PROGRESSI NELLA TERAPIA DELLO SCOMPENSO CARDIACO:
IL DISPOSITIVO COME TECNOLOGIA RISOLUTIVA

SEDE UNIONE INDUSTRIALI
PIAZZA DEI MARTIRI – NAPOLI

4 DICEMBRE
2023
15.00 - 18.30

Terapia di Modulazione della Contrattilità Cardiaca

Tecnologia

Meccanismo di azione

Ambiti di applicazione

Dott. Daniele Masarone

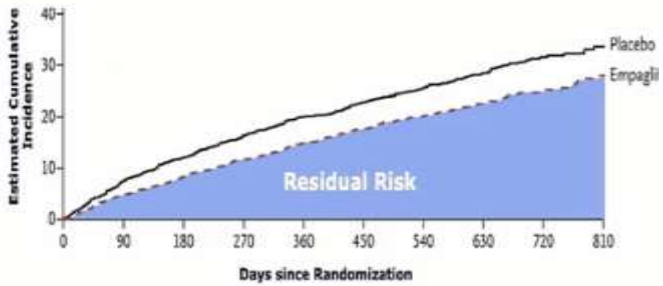
UOSD Scompenso Cardiaco

AOS dei Colli

Ospedale Monaldi

The war against heart failure: the *Lancet* lecture

Eugene Braunwald

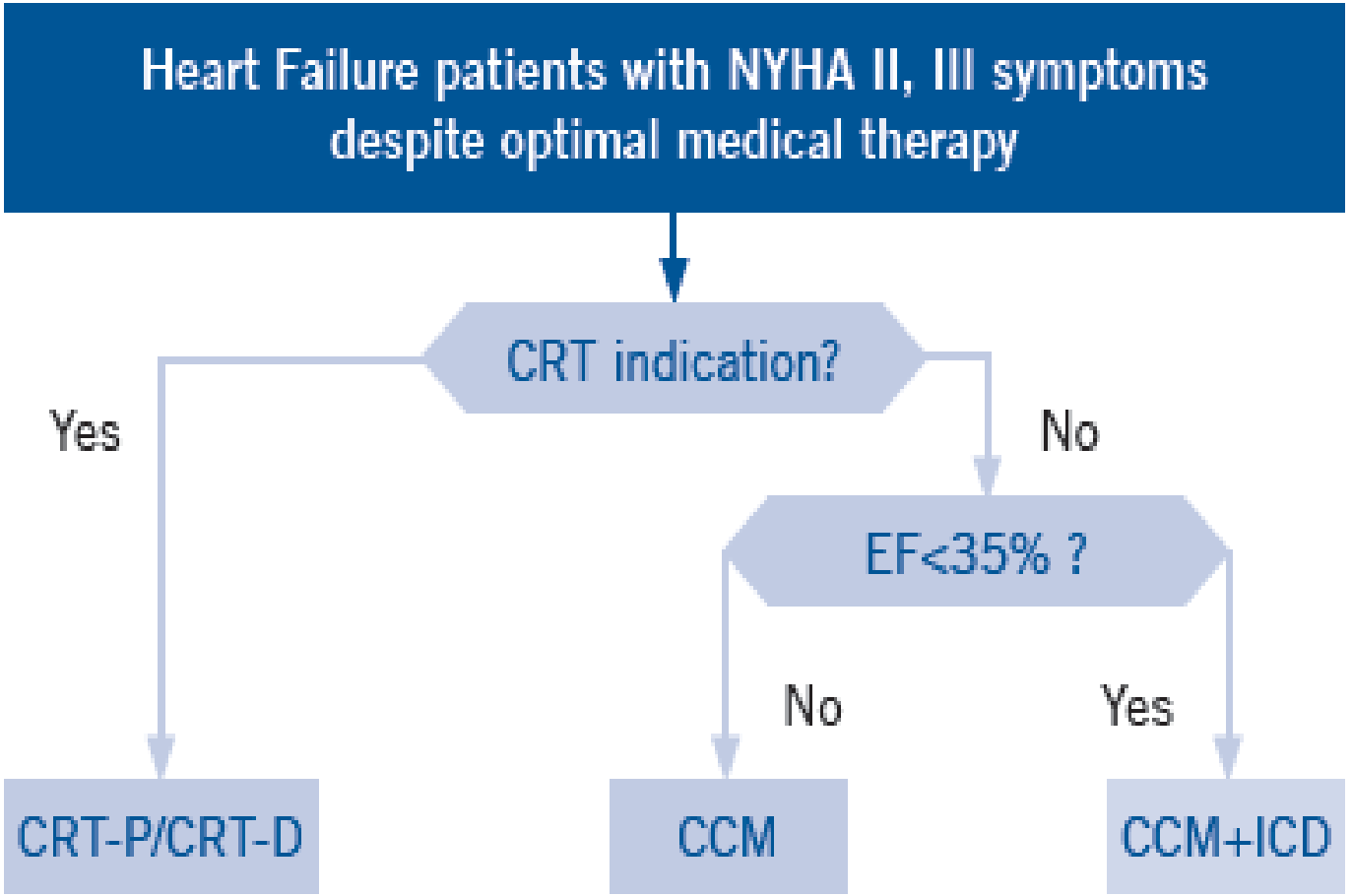


19.4%

Residual risk of CV death or hospitalization despite optimal GDMT

Packer M NEJM 2020

CCMT solves an unmet need in the treatment of HF



More than 17m patients globally with NYHA II/III despite OMT

- 30% eligible for CRT
- 70% eligible for CCM

Abraham WT. Heart Fail. Clin. 2021

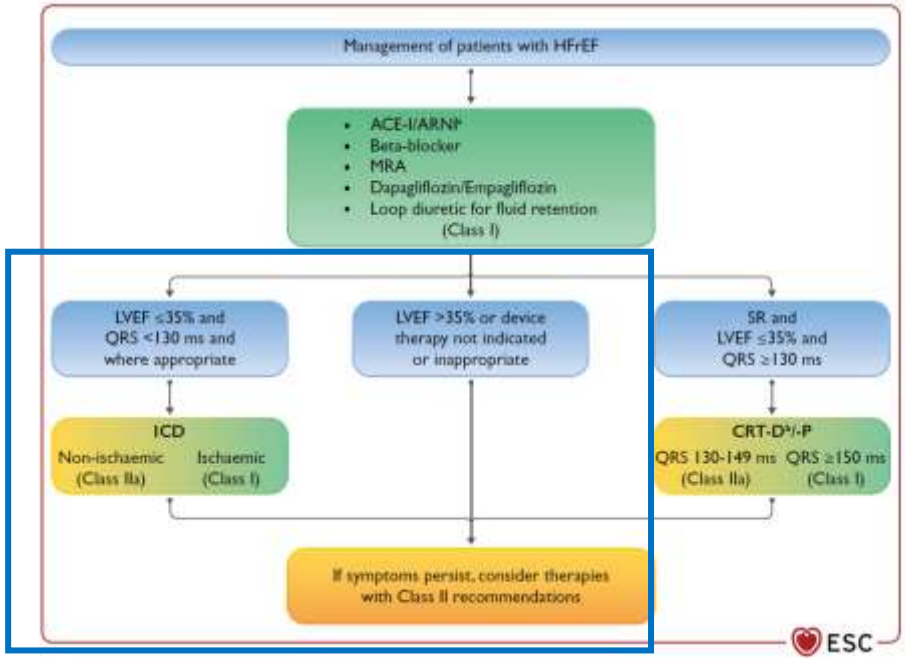
ESC European Society of Cardiology
European Heart Journal (2021) 00, 1–128
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

6.3 Devices under evaluation

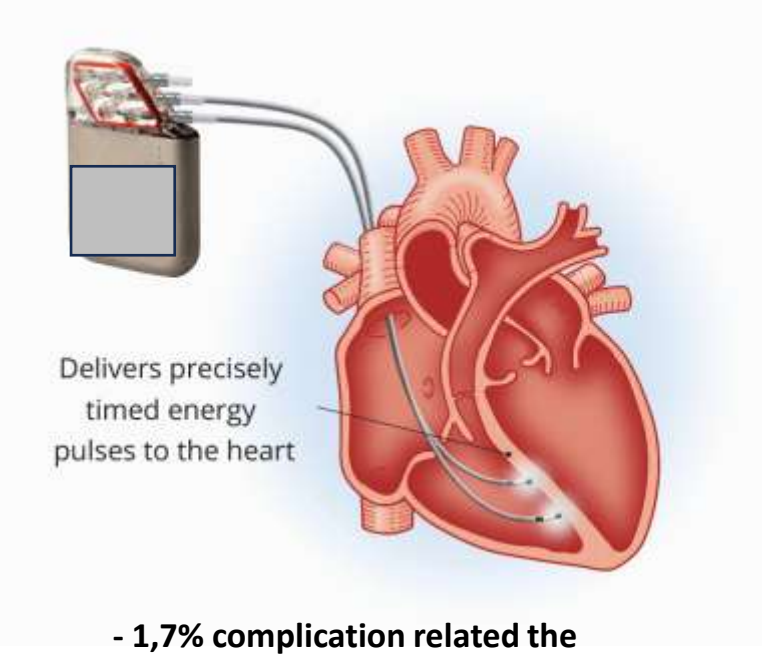
Cardiac contractility modulation (CCM) has been evaluated in patients with NYHA class III–IV HF, with an LVEF ≥25% to ≤45% and QRS duration <130 ms, and was associated with a small improvement in exercise tolerance and QOL.[241,242]



