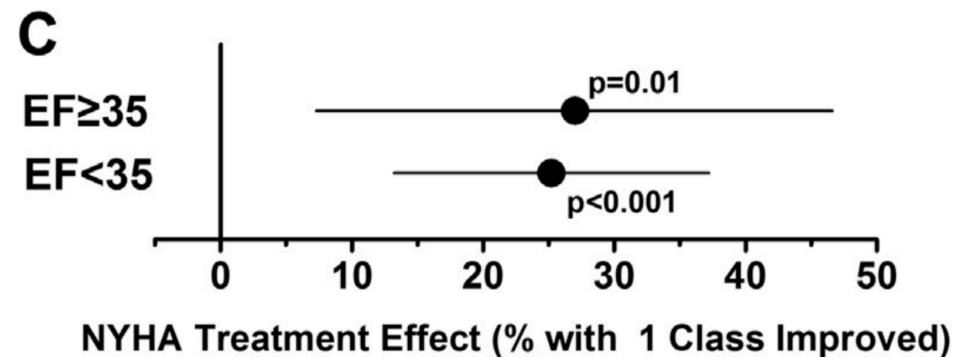
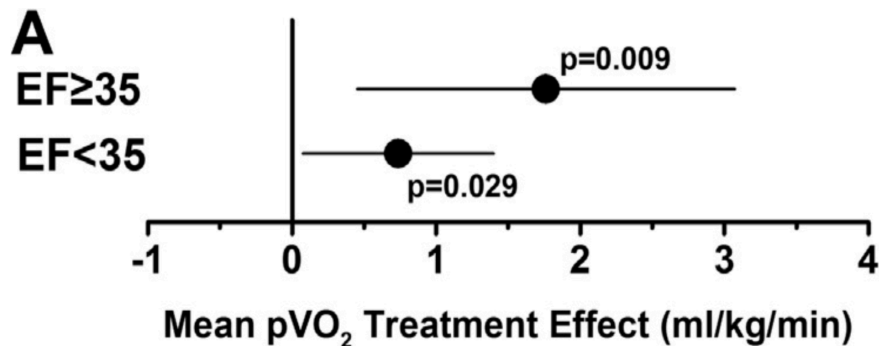
Registo prospetivo Multicentrico 140 doentes

Eventos Adversos Graves



A Randomized Controlled Trial to Evaluate the Safety and Efficacy of Cardiac Contractility Modulation

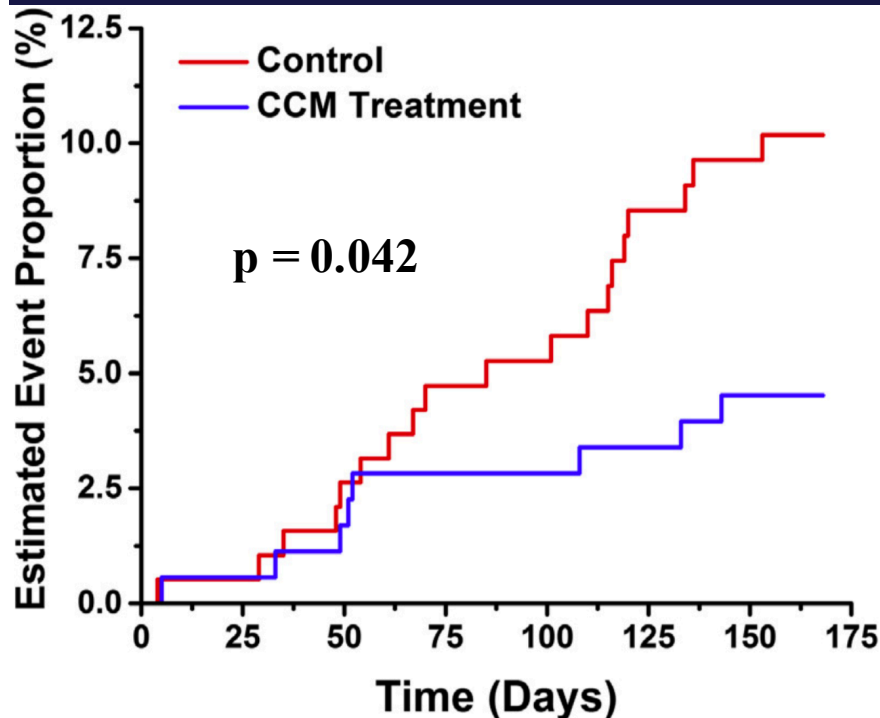
Estudo Randomizado MCC vs TMO - 160 doentes NYHA II e III QRS<130ms



A Randomized Controlled Trial to Evaluate the Safety and Efficacy of Cardiac Contractility Modulation

Estudo Randomizado MCC vs TMO - 160 doentes NYHA II e III QRS<130ms

Mortalidade e Hospitalização IC



Sobrevida MCC 98%
Sobrevida TMO 95%
pNS

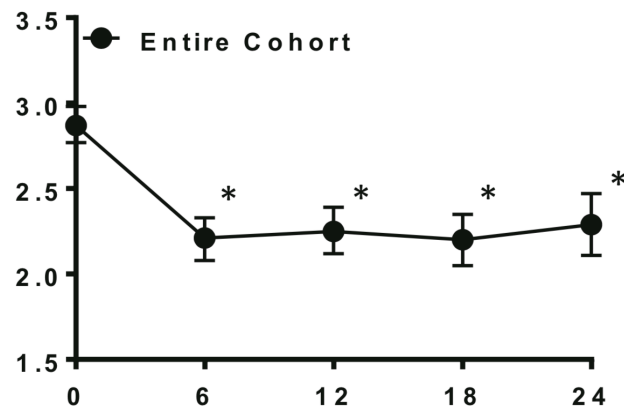
Ausência HIC MCC 78%
Ausência HIC TMO 78%
pNS

MCC 2 Mortes
TMO 4 Mortes
1-Pós Ablação TV
2-TEP pós Op

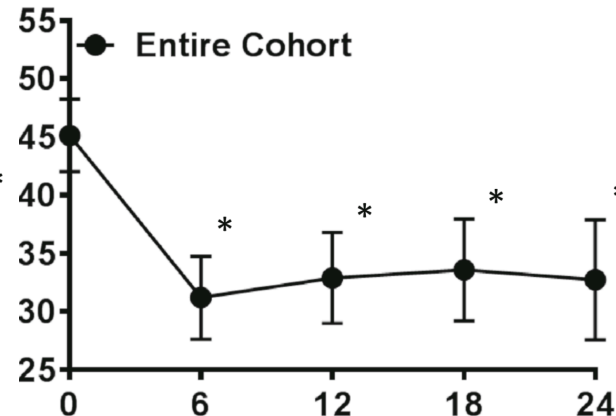
Clinical effects of long-term cardiac contractility modulation (CCM) in subjects with heart failure caused by left ventricular systolic dysfunction

