

# PLACE

The logo for PLACE consists of the word "PLACE" in a large, dark red, serif font. To the right of the text is a stylized graphic of a heart, composed of several overlapping, curved, red and white lines that create a sense of motion and depth.

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

**ROMA**

Centro Congressi  
di Confindustria

**Auditorium  
della Tecnica**

**9ª Edizione**

**30 Settembre**

**1 Ottobre**

**2022**



**CARDIAC CONTRACTILITY MODULATION: UN'OPZIONE TERAPEUTICA  
PER IL TRATTAMENTO DELLO SCOMPENSO CARDIACO**

## **INDICAZIONE DELLA TERAPIA CCM NELLA VITA REALE: PRO E CONTRO**

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**AOU Maggiore della Carità, Novara**

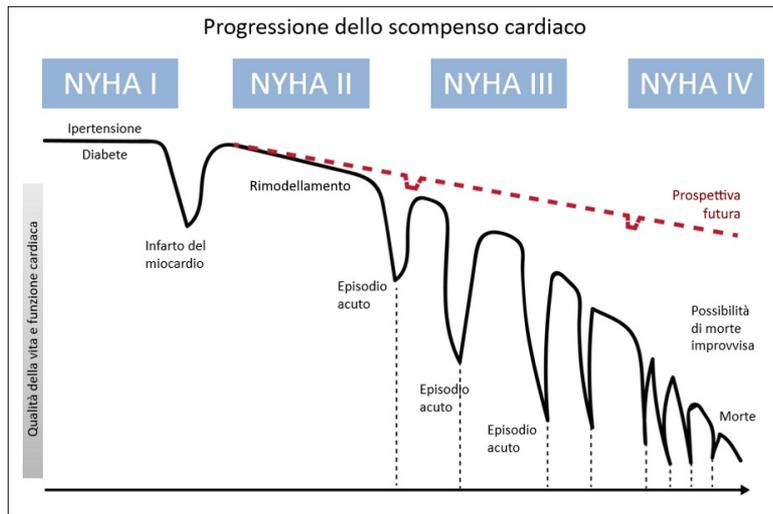


# Evoluzione dell'HF

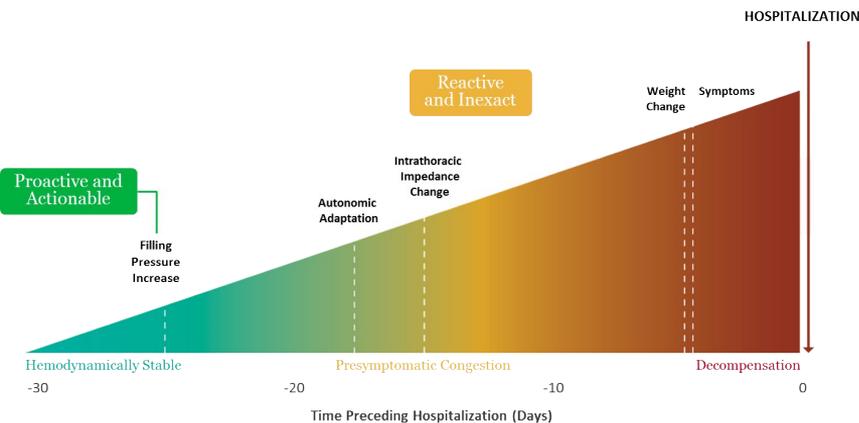
Gestione ottimale del paziente con scompenso:

- Obiettivo prognostico (qualità di vita, sopravvivenza)
- Obiettivo diagnostico (riduzione ricoveri e costi sociali)

**Ogni evento acuto ha conseguenze irreversibili sulla funzionalità cardiaca**



CCM?