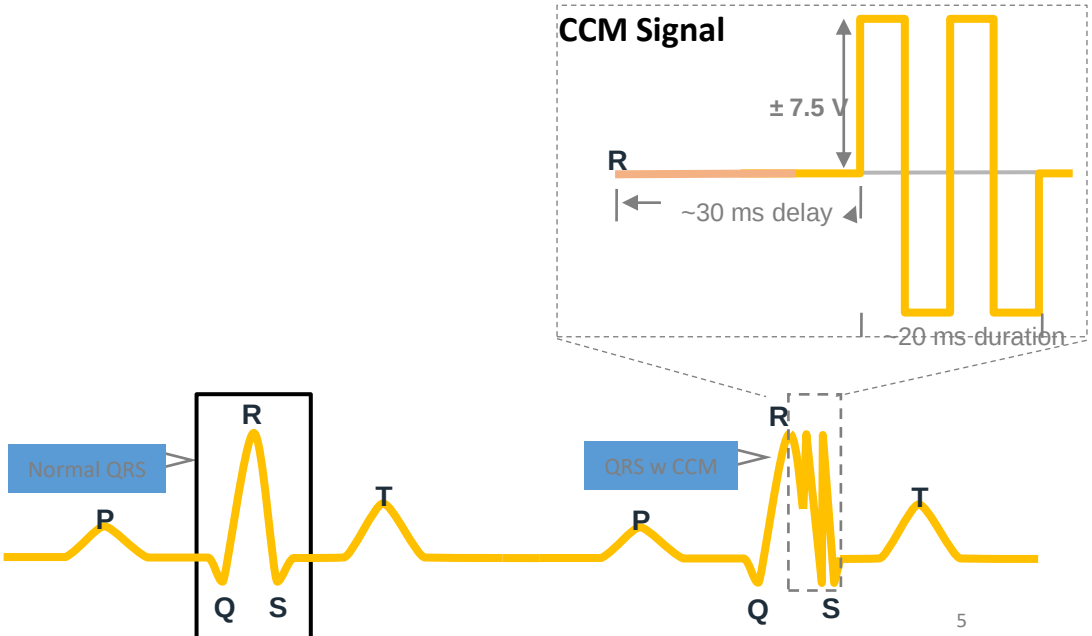
Supplementary Table 9 Interventions aiming to improve quality of life and/or exercise capacity in symptomatic patient with heart failure with reduced ejection fraction

	Intervention	Additional criteria beyond the presence of symptomatic HFrEF (if any)
DRUGS	Sacubitril/valsartan[77,78]	
	Dapagliflozin[79]	
	Diuretics[80]	fluid overload
	Ferric carboxymaltose i.v.[21–23]	iron deficiency
	Ivabradine[81–86]	SR >70 b.p.m.
	Tromtesicdine[87–89]	
DEVICES AND INVASIVE PROCEDURES	CRT[90,91]	Eligibility for CRT
	Pulmonary vein isolation[92–94]	AF
	Percutaneous correction of severe functional mitral regurgitation[95–98]	Severe functional mitral regurgitation
	Cardiac contractility modulation[99–101]	QRS <130 ms, LVEF 25–45%
	Baroreflex activation therapy[102–104]	
	Phrenic nerve stimulation[105–107]	Central sleep apnoea

Erogazione della terapia CCM



- Stimoli non eccitatori, bifasici (applicati durate il periodo refrattario assoluto a ~ 30 ms delay), ad elevate energia: durata di almeno 20 ms ed ampiezza programmabile da 4 a 7.5 V
- Max frequenza di sincronizzazione: 110bpm

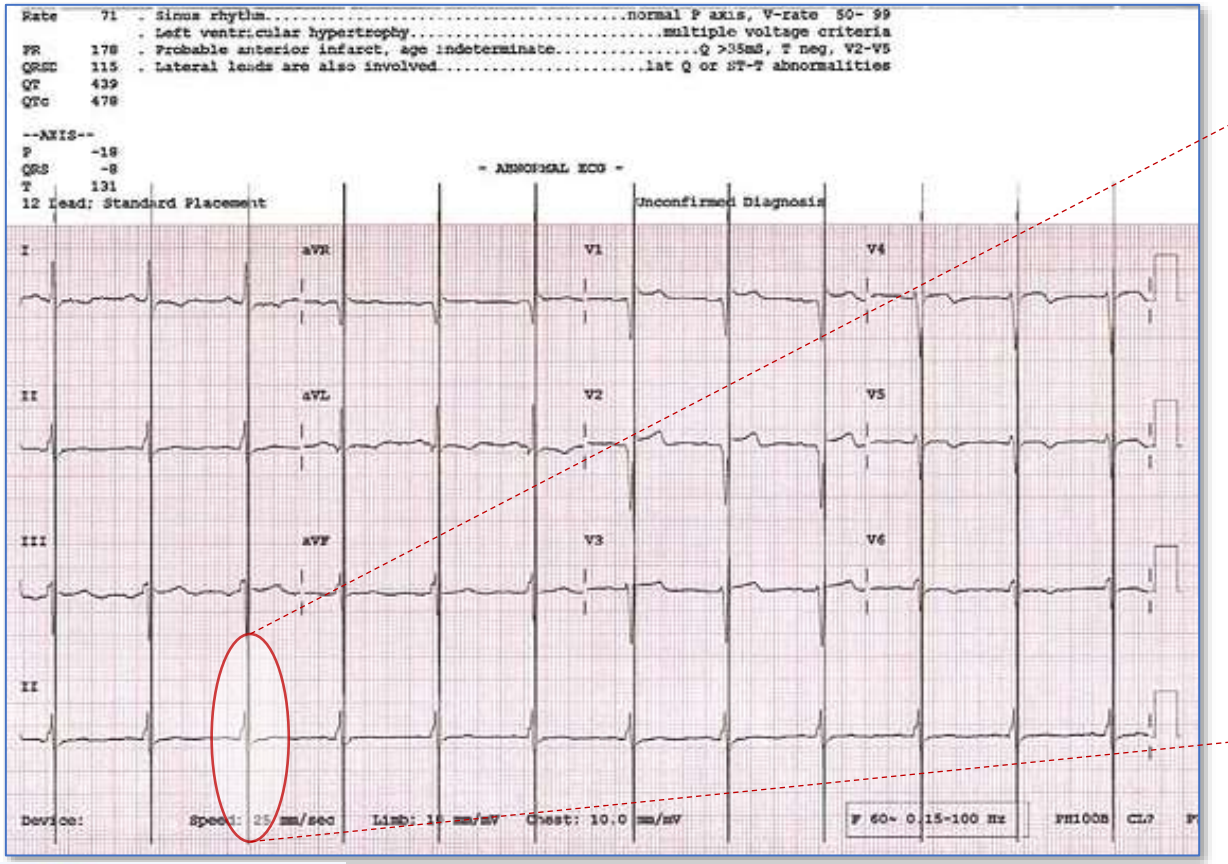


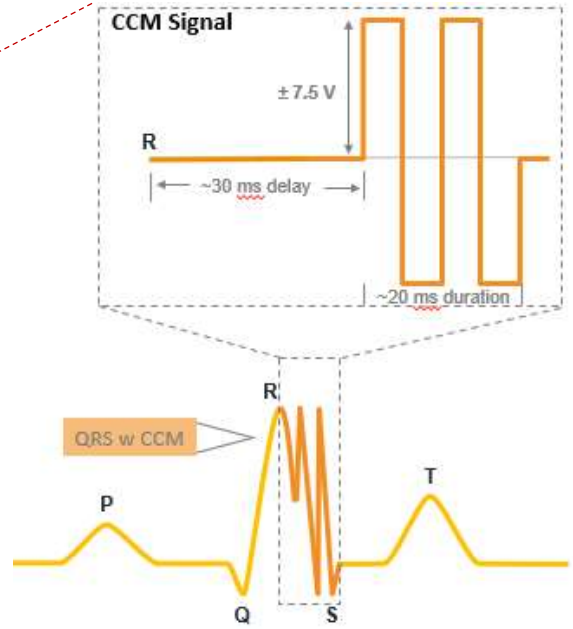
- 1,7% complication related the procedure→ Fix HF5C2

- **Event free-rate: 93,6% (device and procedure-related complications)→ HFpEF Pilot**

5

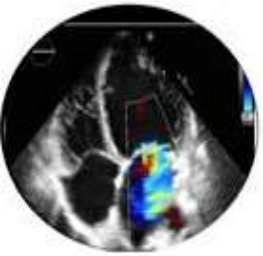
Erogazione della terapia CCM





Esempio di 7 ore di fasi con terapia CCM rilasciata, separati da 2.4 ore di fase in riposo.

CCMT
Mechanism of Action



Minutes

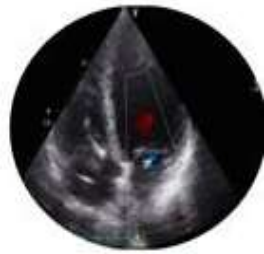
- Upregulation of SERCA2a
- Increased phosphorylation of titin
- Increased phosphorylation of PLB
- Increased phosphorylation of PKA and PKG

Hours

- Reverse of the maladaptive fetal gene program
- Reduction of cardiac fibrosis
- Decreased sympathetic activity

Months

- Improved ejection fraction reserve
- Improved diastolic filling index



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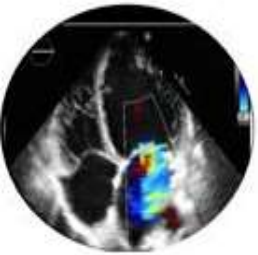
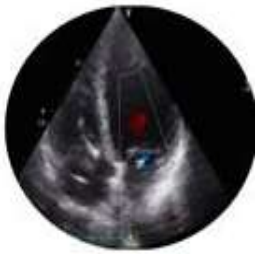
CCMT
Mechanism of Action



Minutes	Hours	Months
• Upregulation of SERCA2a • Increased phosphorylation of titin • Increased phosphorylation of PLB • Increased phosphorylation of PKA and PKG	• Reverse of the maladaptive fetal gene program • Reduction of cardiac fibrosis • Decreased sympathetic activity	• Improved ejection fraction reserve • Improved diastolic filling index

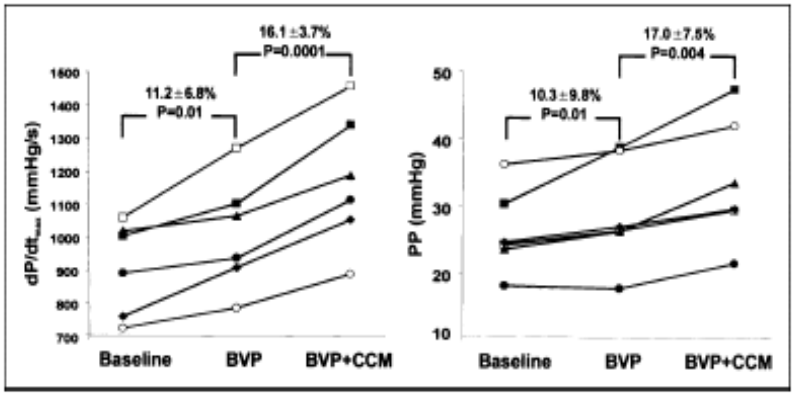


Masarone D . Heart Rhythm 2023

Cardiac Contractility Modulation by Electric Currents Applied During the Refractory Period in Patients With Heart Failure Secondary to Ischemic or Idiopathic Dilated Cardiomyopathy