Registo Multicêntrico – 143 doentes – Seguimento 24 meses

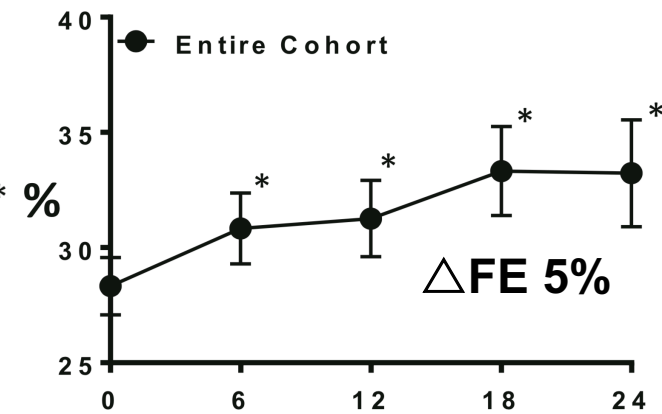
Classe NYHA



MLWHFQ Score



Fração Ejeção



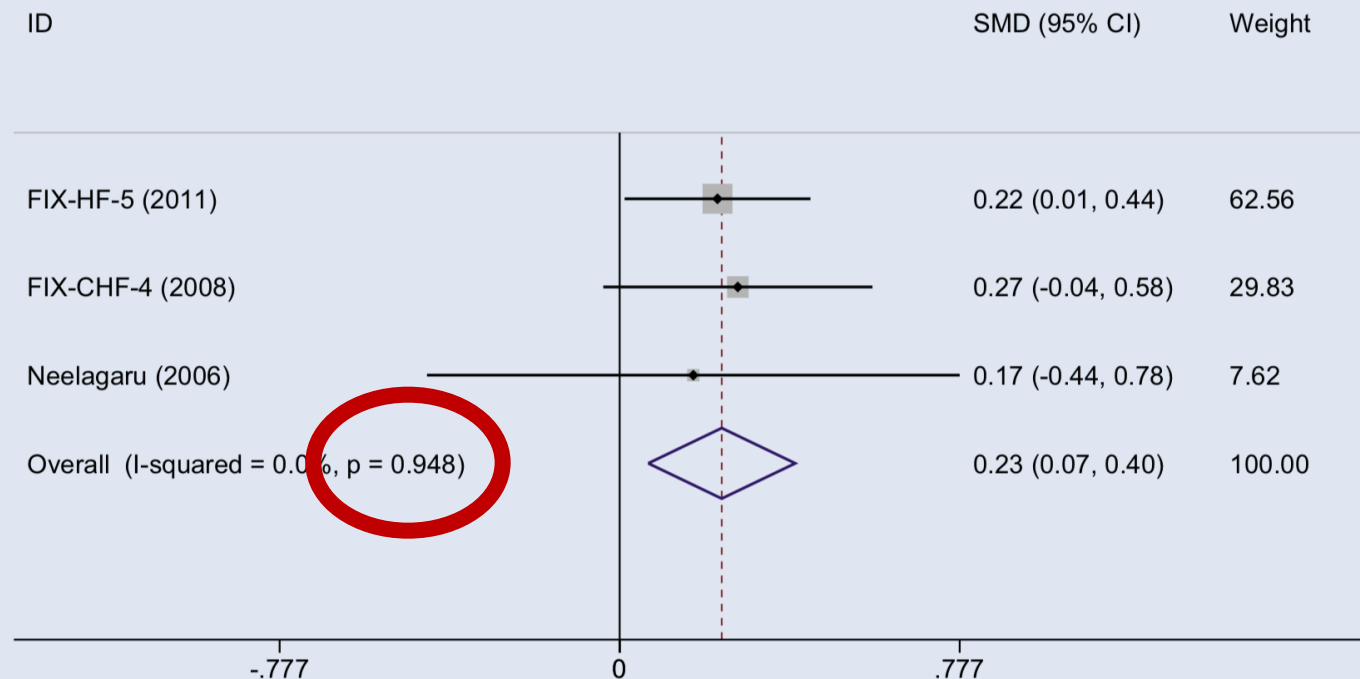
Efeitos Adversos Graves relacionados com o Sistema 17%