Timing dei sintomi relativi ad episodi acuti di HF



# FIX-5C (2018)

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

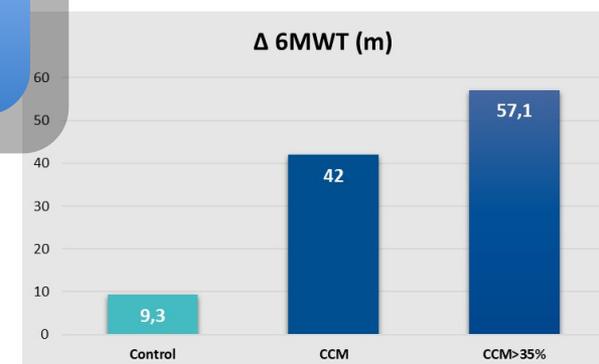
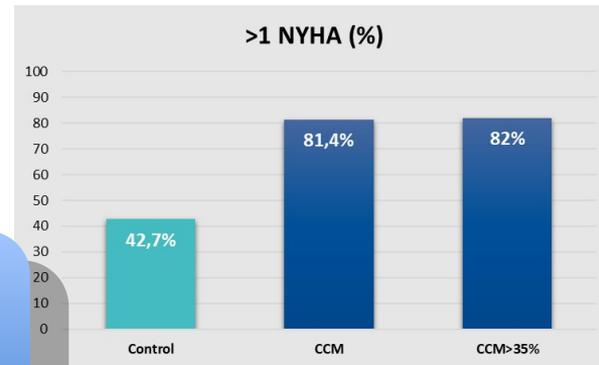
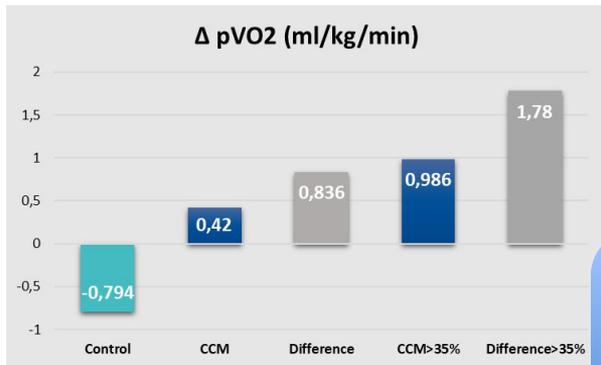
William T. Abraham, MD,<sup>a</sup> Karl-Heinz Kuck, MD,<sup>b</sup> Rochelle L. Goldsmith, PhD,<sup>c</sup> JoAnn Lindenfeld, MD,<sup>d</sup> Vivek Y. Reddy, MD,<sup>e</sup> Peter E. Carson, MD,<sup>f</sup> Douglas L. Mann, MD,<sup>g</sup> Benjamin Saville, PhD,<sup>h</sup> Helen Parise, ScD,<sup>i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

### OBJECTIVE

Confirm a subgroup analysis of the prior FIX-HF-5 study showing that cardiac contractility modulation (CCM) improved exercise tolerance and quality of life in patients with **EF between 25% and 45%**.



# FIX-HF-5C Study: EF 35-45% subgroup analysis



Even stronger effects in patients with EF 35-45%

# CCM-REG (2018)



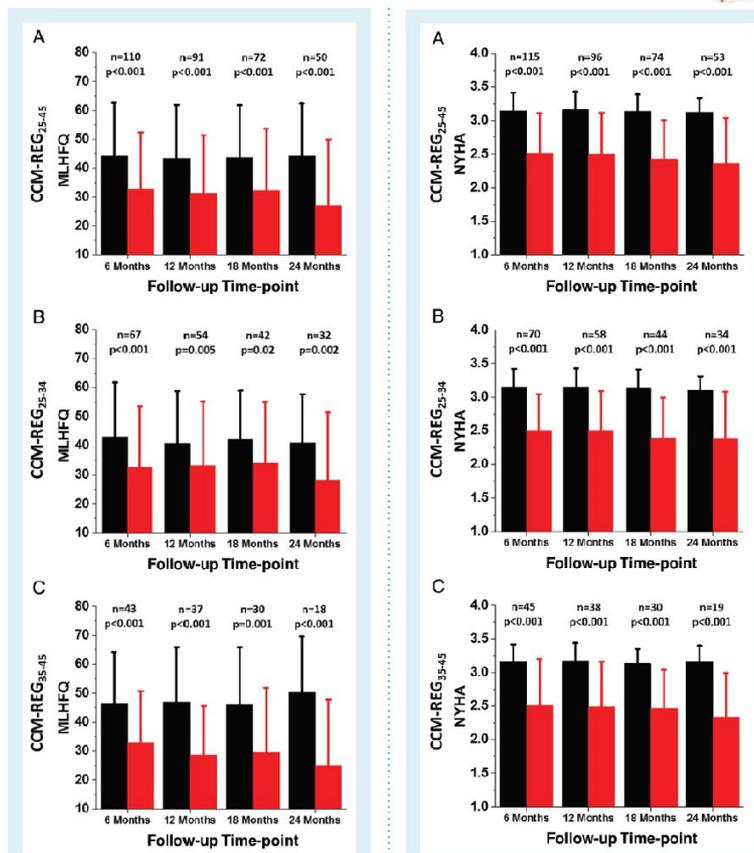
European Journal of Heart Failure (2019)  
doi:10.1002/ehf.1374