Carlo Pappone, MD, PhD, Salvatore Rosanio, MD, PhD, Daniel Burkhoff, MD, PhD, Yuval Mika, DSc, Gabriele Vicedomini, MD, Giuseppe Augello, MS, Itzhak Shemer, MD, David Prutchi, DSc, Walid Haddad, PhD, Ricardo Aviv, DSc, Yehuda Snir, DSc, Itzhak Kronzon, MD, Ottavio Alfieri, MD, and Shlomo A. Ben-Haim, MD, PhD

Pappone C. et al. Am J Card 2002



ELSEVIER

The European Journal of Heart Failure

www.elsevier.com/locate/ejheart

Cardiac contractility modulation by non-excitatory currents: Studies in isolated cardiac muscle

Corinna B. Brunckhorst[a,1], Isaac Shemer[b,c,1,*], Yuval Mika[c], Shlomo A. Ben-Haim[c], Daniel Burkhoff[c]

[a]Institute of Cardiology, University Hospital Zurich, Ramistr 100, Zurich 8091, Switzerland
[b]Department of Physiology and Biophysics, The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa 31096, Israel
[c]IMPULSE Dynamics, Orangeburg, NY, USA

Received 25 August 2006; accepted 9 May 2005
Available online 3 October 2005

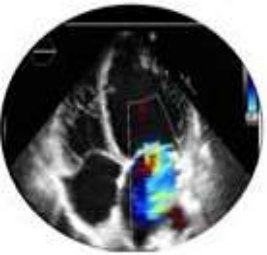
Brunckhorst C. et al. EJHF 2006

Table 1
Characteristics of CCM signal inotropic effect

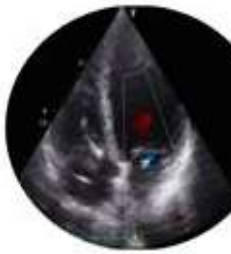
	Rabbit papillary muscle			Human failing trabecular muscle		
	Baseline	CCM	Effect [%]	Baseline	CCM	Effect [%]
Anodic CCM						
n	16			3		
Time to reach 90% of steady state (beats)	–	4.4±0.2		–	4.8±0.6	
Peak force (mg/mm^2)	361±69	599±105	68±15*	333±129	428±131	29.8±2.8*
Time to peak force (ms)	94±3	105±4	11.9±2.2*	180±107	193±17	7.9±2.1*
Twitch duration at 80% relaxation (ms)	146±7l	151±7	3.7±0.4*	340±61	371±48	9.1±2.6
Time to 50% relaxation (ms)	46.8±4.1	45.2±4.0	− 3.5±1.10*	131±14.1	133±16.7	1.3±2.1
Maximal rate of relaxation (g/mm^2/ms)	−4.2±1.3	−7.8±2.2	93±34*	−3.39±2.04	−4.08±2.52	16.8±4.1*
Cathodic CCM						
n	11			3		
Time to reach 90% of steady state (beats)	–	4.2±0.4		–	4.0±02	
Peak force (mg/mm^2)	394±106	320±82	−17.1±2.8*	330±60	260±4	−19.7±14.0*
Time to peak force (ms)	89±3	86±3	−4.1±0.2	188±21	179±24	−4.8±2.4
Twitch duration at 80% relaxation (ms)	149±11	150±12	0.9±0.4	348±32	357±46	2.4±4.0
Time to 50% relaxation (ms)	50.2±2.1	52.6±2.3	4.9±0.5*	136.4±23.0	139.9±20.5	3.2±2.9
Maximal rate of relaxation (g/mm^2/ms)	−5.2±1.3	−4.1±1.3	−19.1±3.3*	−4.14±2.25	−2.83±1,03	−22.3±17.3*

* $p<0.05$.

CCMT
Mechanism of Action



Minutes	Hours	Months
• Upregulation of SERCA2a • Increased phosphorylation of titin • Increased phosphorylation of PLB • Increased phosphorylation of PKA and PKG	• Reverse of the maladaptive fetal gene program • Reduction of cardiac fibrosis • Decreased sympathetic activity	• Improved ejection fraction reserve • Improved diastolic filling index



Masarone D. Heart Rhythm 2023

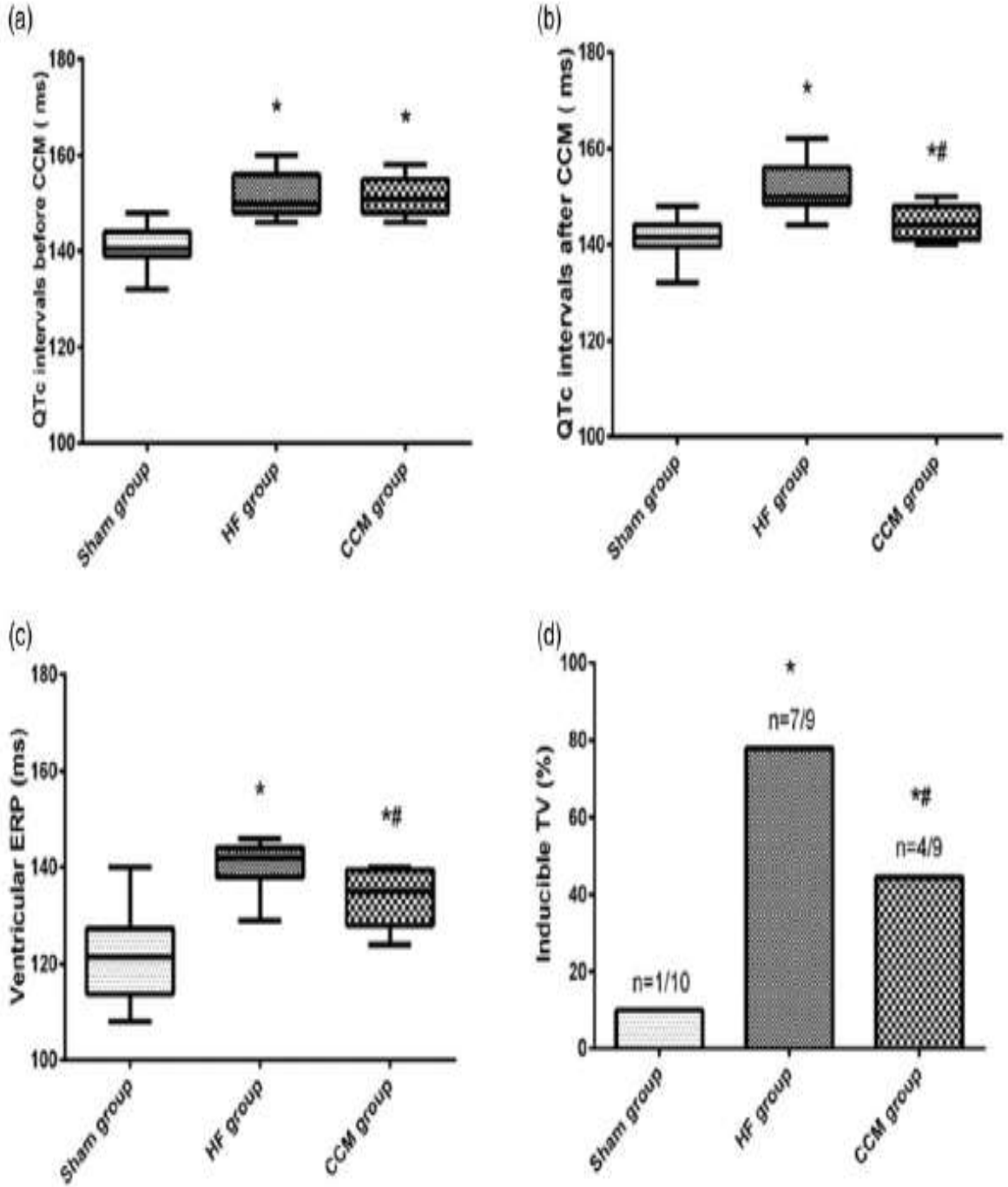
Pre-Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Cardiac contractility modulation attenuates structural and electrical remodeling in a chronic heart failure rabbit model

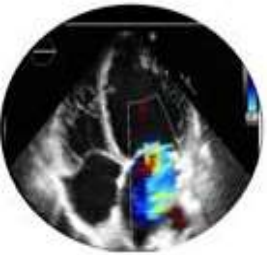
Bin Ning[1], Feifei Zhang[2], Xuelian Song[2], Qingqing Hao[2], Yingxiao Li[2], Rong Li[2] and Yi Dang[2]

SAGE



Bin N. J Int Med Res. 2020

CCMT
Mechanism of Action



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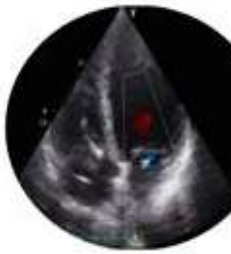
• Upregulation of SERCA2a • Increased phosphorylation of titin • Increased phosphorylation of PLB • Increased phosphorylation of PKA and PKG	• Reverse of the maladaptive fetal gene program • Reduction of cardiac fibrosis • Decreased sympathetic activity	• Improved ejection fraction reserve • Improved diastolic filling index



Masarone D. Heart Rhytm 2023

ORIGINAL RESEARCH

Impact of Cardiac Contractility Modulation on Left Ventricular Global and Regional Function and Remodeling

Cheuk-Man Yu, MD,* Joseph Yat-Sun Chan, MB,* Qing Zhang, MM, PHD,*
Gabriel W. K. Yip, MD,* Yat-Yin Lam, MB,* Anna Chan, MB,*
Daniel Burkhoff, MD, PHD,†‡ Pui-Wai Lee, MB,* Jeffrey Wing-Hong Fung, MD*
Hong Kong, China; and New York and Orangeburg, New York