The safety and efficacy of cardiac contractility modulation in heart failure

A meta-analysis of clinical trials

Meta-análise 4 estudos
723 Doentes

Consumo pico O₂

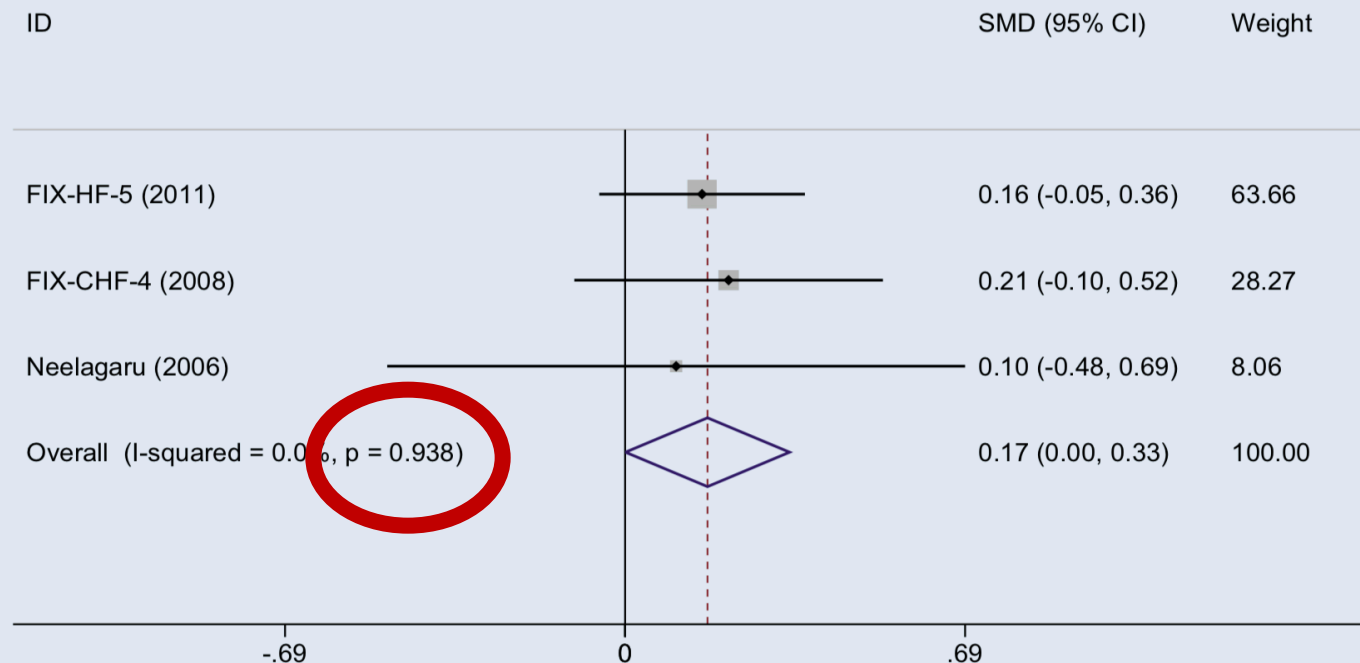


The safety and efficacy of cardiac contractility modulation in heart failure

A meta-analysis of clinical trials

Meta-análise 4 estudos
723 Doentes

Prova de Marcha 6 min

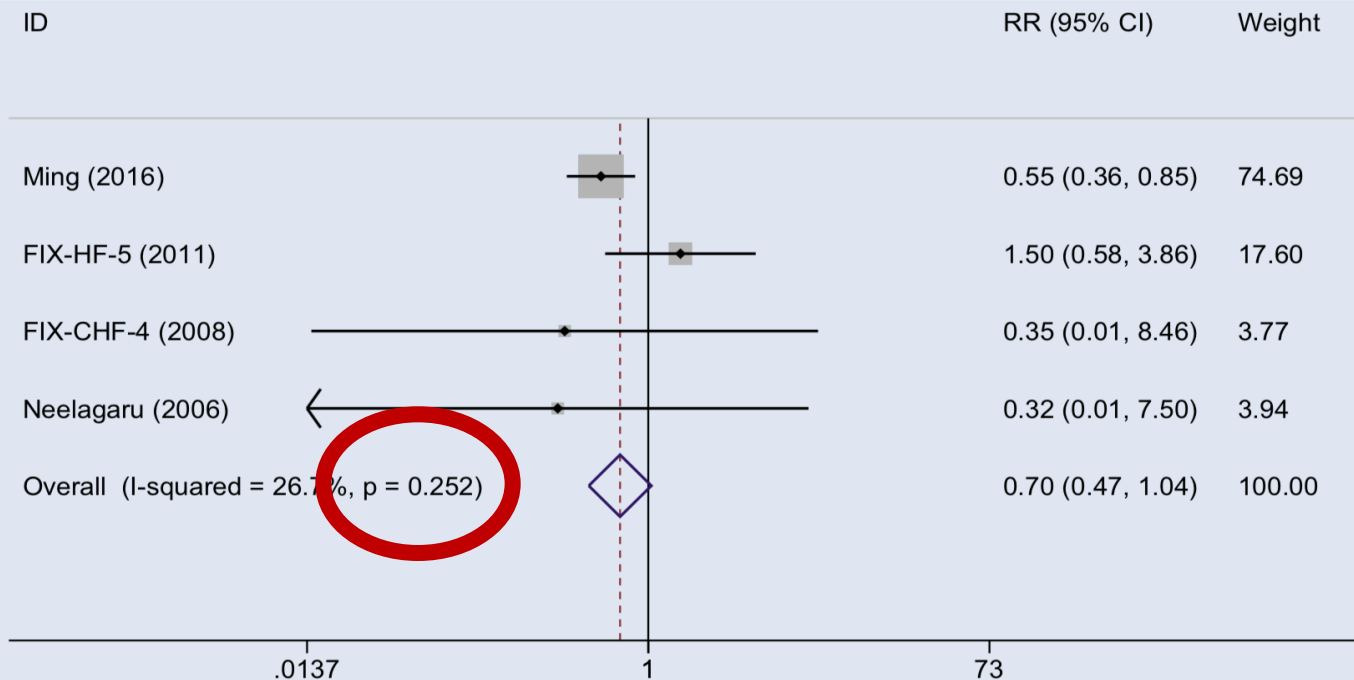


The safety and efficacy of cardiac contractility modulation in heart failure

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723 Doentes

Mortalidade Global

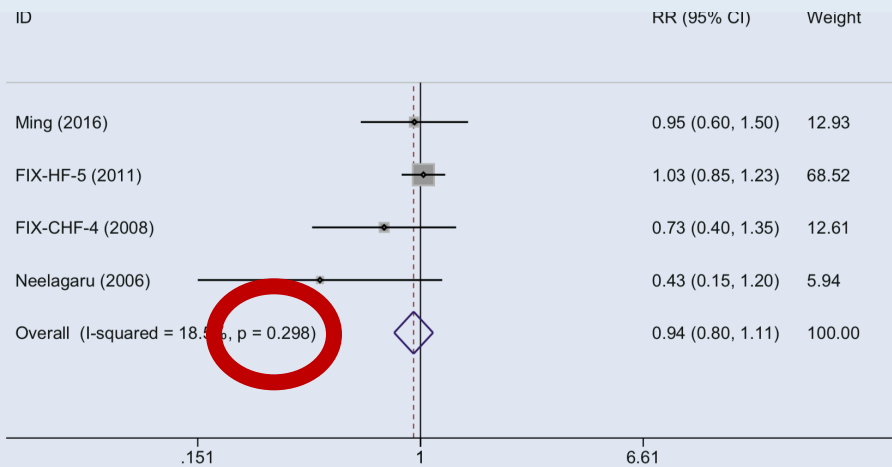


The safety and efficacy of cardiac contractility modulation in heart failure

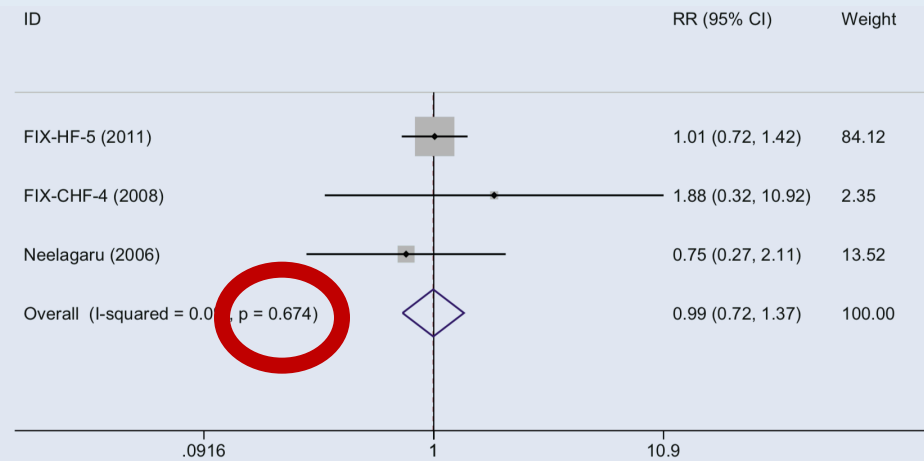
A meta-analysis of clinical trials

Meta-análise 4 estudos 723 Doentes

Internamentos Global



Agravamento IC



Conclusão

Modulação da Contractilidade Cardíaca



European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

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2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

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O Benefício da terapêutica de ressincronização está bem fundamentado

Estudos clínicos avaliando a terapêutica de ressincronização em doentes com IC

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, randomized RV vs. LV vs. BiV, 12 months	III–IV	NA	≥150	Peak VO ₂ , 6MWD	NYHA class, QoL, hospitalizations	CRT-P improved NYHA class, QoL and 6MWD and reduced hospitalizations
MIRACLE ⁴⁹	453	Double-blinded, randomized CRT vs. OMT, 6 months	III–IV	≤35%	≥130	NYHA class, 6MWD, QoL	Peak VO ₂ , LVEDD, LVEF, MR clinical composite response	CRT-P improved NYHA class, QoL and 6MWD and reduced LVEDD, MR and increased LVEF
MIRACLE-ICD ⁵⁴	369	Double-blinded, randomized CRT-D vs. ICD, 6 months	III–IV	≤35%	≥130	NYHA class, 6MWD, QoL	Peak VO ₂ , LVEDD, LVEF, MR clinical composite response	CRT-D improved NYHA class, QoL, peak VO ₂
CONTA-CD ⁵³	490	Double-blinded randomized CRT-D vs. ICD, 6 months	II–III–IV	≤35%	≥120	NYHA class, 6MWD, QoL	LV volume, LVEF composite of mortality, VT/VF, hospitalizations	CRT-D improved 6MWD, NYHA class, QoL, reduced LV volume and increased LVEF
MIRACLE-ICD II ⁶⁰	186	Double-blinded, randomized CRT-D vs. ICD, 6 months	II	≤35%	≥130	Peak VO ₂	VE/CO ₂ , NYHA, QoL, 6MWD, LV volumes and EF, composite clinical endpoint	CRT-D improved NYHA, VE/CO ₂ and reduced LV volumes and improved LVEF

Trial (ref)	No.	Design	NYHA	LVEF	QRS	Primary endpoints	Secondary endpoints	Main Findings
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 reduce 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

Mais de 8000 doentes incluídos em estudos clínicos randomizados e aleatorizados

Recomendações para Ressincronização no Tratamento da IC

Recomendações	Classe	Nível
BRE com QRS > 150 ms em ritmo sinusal. TRC recomendada nos doentes com IC sintomática e FEj < 35% apesar da TMO para melhoria sintomática reduzir a mortalidade e morbilidade.	I	A
BRE com QRS 130-149ms em ritmo sinusal. TRC recomendada nos doentes com IC sintomática e FEj < 35% apesar da TMO para melhoria sintomática reduzir a mortalidade e morbilidade.	I	B
Não-BRE QRS > 150 ms em ritmo sinusal. TRC deve ser ponderada nos doentes com IC sintomática e FEj < 35% apesar da TMO para melhoria sintomática reduzir a mortalidade e morbilidade.	Ila	B
Não-BRE QRS 130-149ms em ritmo sinusal. TRC deve ser ponderada nos doentes com IC sintomática e FEj < 35% apesar da TMO para melhoria sintomática reduzir a mortalidade e morbilidade.	Ilb	B
Doentes em FA e QRS > 130 ms. TRC deve ser ponderada em doentes com IC classe III-IV de NYHA e FEj < 35% apesar da TMO para melhoria sintomática reduzir a mortalidade e morbilidade, desde que exista uma estratégia que assegure pacing BiV ou seja espectável regresso a ritmo sinusal.	Ila	B
Portadores de CDI ou pacemaker. Upgrade para TRC deve ser considerado nos doentes com elevada percentagem de pacing e agravamento da IC apesar da TMO. Não se aplica a doentes com IC estável.	Ilb	B
A TRC está contra-indicada nos doentes com QRS < 130 ms.	III	A