RESEARCH ARTICLE

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

Stefan D. Anker<sup>1,2†</sup>, Martin Borggrefe<sup>3,4,5†</sup>, Hans Neuser<sup>6</sup>, Marc-Alexander Ohlow<sup>7</sup>, Susanne Röger<sup>3,4,5</sup>, Andreas Goette<sup>8,9</sup>, Bjoern A. Remppis<sup>10</sup>, Karl-Heinz Kuck<sup>11</sup>, Kevin B. Najarian<sup>12</sup>, David D. Gutterman<sup>13</sup>, Benny Rousso<sup>14</sup>, Daniel Burkhoff<sup>15</sup>, and Gerd Hasenfuss<sup>2\*</sup>

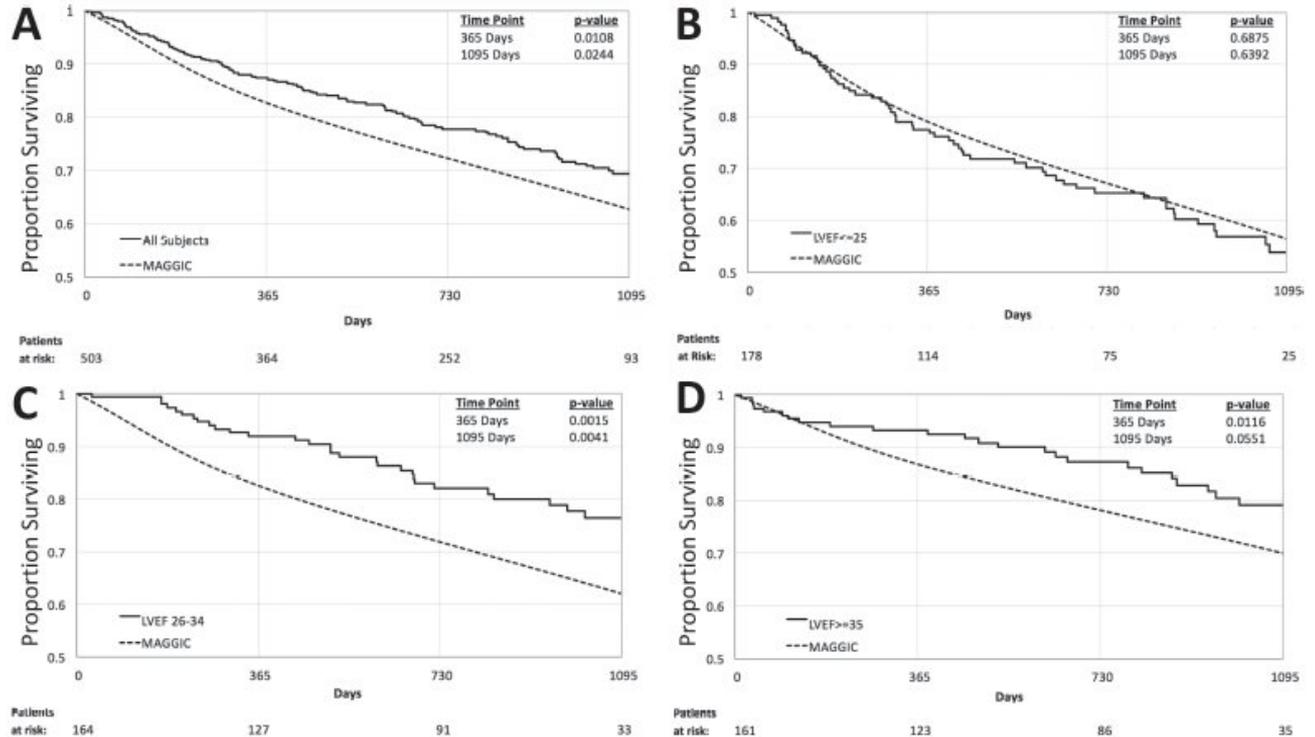
Symptoms and quality of life (NYHA class, MLHFQ) showed sustainable improvement and of similar magnitude to the ones observed in the randomized studies. LVEF also improved during the early follow-up period, as in prior studies.