Yu C. et al. JACC Card Imag 2009

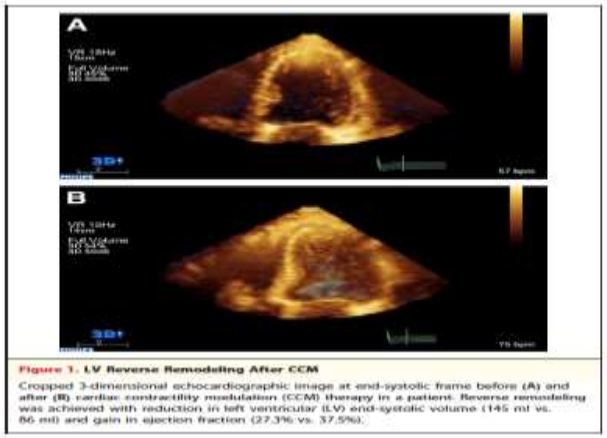


Figure 1. LV Reverse Remodeling After CCM
Cropped 3-dimensional echocardiographic image at end-systolic frame before (A) and after (B) cardiac contractility modulation (CCM) therapy in a patient. Reverse remodeling was achieved with reduction in left ventricular (LV) end-systolic volume (145 ml vs. 86 ml) and gain in ejection fraction (27.3% vs. 37.5%).

applied sciences

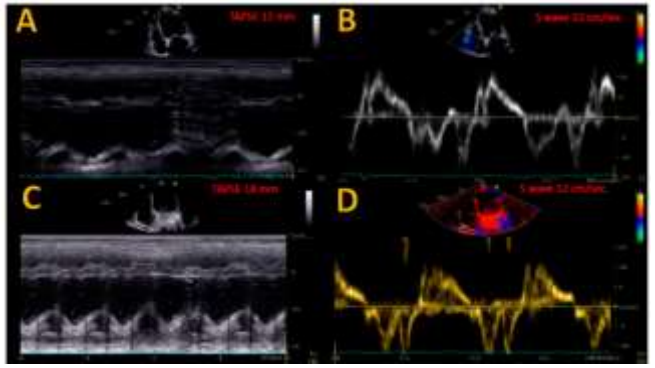
MDPI

Article

Effects of Cardiac Contractility Modulation Therapy on Right Ventricular Function: An Echocardiographic Study

Carla Contaldi [1,*], Stefano De Vivo [2], Maria L. Martucci [1], Antonio D'Onofrio [2], Ernesto Ammendola [1], Gerardo Nigro [3], Vittoria Errigo [1], Giuseppe Pacileo [1] and Daniele Masarone [1]

Contaldi C. et al. Appl. Sci 2022



Journal of Clinical Medicine

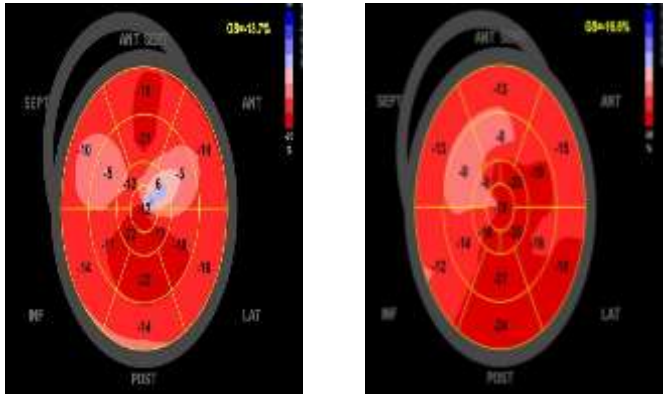
MDPI

Article

The Effects of Device-Based Cardiac Contractility Modulation Therapy on Left Ventricle Global Longitudinal Strain and Myocardial Mechano-Energetic Efficiency in Patients with Heart Failure with Reduced Ejection Fraction

Daniele Masarone [1,*], Michelle M. Kittleson [2], Stefano De Vivo [3], Antonio D'Onofrio [3], Ernesto Ammendola [1], Gerardo Nigro [4], Carla Contaldi [1], Maria L. Martucci [1], Vittoria Errigo [1] and Giuseppe Pacileo [1]

Masarone D. et al. J Clin Med 2022



HeartRhythm Heart Rhythm Society

Basic Science of Cardiac Contractility Modulation Therapy: Molecular and Electrophysiological Mechanisms

Daniele Masarone, MD;PhD • Michelle M. Kittleson, MD;PhD • Antonio D'Onofrio, MD • Luigi Falco, MD • Isabella Fumarolo, MD • Massimo Massetti, MD • Filippo Crea, MD • Nadia Aspromonte, MD • Giuseppe Pacileo, MD • Show less

CCMT
Mechanism of Action

HFpEF

- Reduction of cardiac fibrosis
- Increase in titin phosphorylation

HFrEF

- Increase in peak cytosolic calcium concentrations
- Metabolic remodelling
- Reverse of fetal gene programs
- Rebalancing Cardiac Autonomic Tone
- Reduction of cardiac fibrosis
- Electrophysiological remodeling

Published: September 26, 2023 • DOI: https://doi.org/10.1016/j.hrthm.2023.09.021

Masarone D. Heart Rhythm 2023

Randomized Clinical Trial History

- All randomized studies showed significant impact on exercise tolerance and quality of life
- Peak VO2 endpoint consistently positive across all trials
- Subgroup analyses (whether or not pre-specified) demonstrated greatest benefits in HF patients with moderately reduced ejection fractions ranging from 35% to 45%

CCM-REG	CCM Registry		Opt IVs, Smart	Germany, Russia, France	503
FIX-HF-5C2	2-Lead CCM Device		OptSmart (2-lead)	US, Germany	60
HFpEF Pilot	FE>50%		OptSmart (2-lead)	EU, Australia	47
Total					1,751

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

William T. Abraham, MD,[a] Karl-Heinz Kuck, MD,[b] Rochelle L. Goldsmith, PhD,[c] JoAnn Lindenfeld, MD,[d] Vivek Y. Reddy, MD,[e] Peter E. Carson, MD,[f] Douglas L. Mann, MD,[g] Benjamin Saville, PhD,[h] Helen Parise, ScD,[i] Rodrigo Chan, MD,[j] Phi Wiegn, MD,[k] Jeffrey L. Hastings, MD,[k] Andrew J. Kaplan, MD,[l] Frank Edelmann, MD,[m] Lars Luthje, MD,[m] Rami Kahwash, MD,[n] Gery F. Tomassoni, MD,[o] David D. Gutterman, MD,[p] Angela Stagg, BS,[q] Daniel Burkhoff, MD, PhD,[r] Gerd Hasenfuß, MD[s]

OBJECTIVES *The authors sought to confirm a subgroup analysis of the prior FIX-HF-5 (Evaluate Safety and Efficacy of the OPTIMIZER System in Subjects With Moderate-to-Severe Heart Failure) study showing that cardiac contractility modulation (CCM) improved exercise tolerance (ET) and quality of life in patients with ejection fractions between 25% and 45%.*

- 160 patients **randomized** 1:1: at 20 US sites and 8 EU sites
- Target population: Heart failure patients with **EF 25% to 45%**
- **Primary Efficacy Endpoint:** Improvement in **peak VO2**
- **Primary Safety Endpoint:** Proportion of Treatment group that did **not** experience an Optimizer device or Optimizer procedure related **complication** through 24-weeks greater than **70%**
- Major **Secondary Efficacy Endpoint:**
  - Minnesota Living with Heart Failure **Quality of Life** (QoL) Score
- Granted Expedited Access Pathway by the FDA qualifying for priority review

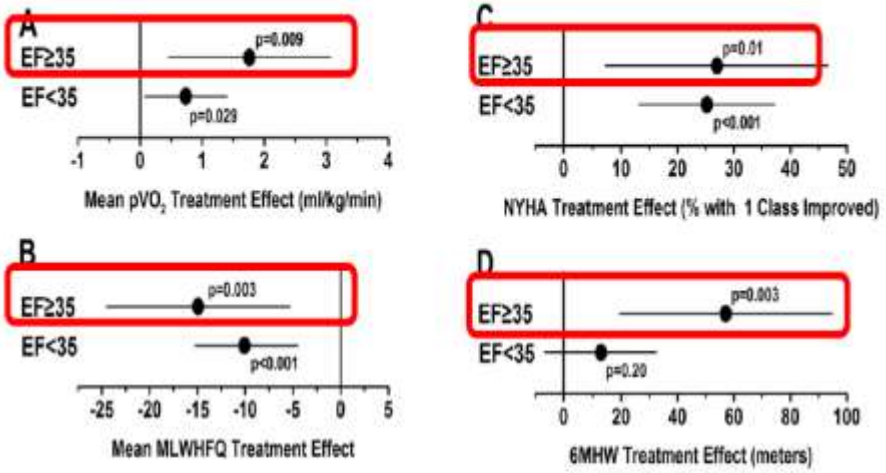
Abraham WT T. JACC 2019

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

(J Am Coll Cardiol HF 2018;6:874-83)

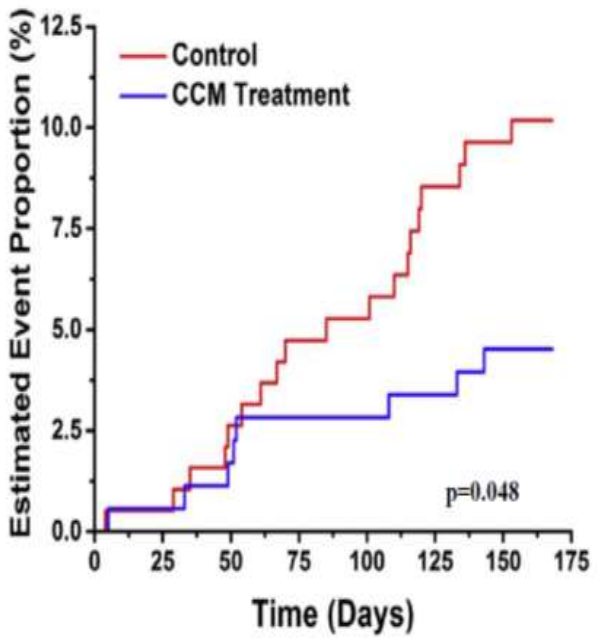
William T. Abraham, MD,[a] Karl-Heinz Kuck, MD,[b] Rochelle L. Goldsmith, PsD,[c] JoAnn Lindenfeld, MD,[d] Vivek Y. Reddy, MD,[e] Peter E. Carson, MD,[f] Douglas L. Mann, MD,[g] Benjamin Saville, PsD,[h] Helen Parise, ScD,[i] Rodrigo Chan, MD,[j] Phi Wiegn, MD,[k] Jeffrey L. Hastings, MD,[k] Andrew J. Kaplan, MD,[l] Frank Edelmann, MD,[m] Lars Luthje, MD,[m] Rami Kahwash, MD,[n] Gery F. Tomassoni, MD,[o] David D. Gutterman, MD,[p] Angela Stagg, BS,[q] Daniel Burkhoff, MD, PsD,[r] Gerd Hasenfuß, MD[s]

Analisi combinata (FIX-HF-5+FIX-HF-5C) su 389 pazienti: 293 con Fe < 35%, 96 con FE≥35%



- Benefici della terapia CCM in tutte le classi di FE
- Responder migliori in FE>35%: +1,76 mL/Kg/min VO2 picco, (+0,9 mL/Kg/min in tutta la popolazione)
- 81% dei pazienti trattati con CCM con miglioramento ≥1 classe NYHA, di cui il 50% con miglioramento di 2 classi funzionali.