Recomendações para Ressincronização no Tratamento da IC

Terapêutica Médica Otimizada

$QRS > 130 \text{ ms}$ e $FEj < 35\%$

**Ritmo sinusal e IC sintomática
ou
FA e IC classe III ou IV da NYHA**

**Portadores de pacemaker ou CDI
com elevada percentagem de
pacing e agravamento da IC**

Objetivos Terapêuticos na IC

Melhoria Sintomática

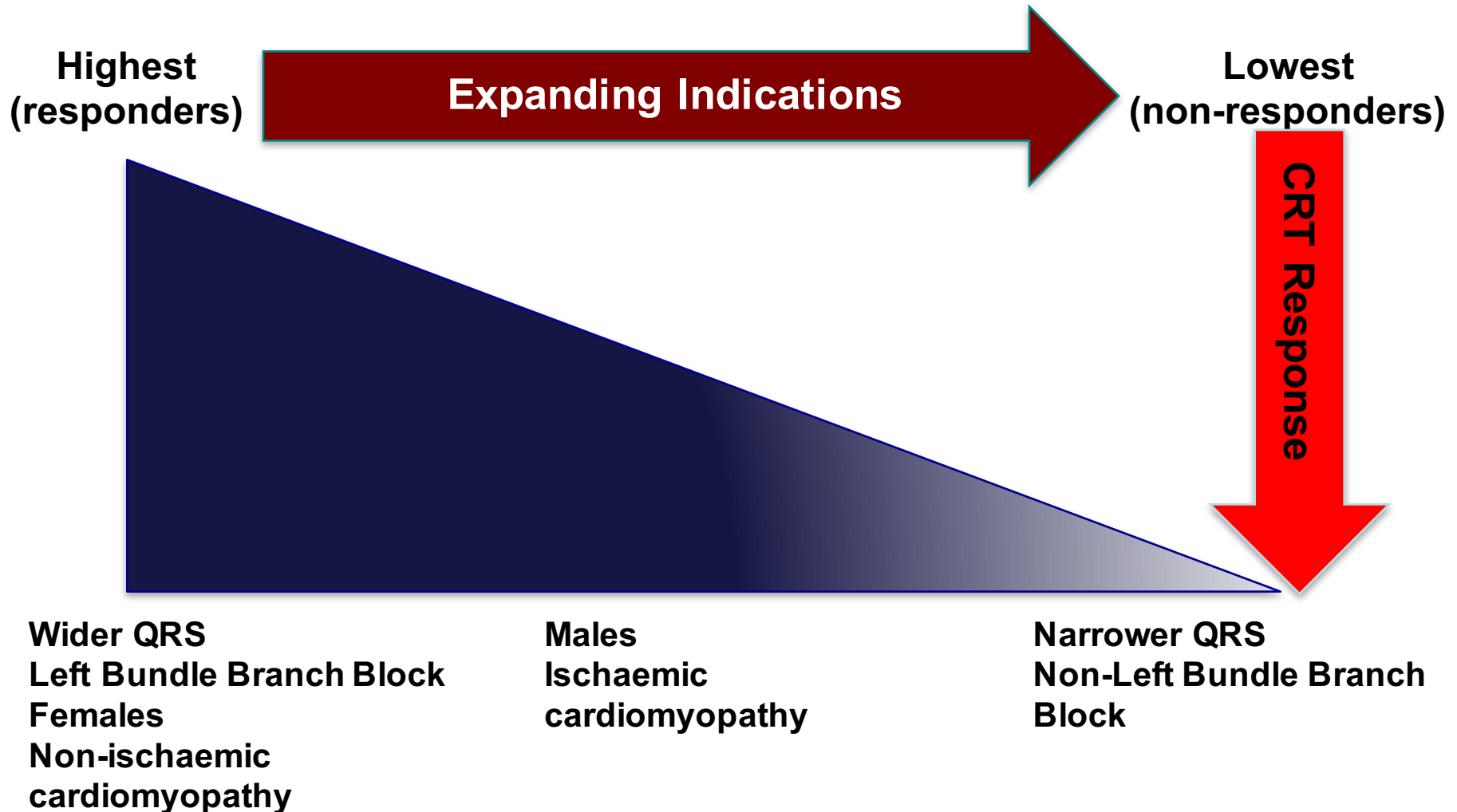
Melhoria da qualidade de vida

Diminuição das hospitalizações

Diminuição da mortalidade

Patient Selection

Magnitude of benefit from CRT



Duração do QRS

Duração do QRS



European Heart Journal (2013) 34, 3547–3556
doi:10.1093/eurheartj/ehz290

FASTTRACK CLINICAL RESEARCH

An individual patient meta-analysis of five randomized trials assessing the effects of cardiac resynchronization therapy on morbidity and mortality in patients with symptomatic heart failure

John G. Cleland^{1*}, William T. Abraham², Cecilia Linde³, Michael R. Gold⁴, James B. Young⁵, J. Claude Daubert⁶, Lou Sherfese⁷, George A. Wells⁸, and Anthony S.L. Tang⁹

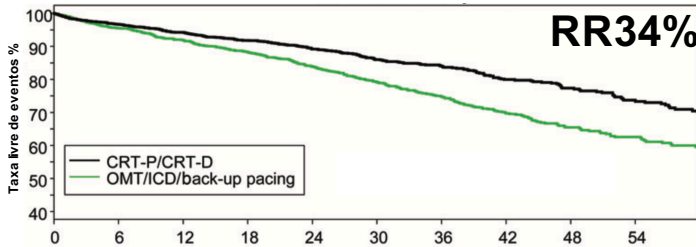
Meta-análise de 5 estudos

3872 doentes

Benefício do CRT vs TMO

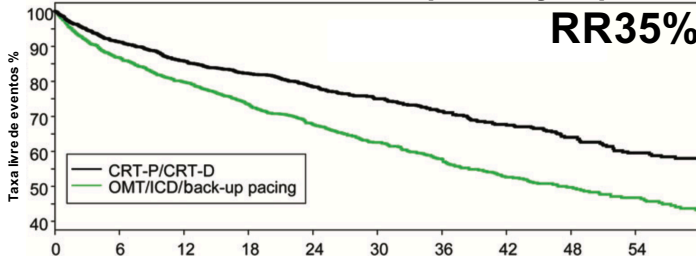
Mortalidade Global

RR34%

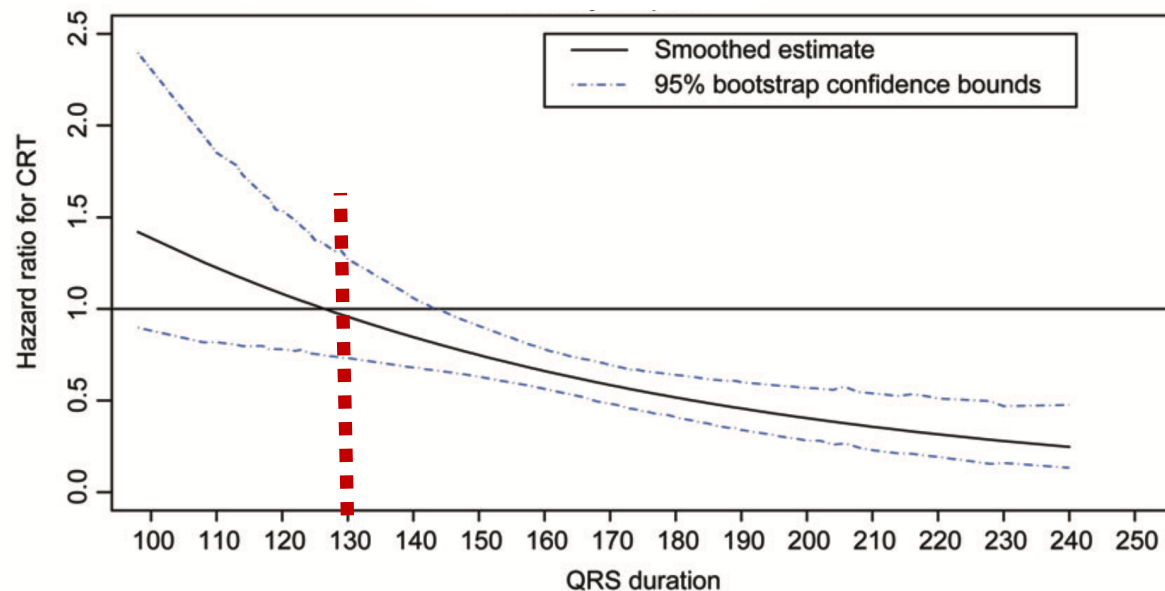


Mortalidade Global e Hospitalização por IC

RR35%



Mortalidade Global



Morfologia do QRS

Morfologia do QRS

Effectiveness of Cardiac Resynchronization Therapy by QRS Morphology in the Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy (MADIT-CRT)