# Survival rate based on LVEF terciles CCM REG (2021)

- In the overall cohort, survival at 1- and 3-year follow-up was significantly better than predicted by the MAGGIC risk score.
- This was especially apparent for the LVEF 26–34% and LVEF ≥35% subgroups.





# CCM and NYHA II vs III/IV (Maintained Study)

Clinical Research in Cardiology  
<https://doi.org/10.1007/s00392-022-02089-w>

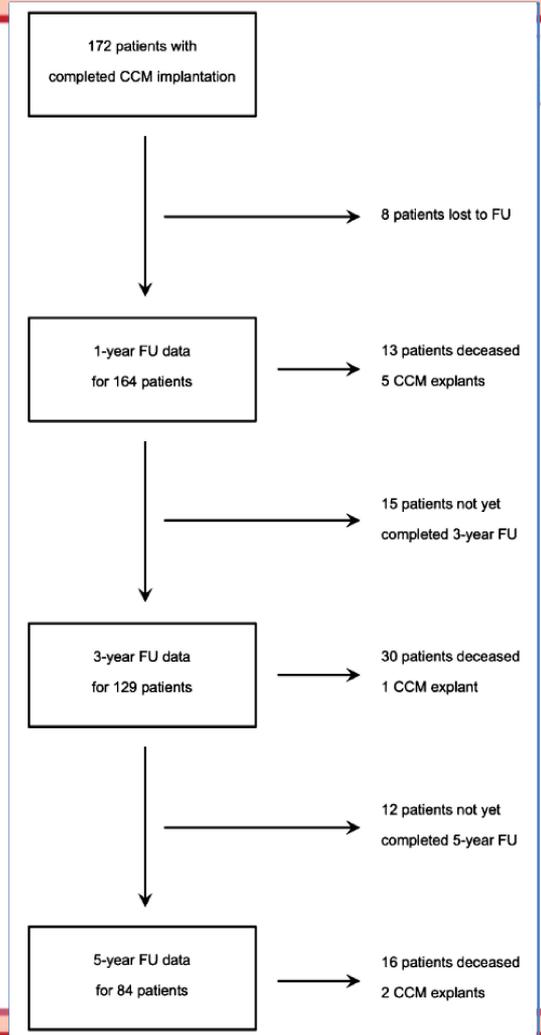
ORIGINAL PAPER



Should HF<sub>rEF</sub> patients with NYHA class II expect benefit from CCM therapy? Results from the MAINTAINED observational study

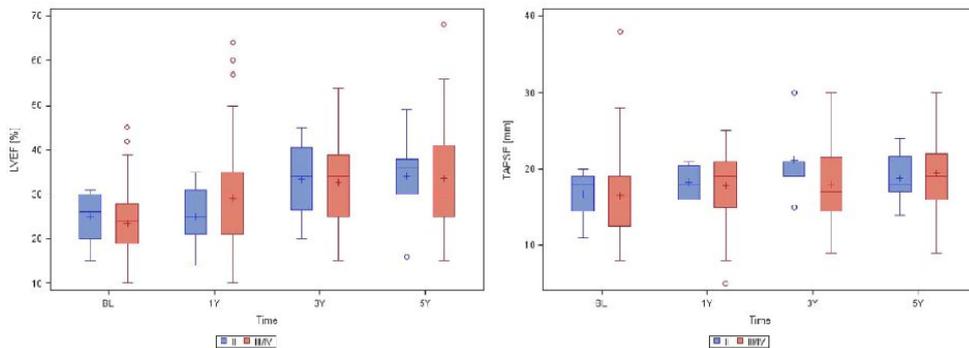
Christian Fastner<sup>1,2</sup> · Goekhan Yuceel<sup>1</sup> · Svetlana Hetjens<sup>3</sup> · Boris Rudic<sup>1</sup> · Gereon Schmiel<sup>1</sup> · Matthias Toepel<sup>1</sup> · Volker Liebe<sup>1</sup> · Mathieu Kruska<sup>1</sup> · Martin Borggrefe<sup>1</sup> · Daniel Burkhoff<sup>4</sup> · Ibrahim Akin<sup>1</sup> · Daniel Duerschmied<sup>1</sup> · Juergen Kuschyk<sup>1</sup>

In clinical practice, patients with mildly symptomatic heart failure in NYHA class II experience significant improvement in LVEF under CCM therapy. Patients with more advanced heart failure additionally benefit from immediate improvement in NYHA class, improvement in RV function over a longer therapy period, and significantly lower mortality compared with the MAGGIC heart failure risk score prognosis.