FIGURE 5 Heart Failure and Mortality Events



A 24 settimane, il gruppo CCM aveva maggiore sopravvivenza libera da morte cardiaca e ospedalizzazioni per SC: 97,1% nel gruppo studio vs 89,2% nel gruppo controllo

Abraham WT T. JACC 2019

A comprehensive individual patient data meta-analysis of the effects of cardiac contractility modulation on functional capacity and heart failure-related quality of life

Francesco Giallauria[1]*, Gianluigi Cuomo[1], Alessandro Parlato[1], Nirav Y. Raval[2], Jürgen Kuschyk[3] and Andrew JS Stewart Coats[4]

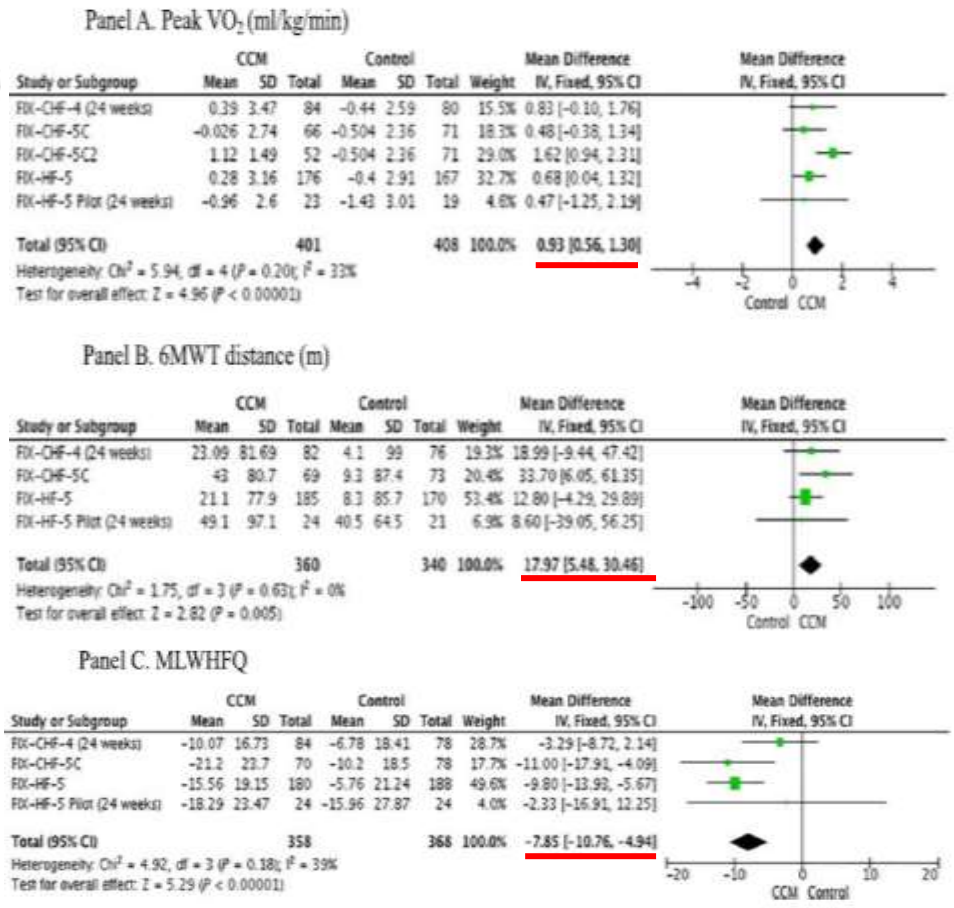
ESC HEART FAILURE
ESC Heart Failure (2020)
Published online in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/ehf2.12902

ORIGINAL RESEARCH ARTICLE

Effetti statisticamente significativi e clinicamente utili della terapia CCM sono emersi rispetto a :

- Capacità Funzionale (CPET);
- Capacità di Esercizio (6MWT);
- Qualità della Vita (MLWHFQ).

Tutti gli endpoint hanno dimostrato differenze non significative tra pazienti con età > 60 anni e quelli con età ≤ 60 anni

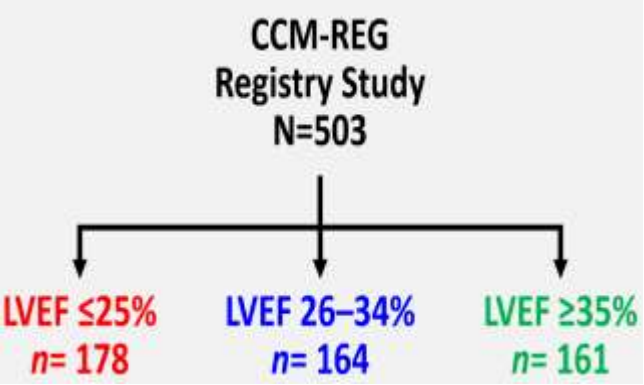


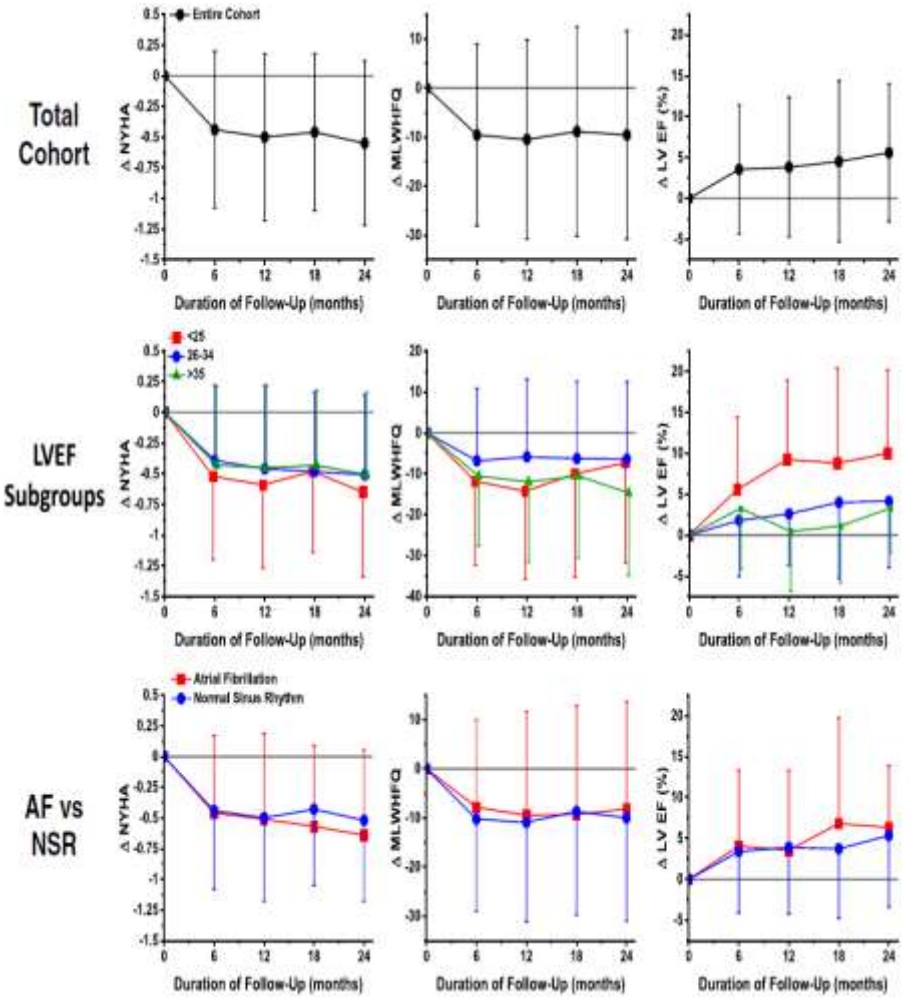
Long-term clinical experience with cardiac contractility modulation therapy delivered by the Optimizer Smart system

Jürgen Kuschyk[1], Peter Falk[2], Thomas Demming[2], Oliver Marx[3], Deborah Morley[4], Ishu Rao[4], and Daniel Burkhoff[5]*

ESC European Society of Cardiology

European Journal of Heart Failure (2021)
doi:10.1002/ejhf.2202





Registro a lungo termine (24 mesi) real world di pazienti impiantati con dispositivo CCM secondo CE Mark del dispositivo (HF sistolico cronico sintomatico→ Fe ≤ 45%, NYHA>II in OMT) per valutare impatto sulla mortalità, QoL, eventi SCC, FE Vsx e QOL.
Età media 66 anni, 60% ischemici, NYHA III 82%, FE 30%, FA 30%.