Wojciech Zareba, MD, PhD; Helmut Klein, MD; Iwona Cygankiewicz, MD, PhD;
W. Jackson Hall, PhD; Scott McNitt, MS; Mary Brown, MS; David Cannom, MD;
James P. Daubert, MD; Michael Eldar, MD; Michael R. Gold, MD, PhD; Jeffrey J. Goldberger, MD;
Ilan Goldenberg, MD; Edgar Lichstein, MD; Heinz Pitschner, MD; Mayer Rashtian, MD;
Scott Solomon, MD; Sami Viskin, MD; Paul Wang, MD; Arthur J. Moss, MD;
on behalf of the MADIT-CRT Investigators

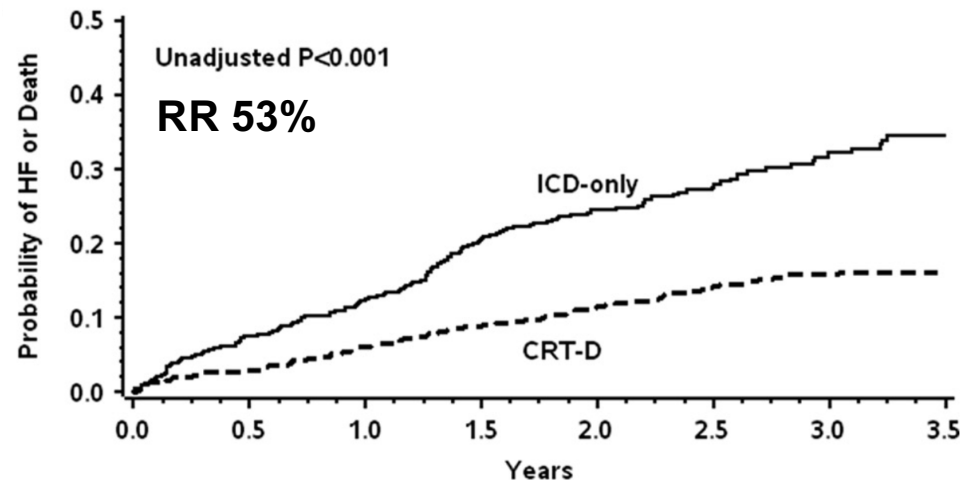
**1817 doentes Classe funcional I-II
QRS ≥ 130 ms FEje $\leq 30\%$**

**Benefício CRT-D vs CDI por
Morfologia do QRS**

Probabilidade de Morte ou HIC

CRT-D vs CDI

Doentes com BRE

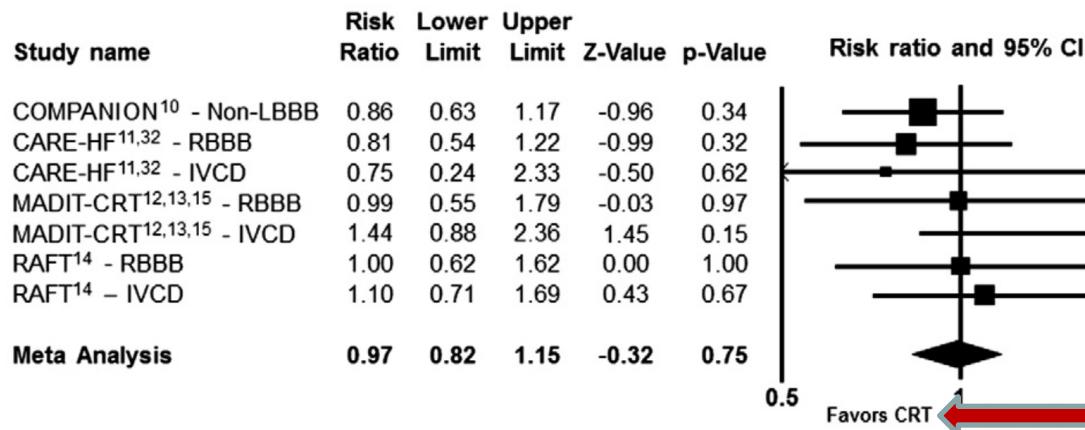
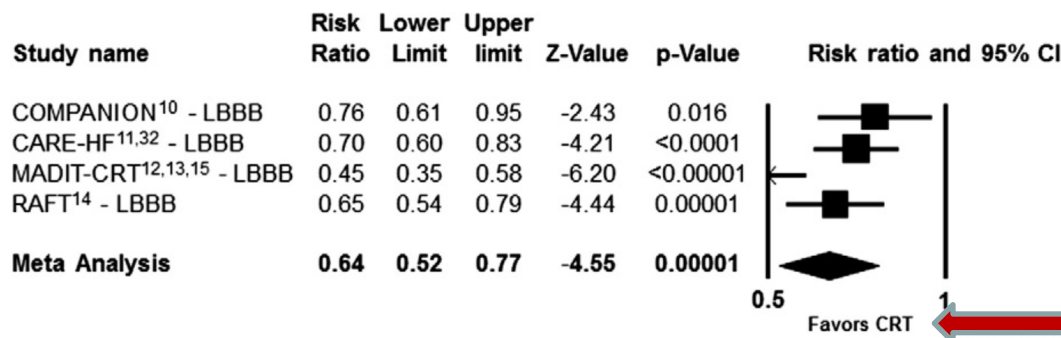


Morfologia do QRS

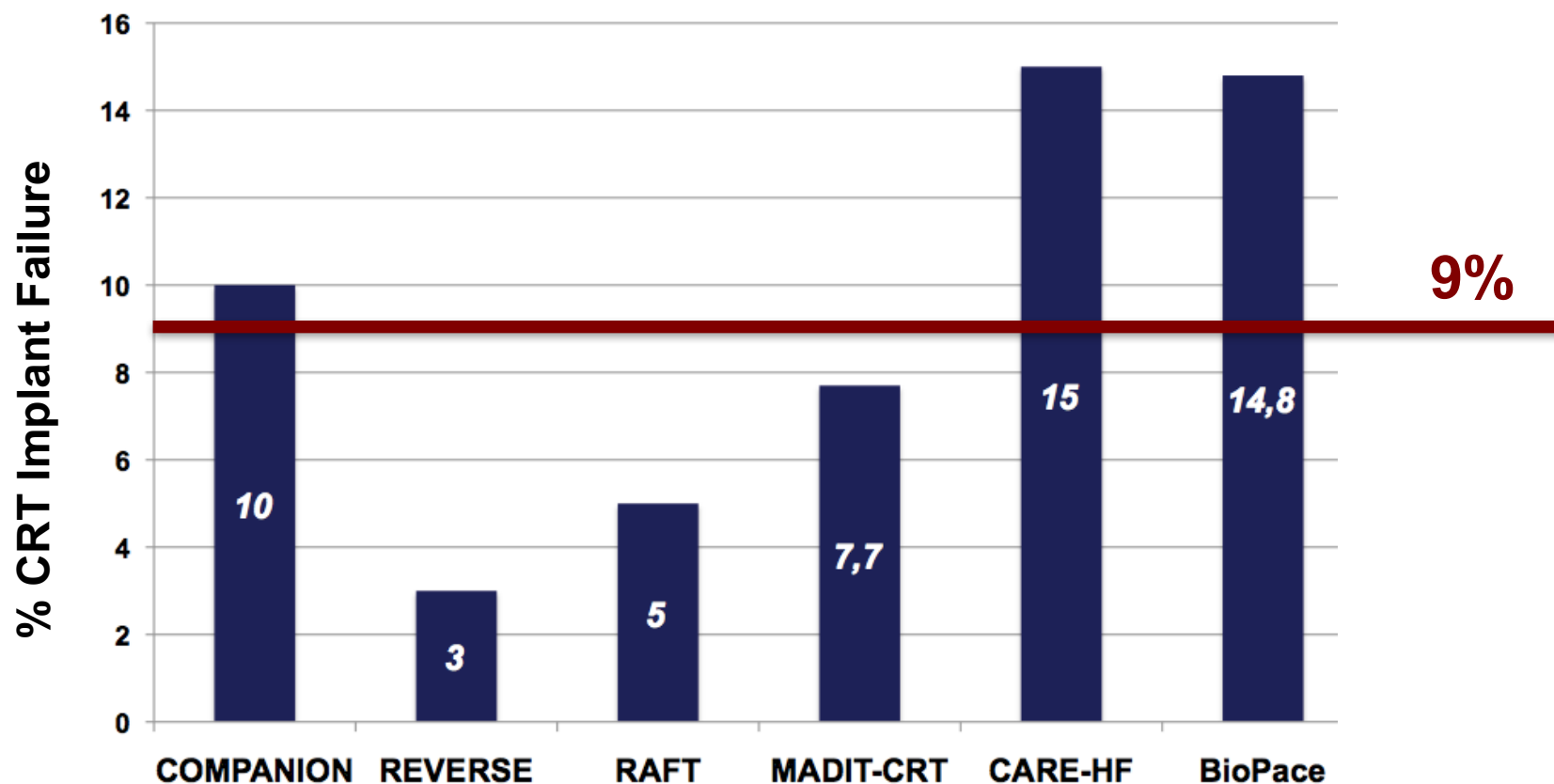
Effect of QRS morphology on clinical event reduction with cardiac resynchronization therapy: Meta-analysis of randomized controlled trials