# CCM and NYHA II vs III/IV (Maintained Study)

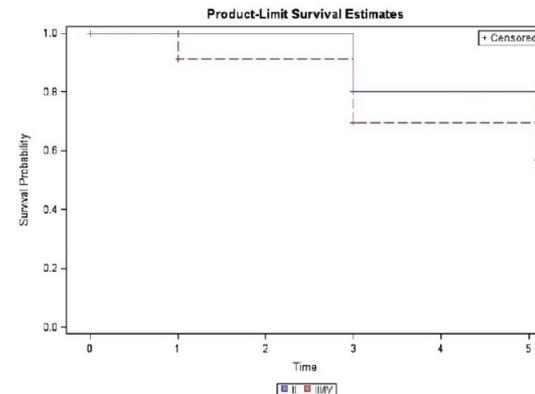


**Fig.2** Changes in LVEF and TAPSE at different follow-up time points. Left figure: boxplot of mean values with standard deviations of left ventricular ejection fraction (LVEF), right figure: regard

ing tricuspid annular plane systolic excursion (TAPSE), *BL* baseline, *FU* follow-up period, *Y* year

For the first time, the present work demonstrated that patients with initial NYHA class III or ambulatory IV can expect broader and more pronounced functional benefits than patients with initial NYHA class II in clinical practice of CCM. Nevertheless, the latter patients also benefited from therapy in relation to LVEF improvement.

**Fig.3** Kaplan Meier analysis of survival over the 5-year period,  $p = 0.60$





## Use of Cardiac Contractility Modulation as Bridge to Transplant in an Obese Patient With Advanced Heart Failure: A Case Report

Daniele Masarone<sup>1\*</sup>, Andrea Petraio<sup>2</sup>, Antonio Fiorentino<sup>3</sup>, Santo Dellegrattaglia<sup>4,5</sup>, Fabio Valente<sup>1</sup>, Ernesto Ammendola<sup>1</sup>, Gerardo Nigro<sup>6</sup> and Giuseppe Pacileo<sup>7</sup>

Use of CCM as a “bridge to transplant” in a young obese patient with advanced heart failure due to non-ischemic dilated cardiomyopathy.

The patient had a poor quality of life and frequent heart failure-related hospitalizations despite the optimal medical therapy and, due to obesity, a suitable heart donor was unlikely to be identified in the short term and due to severe obesity risk of complications after implantation of a left ventricular assist device (LVAD) was very high.

CCM could be used as a bridge to transplant strategy in selected patients with endstage HF<sub>rEF</sub>, not adequately compensated by pharmacological therapy with contraindications to LVAD, such as patients with severe obesity.

**TABLE 2** | Comparison on demographic, clinical, echocardiographic and laboratory parameters between admission and 6 months follow-up.

Parameter	Baseline	6 months follow-up
Weight	128 kg	124
Height	175 cm	175
BMI (Deveraux)	41.8	40.4
BSA (Dubois)	2.39 m <sup>2</sup>	2.36 m <sup>2</sup>
BP	130/80 mmHg	120/70 mmHg
HR	105 b/m	88 b/m
LVEDVI	123.9 ml/m <sup>2</sup>	119.8 ml/m <sup>2</sup>
LVESVI	99.1 ml/m <sup>2</sup>	85.3 ml/m <sup>2</sup>
EF (Simplon biplane)	20%	28%
E/e' average	14	9
LAVI	47 ml/m <sup>2</sup>	43 ml/m <sup>2</sup>
PASP	60 mmHg	35
IVC diameter	24	18
IVC collapsibility index	29.1%	37.4%
NT-proBNP	3,569 pg/ml	2,256 pg/ml
MLWHFQ score	43	14