Il 75% dei pazienti già portatori di ICD

Kuschyck J. EJHF 2021

Long-term clinical experience with cardiac contractility modulation therapy delivered by the Optimizer Smart system

Jürgen Kuschyk[1], Peter Falk[2], Thomas Demming[2], Oliver Marx[3], Deborah Morley[4], Ishu Rao[4], and Daniel Burkhoff[5]*

ESC European Society of Cardiology

European Journal of Heart Failure (2021)
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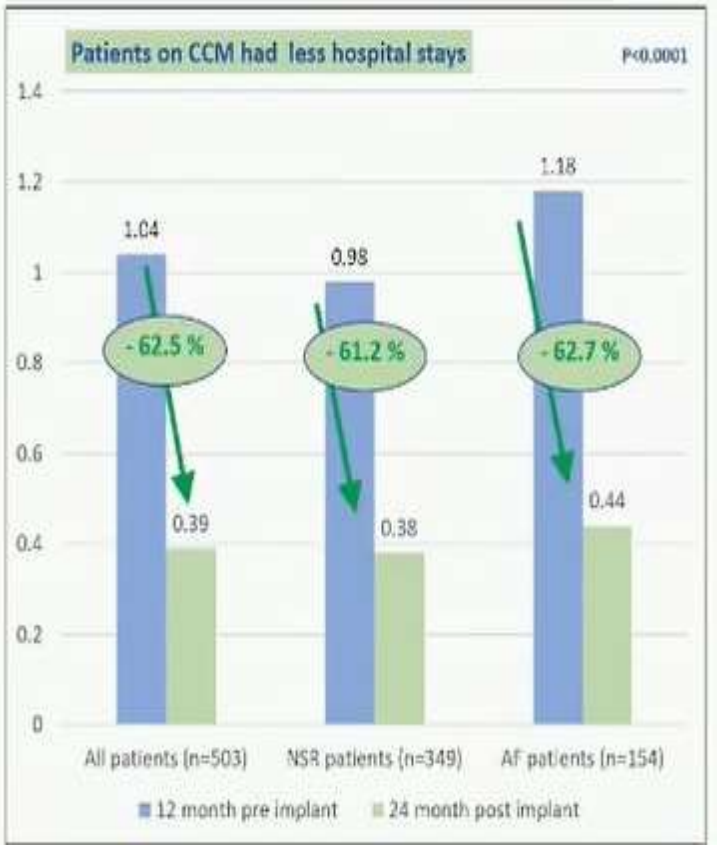
Table 3 Hospitalization rates the year prior to Optimizer implant compared to the 2 years following Optimizer implant in the entire cohort and in the five subgroups of interest

Subgroup	Pre-treatment (1 year prior)				Post-treatment (0–730 days)				
	Patients	Patient-years	Events	Event rate	Patients	Patient-years	Events	Event rate	P-value
All patients									
All cardiovascular events	503	503	523	1.04	503	729	287	0.39	<0.0001
Heart failure events			371	0.74			179	0.25	<0.0001
Non-heart failure cardiovascular events			152	0.30			108	0.15	<0.0001
LVEF ≤25%									
All cardiovascular events	178	178	227	1.28	178	233	123	0.53	<0.0001
Heart failure events			182	1.02			90	0.39	<0.0001
Non-heart failure cardiovascular events			45	0.25			33	0.14	0.0106
LVEF 26–34%									
All cardiovascular events	164	164	157	0.96	164	255	99	0.39	<0.0001
Heart failure events			102	0.62			59	0.23	<0.0001
Non-heart failure cardiovascular events			55	0.34			40	0.16	0.0002
LVEF ≥35%									
All cardiovascular events	161	161	139	0.86	161	242	65	0.27	<0.0001
Heart failure events			87	0.54			30	0.12	<0.0001
Non-heart failure cardiovascular events			52	0.32			35	0.14	0.0002
Normal sinus rhythm									
All cardiovascular events	349	349	342	0.98	349	530	200	0.38	<0.0001
Heart failure events			229	0.66			130	0.25	<0.0001
Non-heart failure cardiovascular events			113	0.32			70	0.13	<0.0001
Atrial fibrillation									
All cardiovascular events	154	154	181	1.18	154	198	87	0.44	<0.0001
Heart failure events			142	0.92			49	0.25	<0.0001
Non-heart failure cardiovascular events			39	0.25			38	0.19	0.2189

LVEF, left ventricular ejection fraction.



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ESC European Society of Cardiology
European Journal of Heart Failure (2023)
doi:10.1002/ejhf.2874
POSITION PAPER

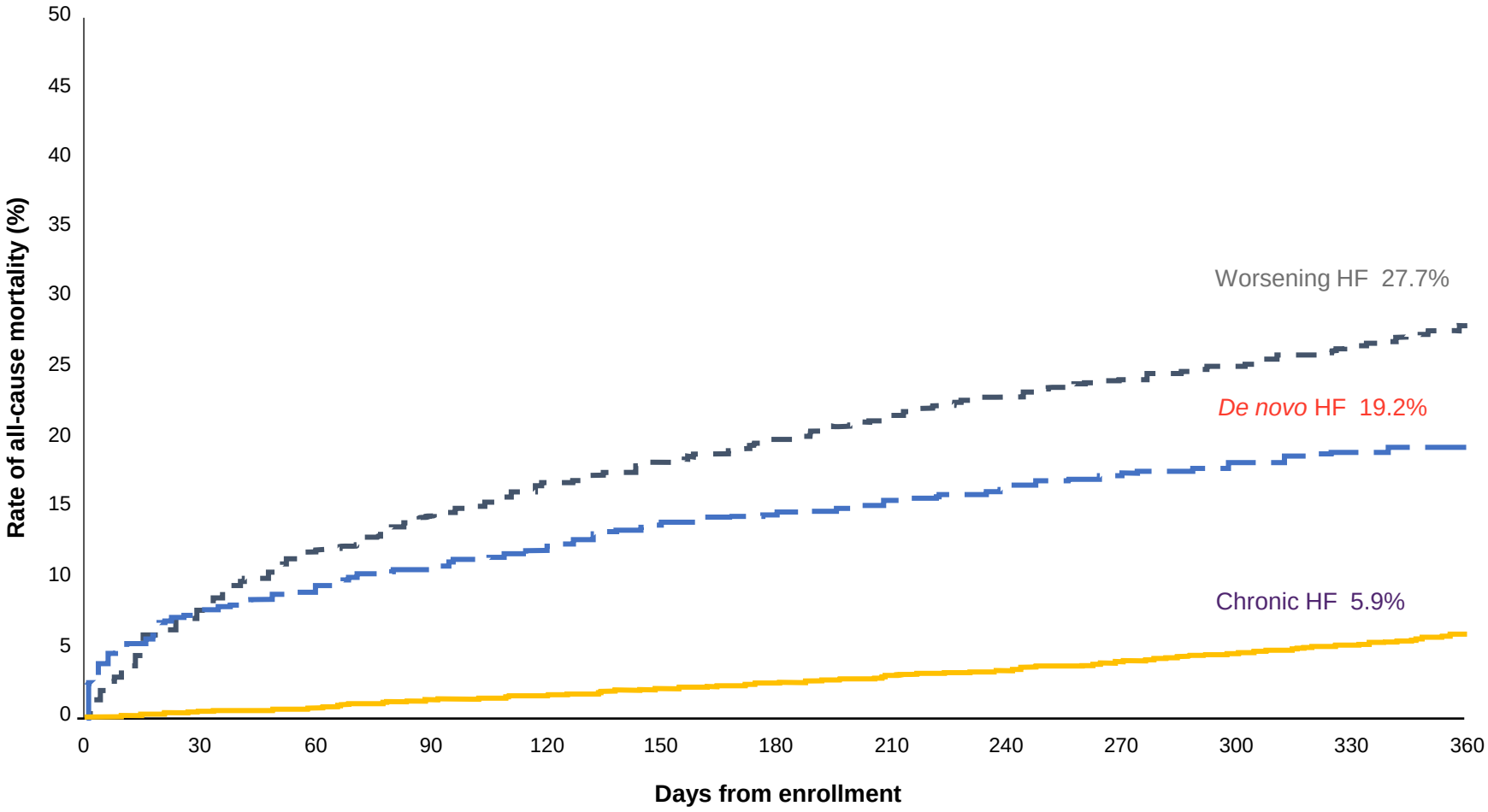
Worsening of chronic heart failure: definition, epidemiology, management and prevention. A clinical consensus statement by the Heart Failure Association of the European Society of Cardiology

Marco Metra[1,2], Daniela Tomasoni[1,2], Marianna Adamo[1*], Antoni Bayes-Genis[3], Gerasimos Filippatos[4], Magdy Abdelhamid[5], Stamatis Adamopoulos[6], Stefan D. Anker[7], Laura Antohi[7,8], Michael Böhm[9], Frieder Braunschweig[10], Tuvia Ben Gal[11], Javed Butler[12], John G.F. Cleland[13], Alain Cohen-Solal[14], Kevin Damman[15], Finn Gustafsson[16], Loreena Hill[17], Ewa A. Jankowska[18], Mitja Lainscak[19], Lars H. Lund[8], Theresa McDonagh[20], Alexandre Mebazaa[21], Brenda Moura[22,23], Wilfried Mullens[24], Massimo Piepoli[25,26], Piotr Ponikowski[18], Amina Rakisheva[27], Arsen Ristic[28], Gianluigi Savarese[8], Petar Seferovic[28], Rajan Sharma[29], Carlo Gabriele Tocchetti[30], Mehmet Birhan Yilmaz[31], Cristiana Vitale[32], Maurizio Volterrani[32], Stephan von Haehling[33,34], Ovidiu Chioncel[6,7], Andrew J.S. Coats[35], and Giuseppe Rosano[32]

The clinical course of heart failure (HF) is characterized by episodes of worsening symptoms and signs.[1–3] These episodes of worsening HF (WHF) are followed by an increased risk of hospitalizations and death and are a major burden on the health-care system, because of their frequency, urgency and prognostic impact.[1,3–5] Their prevention is a major target of current treatment of HF. The aim of the present clinical consensus statement by the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) is to provide an update on the definition and clinical characteristics of WHF and summarize recent findings for the management and prevention of WHF in clinical practice.