Ilke Sipahi, MD,^a Josephine C. Chou, MD,^a Marshall Hyden, MD,^a Douglas Y. Rowland, PhD,^b Daniel I. Simon, MD,^a and James C. Fang, MD^a *Cleveland, OH*

Meta-analise de 4 estudos 5356 doentes Resposta por Morfologia QRS



Insucesso no Implante



N patients

1212

610

888

746

409

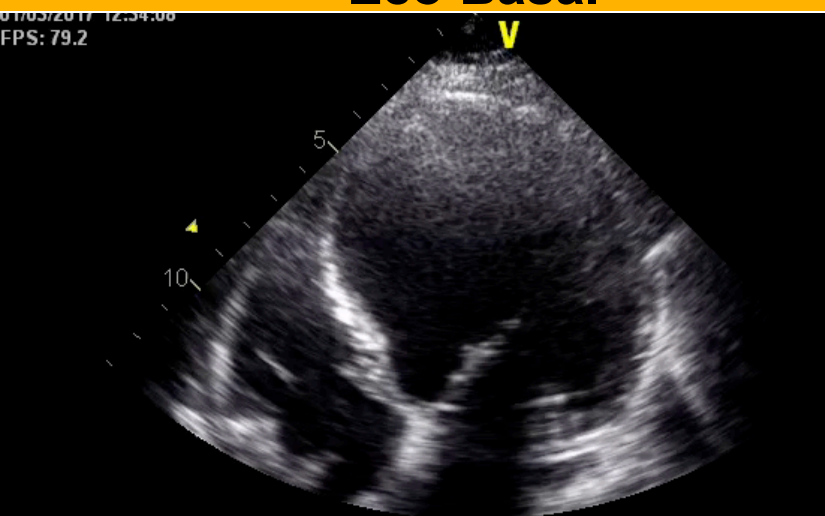
902

Definição de Resposta Segundo a Literatura

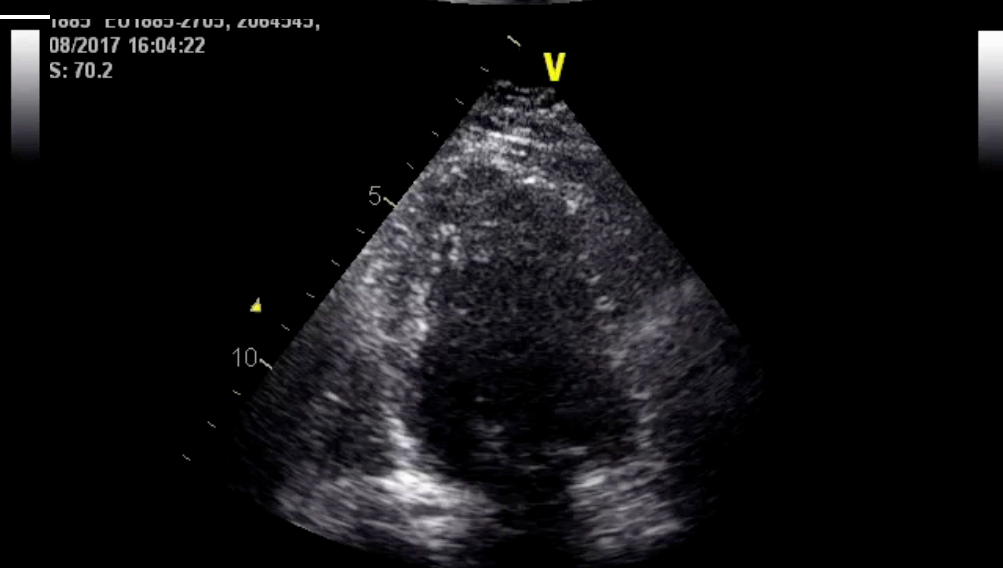
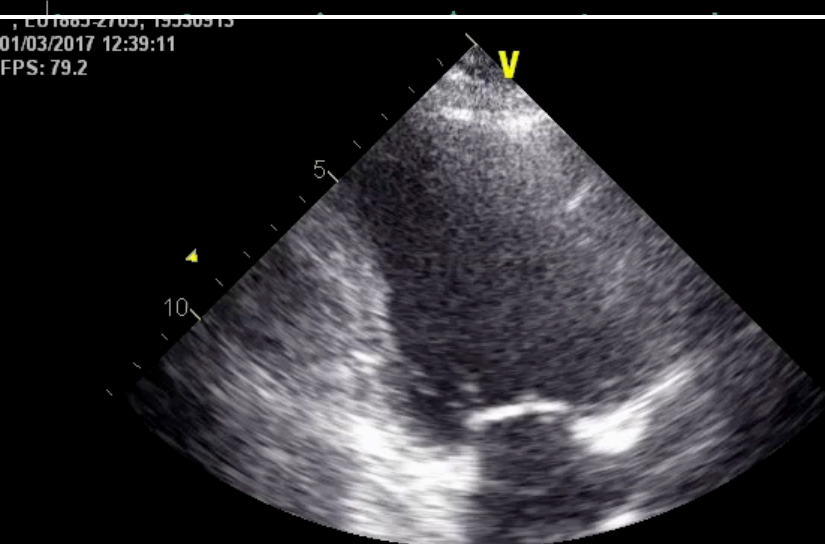
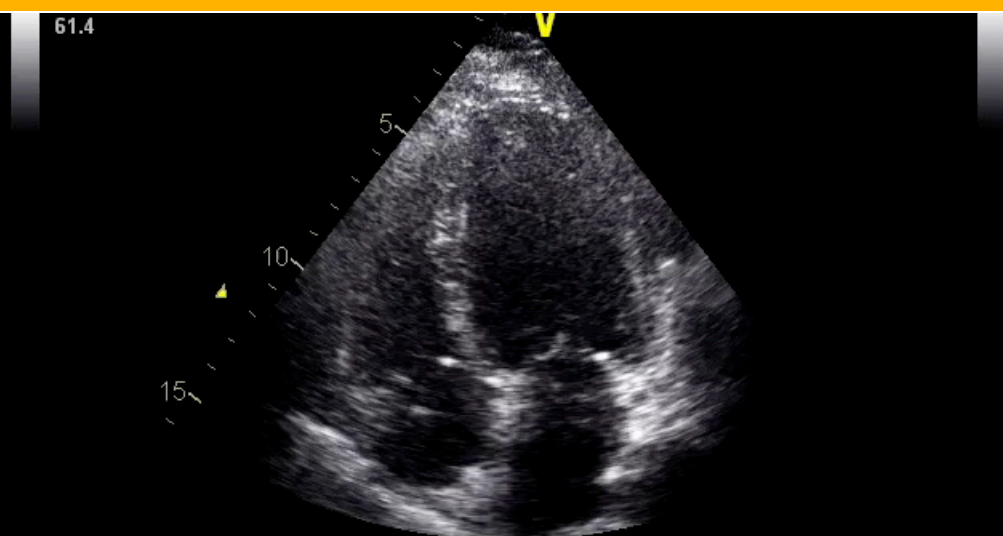
Variáveis Clínicas	Cutoff
Classe Funcional NYHA	↓> 1 classe
Prova de Marcha	↑>50m
NYHA e Prova de Marcha	↓> 1 classe + ↑>25%
QoL	↑>10 ou 15
MLWHF	>10
VO2max	↑>10%
Mortalidade Global	Qualquer evento
Hospitalização IC	Qualquer evento