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

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Theresa A. McDonagh\* (Chairperson) (United Kingdom), Marco Metra\* (Chairperson) (Italy), Marianna Adamo (Task Force Coordinator) (Italy), Roy S. Gardner (Task Force Coordinator) (United Kingdom), Andreas Baumbach (United Kingdom), Michael Böhm (Germany), Haran Burri (Switzerland), Javed Butler (United States of America), Jelena Čelutkienė (Lithuania), Ovidiu Chioncel (Romania), John G.F. Cleland (United Kingdom), Andrew J.S. Coats (United Kingdom), Maria G. Crespo-Leiro (Spain), Dimitrios Farmakis (Greece), Martine Gilard (France), Stephane Heymans

2021	Class	2016	Class
<b>Recommendations for device therapy in HFrEF</b>			
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of a non-ischaemic aetiology, and an LVEF $\leq 35\%$ despite $\geq 3$ months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.	<b>IIa</b>	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 $\leq 35\%$ despite $\geq 3$ months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status, and they have DCM.	<b>I</b>



## CCM nei non-ischemici

International Journal of Cardiology 342 (2021) 49–55

Contents lists available at ScienceDirect

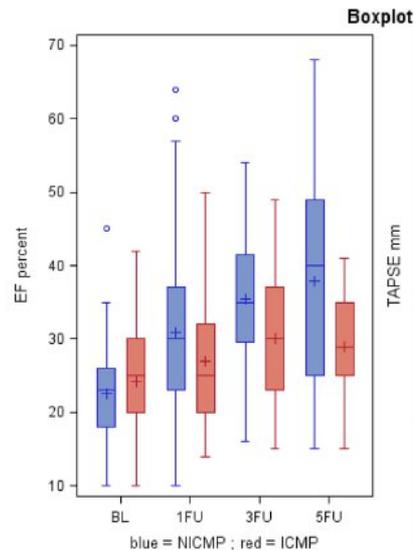
International Journal of Cardiology

journal homepage: [www.elsevier.com/locate/ijcard](http://www.elsevier.com/locate/ijcard)




Check for updates

Cardiac Contractility Modulation in Patients with Ischemic versus Non-ischemic Cardiomyopathy: Results from the MAINTAINED Observational Study



I non-ischemici mostrano un miglioramento della funzione sistolica significativamente maggiore al follow up.



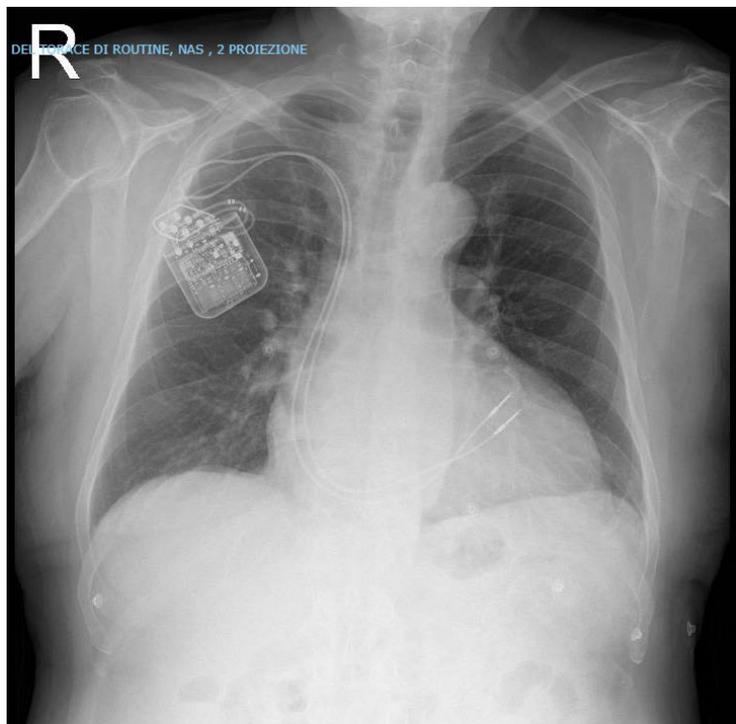
# CCM e FE «borderline»

- Maschio 78aa, iniziale decadimento cognitivo
- CMD postischemica, FA permanente, QRS stretto, FE 35-37% nonostante OMT
- Ripetute acutizzazioni di SCC, NYHA III