Metra et al. Eur J Heart Fail 2023

One-year all-cause mortality rate in patients hospitalized with acute HF or outpatients with chronic HF, prospectively enrolled in the IN-HF outcome registry (N=5,610)



Tavazzi L et al. Circ Heart Fail 2013

Pathophysiologic Targets in the Early Phase of Acute Heart Failure Syndromes

Mihai Gheorghiade, MD,[a,*] Leonardo De Luca, MD,[b] Gregg C. Fonarow, MD,[c] Gerasimos Filippatos, MD,[d] Marco Metra, MD,[e] and Gary S. Francis, MD[f]

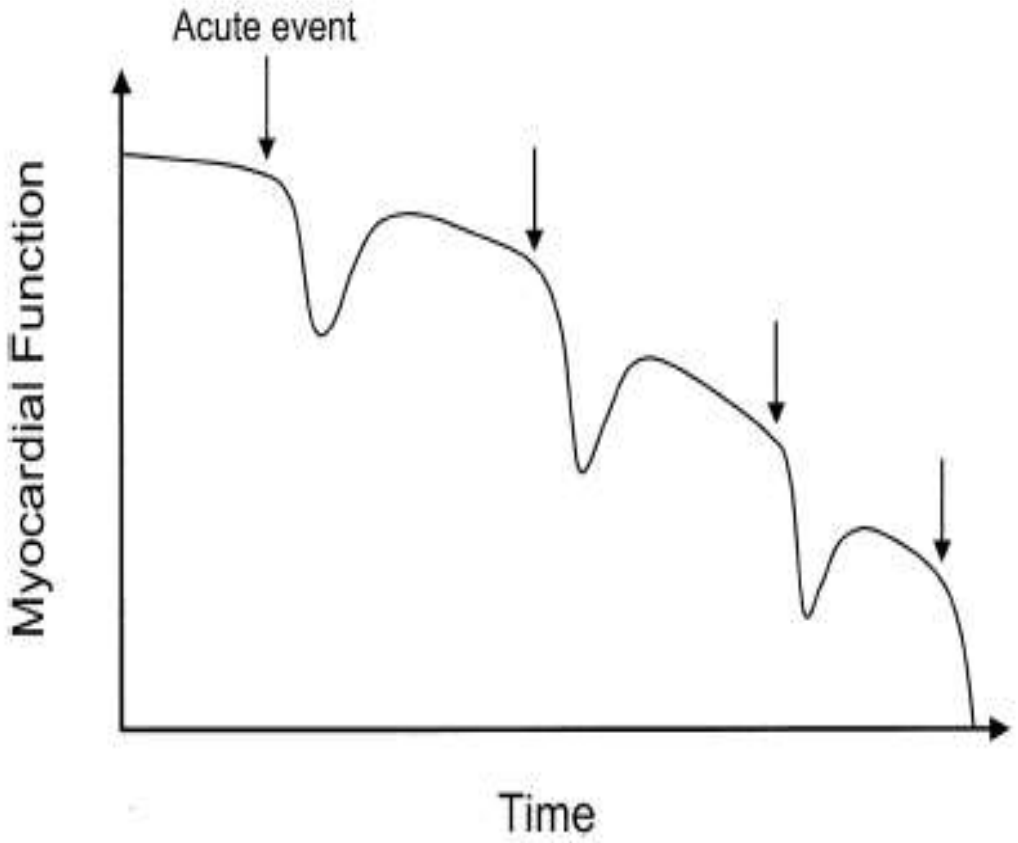


Figure 2. Contribution of acute events to the progression of heart failure. With each admission for acute heart failure syndromes, there is a short-term improvement; however, the patient leaves the hospital with a further decrease in cardiac function.

Gheorgiade M et al. Am Heart J.2005

CCMT in which patients?

- NYHA II with 2 or more WHF episodes in the last 12 months
- NYHA III-IV with at least 1 WHF episodes in the last 12 months
- 25%≤EF ≤45%
- QRS ≤130 ms (in some selected cases also in CRT-D non responder)
- GDMT
- BEV < 10.000; AF with VR < 110 b/min
- No severe tricuspid, aortic, or disproportionate mitral valve regurgitation

How many patients with heart failure are eligible for cardiac contractility modulation therapy?

Rajdip Dulai | Ahmed Chilmeran | Mazin Hassan | Rick A. Veasey | Stephen Furniss | Nikhil R. Patel | Neil Sulke

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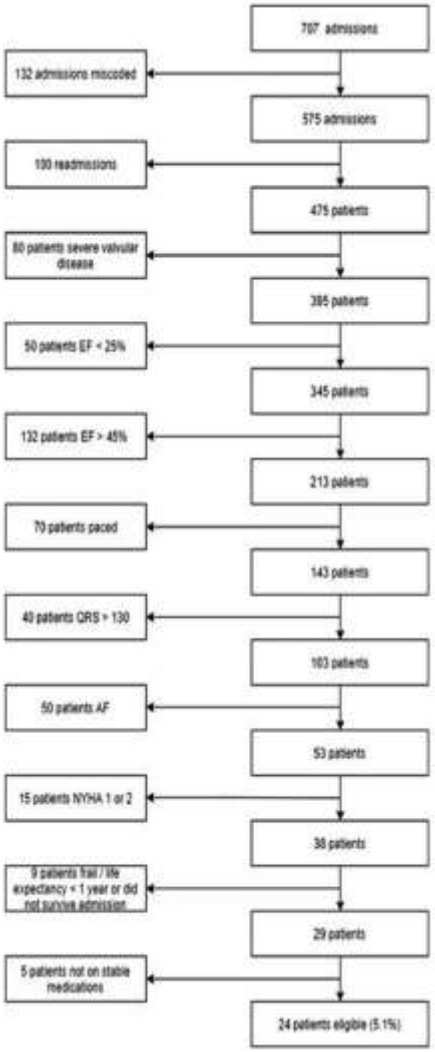
ORIGINAL PAPER
CARDIOVASCULAR MEDICINE

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY



Results: A total of 475 patients were admitted with heart failure during the study period. From this group, 24 (5.1%) patients fulfilled the criteria for CCM therapy. The mean age and ejection fraction were 70.8 ± 10.2 and 32.5% ± 7.4%. The majority of patients were men (71%) and had an ischaemic cardiomyopathy (75%). If patients with atrial fibrillation were included, an additional 18 (3.8%) patients potentially may be eligible for CCM.

Conclusion: Only 5.1% of all patients presenting with heart failure might benefit from cardiac CCM. This is a small proportion of the overall heart failure population. However, this population has no other current option for device therapy of their condition.

TABLE 3 Comparison of baseline characteristics of patients eligible for CCM therapy (Sinus rhythm patients vs atrial fibrillation patients)

	Sinus Rhythm patients (N = 24)	Atrial fibrillation patients (N = 18)	P value
Age	70.9 ± 10.2	77.2 ± 7.7	.03
Male Gender (%)	17 (70.8)	11 (61.1)	.53
Ejection fraction (%)	32.5 ± 7.4	35.7 ± 8.4	.20
QRS duration (msec)	106.0 ± 13.0	102.3 ± 12.4	.36
Ischaemic aetiology (%)	21 (87.5)	12 (66.7)	.14
Hypertension (%)	11 (45.8)	13 (72.2)	.12
Diabetes (%)	9 (37.5)	4 (22.2)	.33
COPD (%)	3 (12.5)	2 (11.1)	1.00
CKD (%)	18 (75.0)	10 (55.6)	.20
MRA (%)	15 (62.5)	7 (38.9)	.21
NYHA class			
3	14 (58.3)	7 (38.9)	.35
4	10 (41.7)	11 (61.1)	.35

Abbreviations: CCM, contractility modulation; CKD chronic kidney disease; COPD Chronic obstructive pulmonary disease; EF, ejection fraction; MRA mineralocorticoid receptor antagonist; NYHA, New York Heart Association.

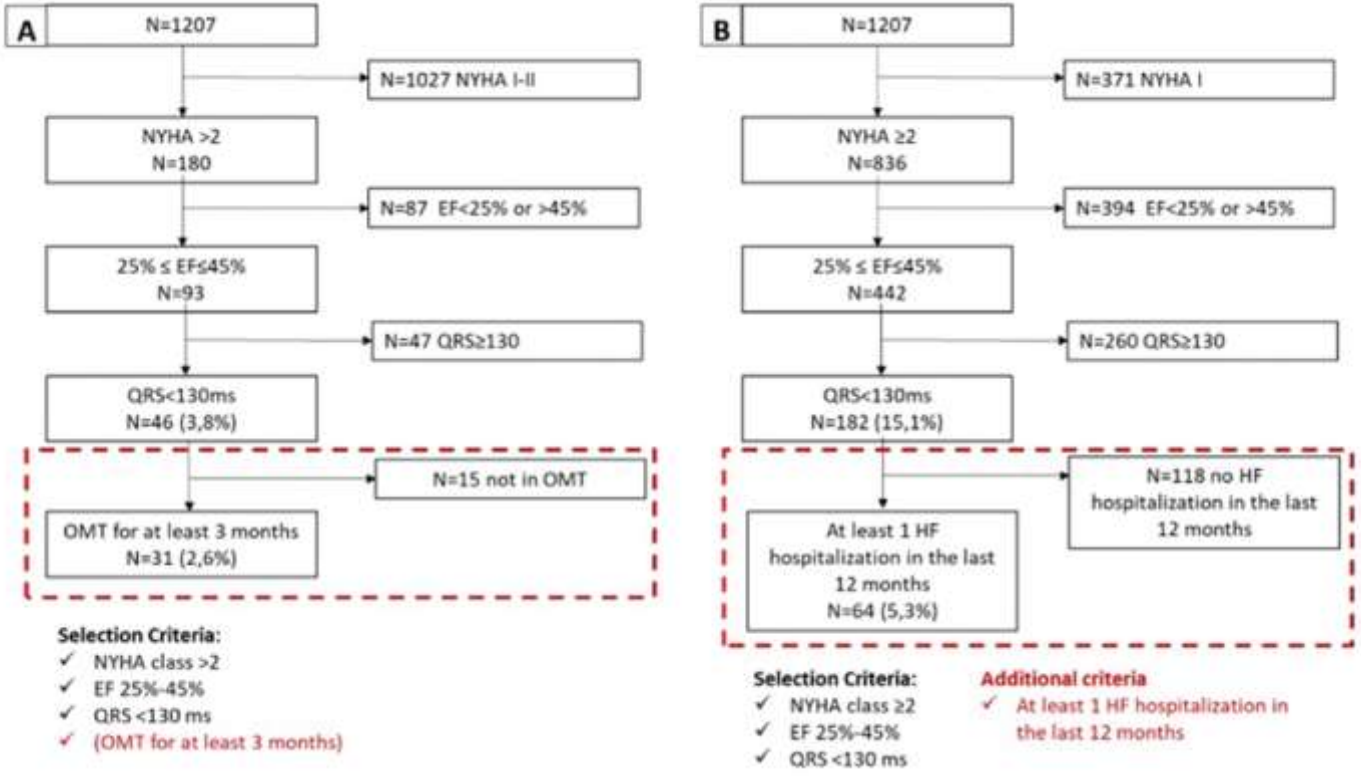
Dulai R et al. IJCP 2020

Expert Review of Medical Devices

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ierd20

Bridging the gap in the symptomatic heart failure patient journey: insights from the Italian scenario