Variáveis Ecocard	Cutoff
Fracção Ejecção VE	↑15%
LVESV	↓10%
LVEDV	↓15%
LVIDs	↓15
LVIDd	↓15
Volume Sistólico	↑15%

Eco Basal

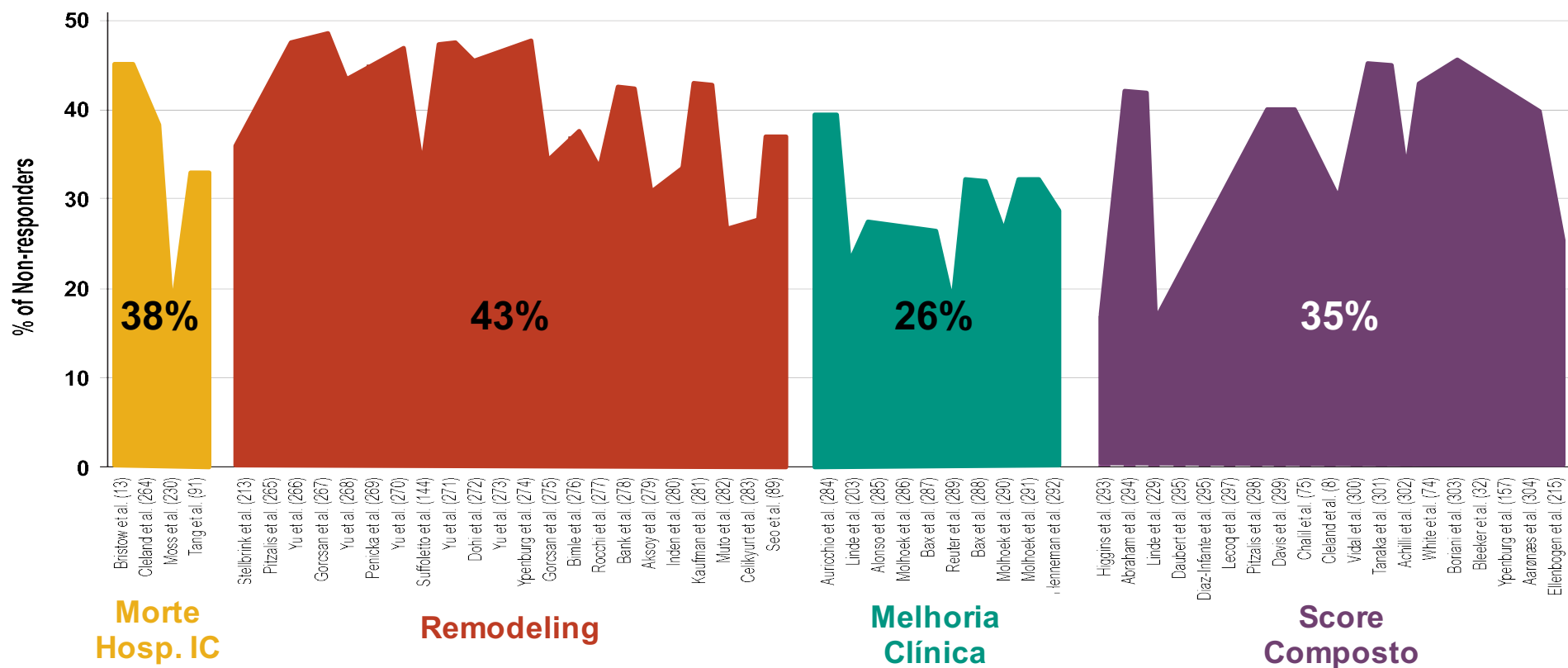


Eco 6 meses

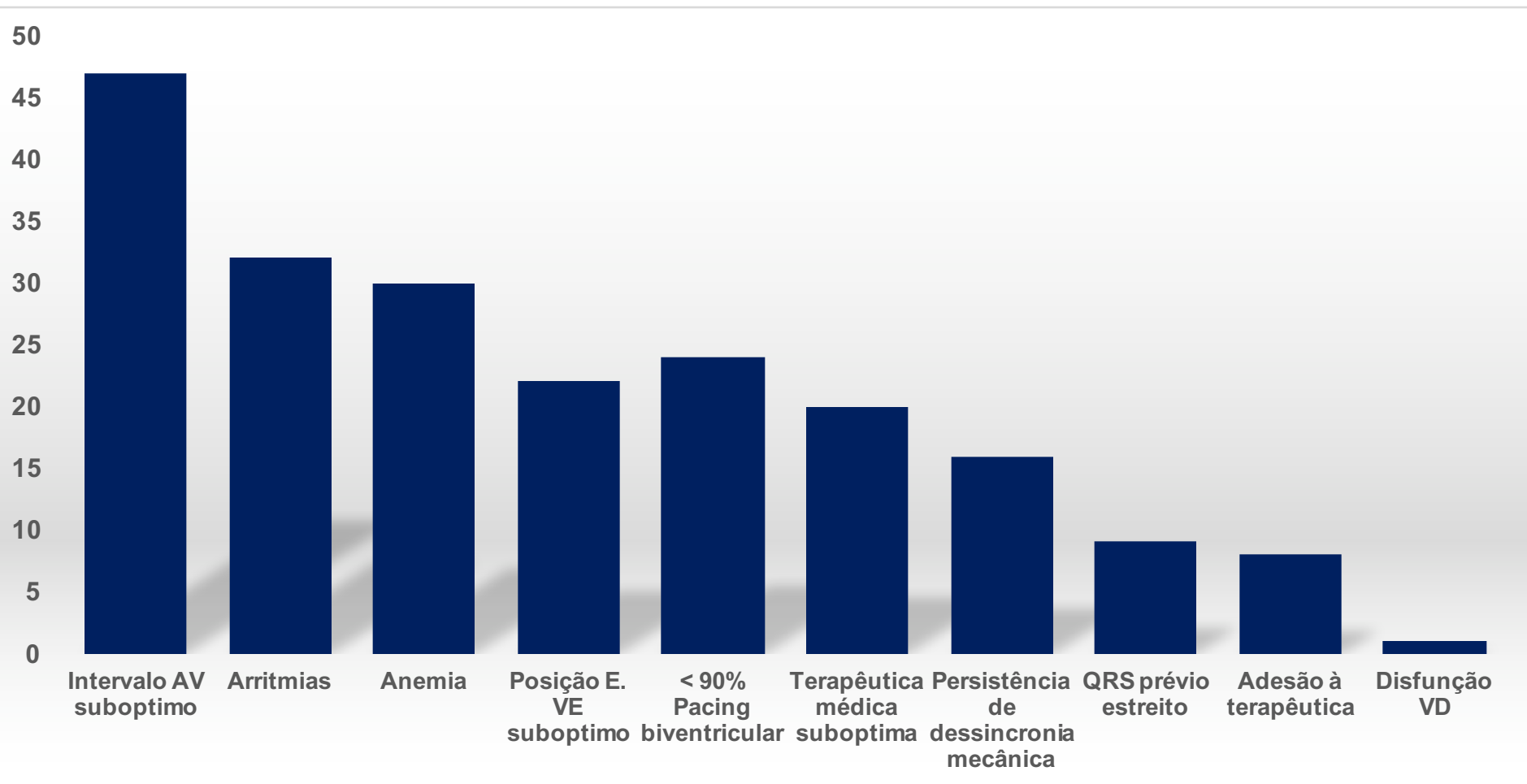


Globalmente consideram-se 30-40% Não Respondedores

Percentagem de não respondedores por estudo clínico e critério de resposta



Possíveis causas de não resposta à terapêutica de Ressincronização

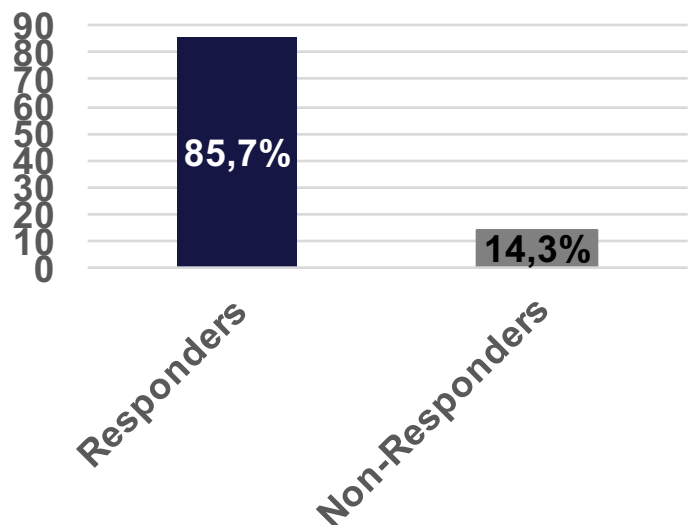




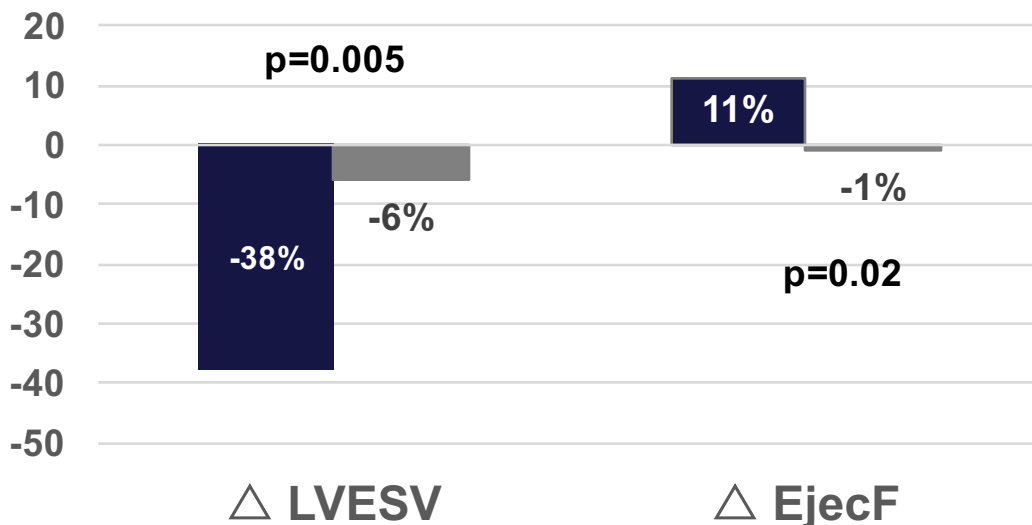
Automatically, operator-independent, assess the conduction delay between RVpacing and the LV available veins to select the LV pacing site. Evaluate the impact of LV site on clinical and remodeling outcomes. 66 Patients follow up 6 months

Response Rate Overall population

Reduction LVESV > 15%
Increase EF > 10%



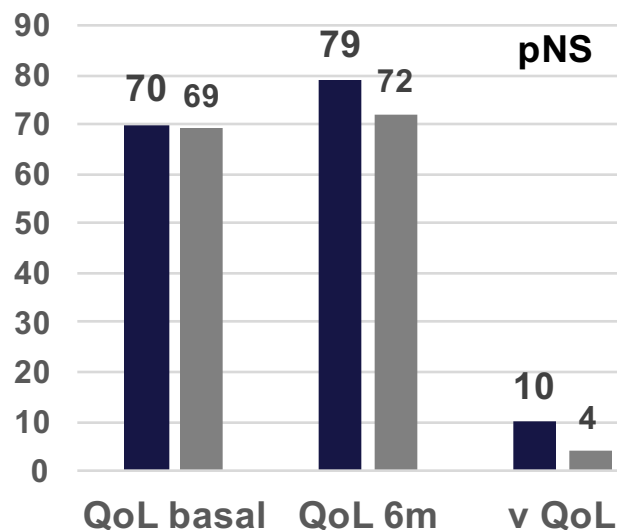