Matteo Ziacchi, Alberto Spadotto, Stefano Ghio, Marta Pellegrino, Luciano Potena, Daniele Masarone, Marco Merlo, Davide Stolfo, Maria Michela Caracciolo, Corinna Inserra, Fabrizio Ammirati, Michele Ciccarelli, Furio Colivicchi, Stefano Bianchi, Giuseppe Patti, Fabrizio Oliva, Giuseppe Arcidiacono, Roberto Rordorf, Daniela Pini, Giuseppe Pacileo, Antonio D'Onofrio, Giovanni Battista Forleo, Matteo Mariani, Francesco Adamo, Alessandro Alonzo, Matteo Ruzzolini, Chiara Ghiglieno, Manlio Cipriani, Giorgio Firetto, Nadia Aspromonte, Francesco Clemenza, Gaetano Maria De Ferrari, Michele Senni, Maria Grazia Bongiorni, Claudio Tondo, Massimo Grimaldi, Francesco Giallauria, Francesco Rametta, Procolo Marchese, Mauro Biffi & Gianfranco Sinagra



Ziacchi M et al. Ex Rev Med Dev 2023

EXPERT REVIEW OF MEDICAL DEVICES
2023, VOL. 20, NO. 7, 525–528
https://doi.org/10.1080/17434440.2023.2217329

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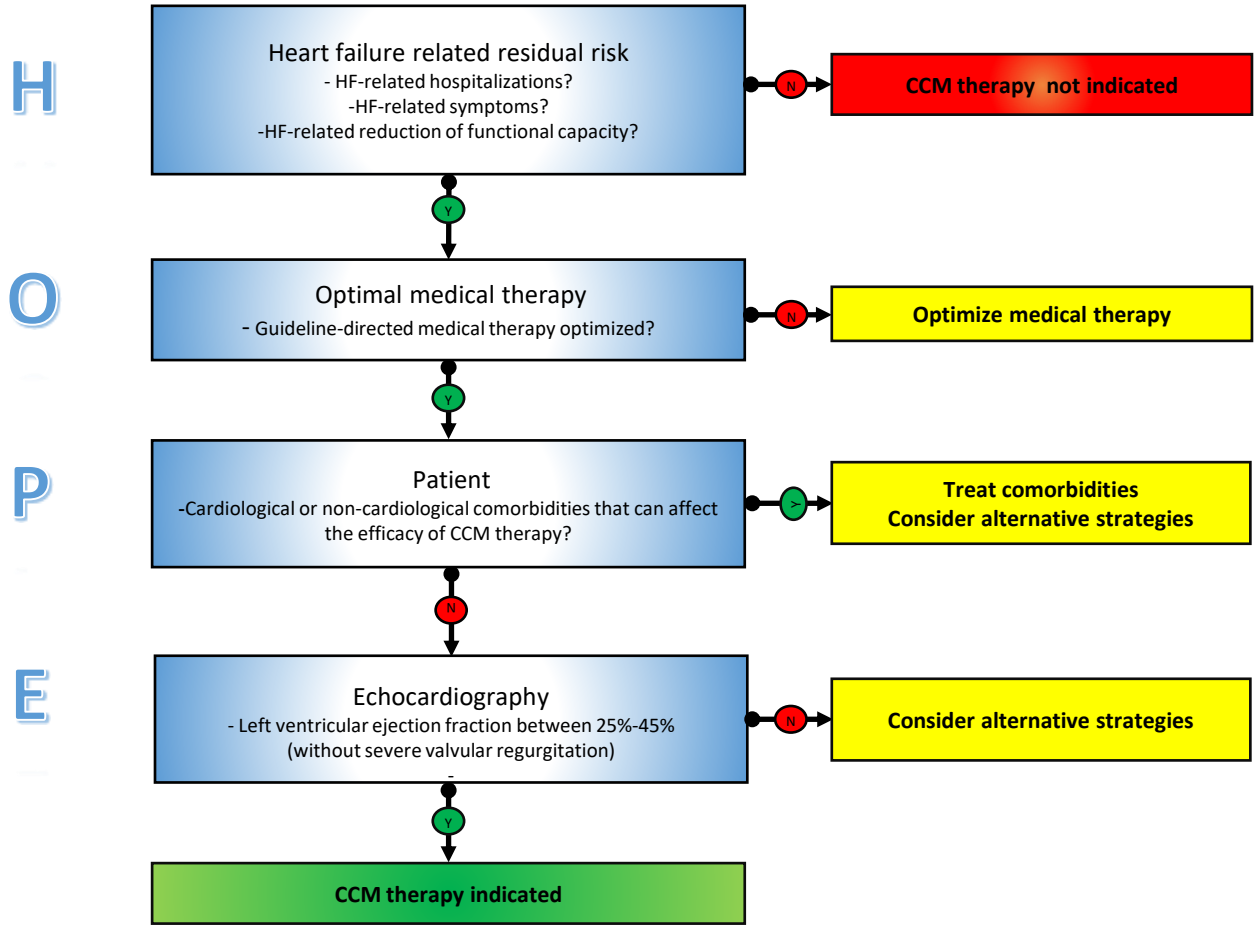
EDITORIAL

HOPE for a better selection of patients for cardiac contractility modulation

Daniele Masarone [a], Ishu Rao [b] and Giuseppe Pacileo [a]

[a]Heart Failure Unit, Department of Cardiology, AORN dei Colli Monaldi Hospital, Naples, Italy; [b]Impulse Dynamics, Inc, Marlton, NJ, USA



Masarone D. Exp Rev Med Dev 2023

Journal of Clinical Medicine

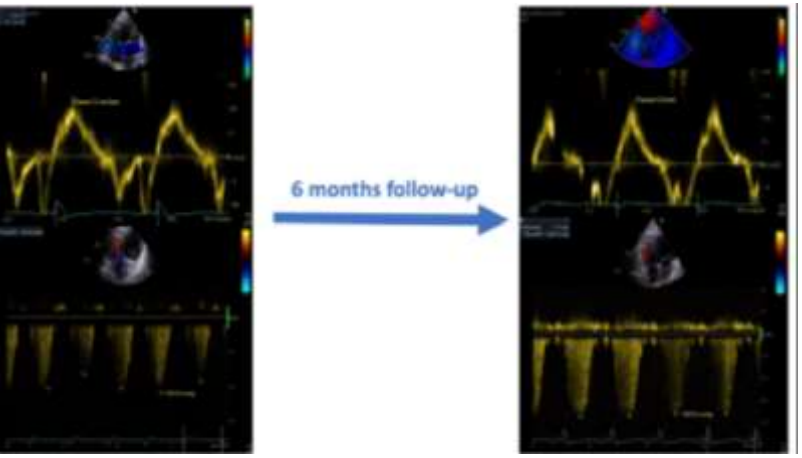
MDPI

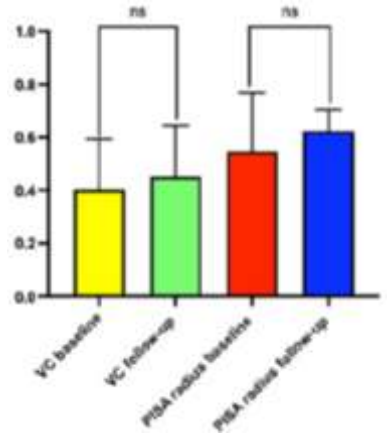
Article

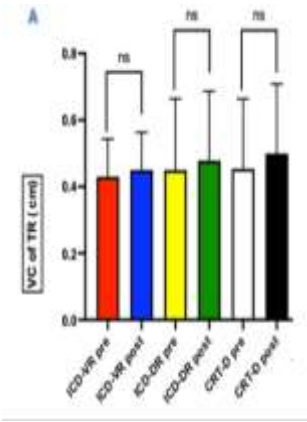
Effects of Cardiac Contractility Modulation Electrodes on Tricuspid Regurgitation in Patients with Heart Failure with Reduced Ejection Fraction: A Pilot Study

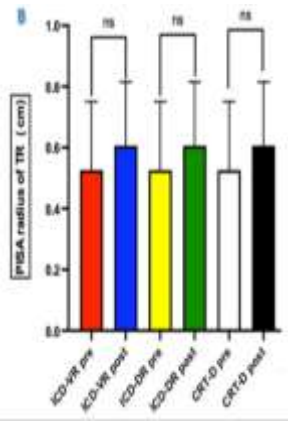
Daniele Masarone [1,*], Michelle M. Kittleson [2], Stefano De Vivo [3], Antonio D'Onofrio [3], Ishu Rao [4], Ernesto Ammendola [1], Vittoria Errigo [1], Maria L. Martucci [1], Gerardo Nigro [5] and Giuseppe Pacileo [1]

Analisi su 30 pazienti sottoposti ad impianto di dispositivo per CCM per la valutazione degli effetti dell'impianto di 2 cateteri transvenosi sulla severità del rigurgito tricuspidalico.









Assessment of CCM in HF With Higher Ejection Fraction (AIM HIGHer)

https://clinicaltrials.gov/ct2/show/NCT05064709

AIM HIGH*er* trial

Studio multicentrico randomizzato, doppio cieco, sham-controlled per la valutazione dell'efficacia della terapia CCM in 1500 pazienti HF con **FE 40%-60%.**

- Endpoint parte 1: 6MWTD e KCCQ a 6 mesi di Fu;
- Endpoint parte 2: Outcome composito di esiti di mortalità, morbilità e QoL (KCCQ CSS) al FU a 18 mesi.

La terapia CCM per HFpEF ha già ricevuto la ***breakthrough device designation*** della FDA

Assessment of Combined CCM and ICD Device in HFrEF (INTEGRA-D Study)

ClinicalTrials.gov Identifier: NCT05855135

Studio di sicurezza

- Riconoscimento di VF indotta all'impianto ed episodi di VT/VF spontanea in pazienti HF in OMT non candidati alla CRT con FE≤ 40%.
- Tasso di complicanze correlate al dispositivo a 6 mesi dal post impianto;
- Valutazione di incidenza di shock inappropriati a 6 mesi dall'impianto

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MAY 18, 2023 / NEWS RELEASES

Cleveland Clinic Performs World's First Implant of Combined Heart Failure Therapies

Novel device improves quality of life

Cleveland Clinic has successfully implanted a dual cardiac device in the first patient in the world as part of a clinical trial, which aims to potentially treat heart failure symptoms.

The INTEGRA-D clinical study will evaluate the safety and effectiveness of a device that combines two proven cardiac therapies into one. Cardiac contractility modulation works to improve the contraction of the heart, while an implantable cardioverter defibrillator (ICD) treats life-threatening arrhythmias that cause sudden cardiac death.

Bruce Wilkoff, M.D., (left) and Niraj Varma, M.D., Ph.D., implanted a dual cardiac device in the first patient in the world on May 17, 2023.