LVESV and Ejection Fraction Variations 0-6 Months



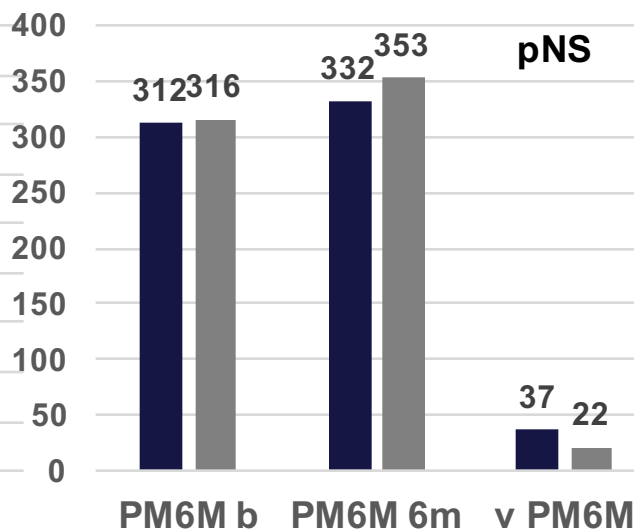


Automatically, operator-independent, assess the conduction delay between RVpacing and the LV available veins to select the LV pacing site.
Evaluate the impact of LV site on clinical and remodeling outcomes.

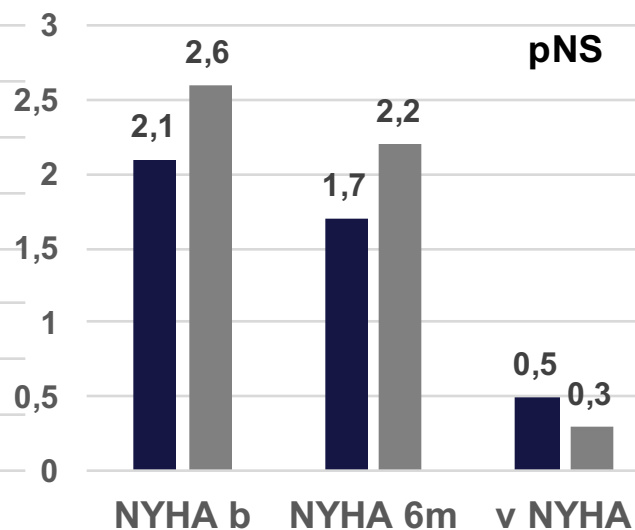
QoL score



PM6M



Classe NYHA



Em doentes selecionados a terapêutica de ressincronização cardíaca produz

Melhoria Sintomática

Melhoria da qualidade de vida

Diminuição das hospitalizações

Diminuição da mortalidade



Donald J. Trump ✓

@realDonaldTrump



If you have HFrEF may God bless you with LBBB and enough money to get a CRT. Congrats to NFMCC 2019, sad for not being there but my friend Kim is giving a huge party.

19:25 PM • 23 Feb 19

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