*Proposto CCM...*



# Follow-up 6 mesi



- FE 38%
- NYHA II
- Soddisfacente compliance (*caregiver!*)
- Non SCC



A.S.L. VC

Azienda Sanitaria Locale  
Vercelli

# Cardiac Contractility Modulation (CCM) Italian Registry: preliminary analysis

M. Matta<sup>1</sup>, C. Devecchi<sup>1</sup>, R. Troccoli<sup>2</sup>, A. Lupi<sup>3</sup>, P. Paffoni<sup>4</sup>, P. Nocerino<sup>5</sup>, G. Dell'Era<sup>6</sup>, G. Manganelli<sup>7</sup>,  
N. Di Belardino<sup>8</sup>, A. Lucifero<sup>9</sup>, V. Giudici<sup>10</sup>, C. D'Agostino<sup>2</sup>, E. Occhetta<sup>1</sup>, F. Rametta<sup>1</sup>

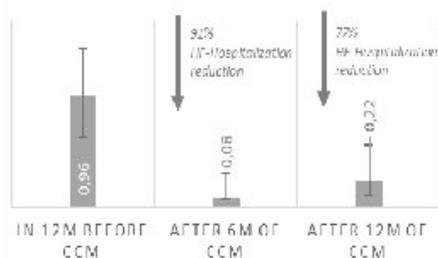
**EHRA 2022**  
Copenhagen,  
April 3-5

(1) Sant'Andrea Hospital, Vercelli, Italy. (2) Polyclinic Hospital of Bari, Italy. (3) Ospedale S.Biagio, Domodossola, Italy. (4) Institute S.S. Trinita, Borgomanero, Italy.  
(5) Santa Maria delle Grazie Hospital, Pozzuoli, Italy. (6) Hospital Maggiore Della Carita, Novara, Italy. (7) Ariano Irpino Hospital, Ariano Irpino, Italy. (8) Anzio-Nettuno Hospital, Anzio, Italy.  
(9) Giovanni Calibita Fatebenefratelli Hospital, Rome, Italy. (10) Bolognini Hospital, Seriate, Italy.

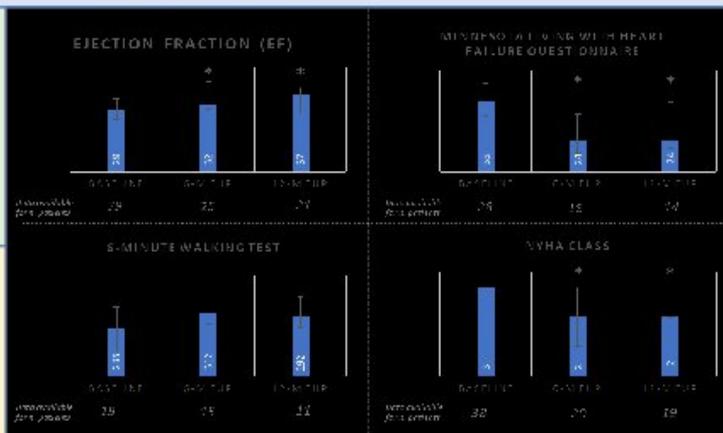
**Purpose and Methods** Cardiac contractility modulation (CCM) is a treatment option for improvement in quality of life (QoL) and reduction of HF-hospitalizations in patients suffering symptomatic **Chronic Heart Failure (HF) with reduced left ventricular ejection fraction (LVEF)** despite optimal medical therapy (OMT). The **CCM Italian Registry** is a prospective, observational, multicentre study investigating the long-term impact of CCM therapy in HF patients on **LVEF, Minnesota Living With HF Questionnaire (MLWHFQ) and 6-minutes walking test (6MWT)**. Preliminary results after 12 months of follow-up are now presented.

**Results** **42 patients** suffering **HF, with LVEF<45% NYHA class>II** despite OMT, have been enrolled and implanted with CCM in 10 Centres. **41 patients (98%) were males**, with a median age of **76 years (70-79)**. The most frequent etiology was **ischemic (29 patients, 69%)**, and **32 (79%) had another implanted device** (24 ICD, 8 CRT-D). **12 (29%) presented permanent atrial fibrillation (AF)**. **Thirty-eight (90%) patients were treated with beta-blockers** and **32 (76%) received sacubitril/valsartan (15) or ACE-inhibitors (17)**. A significant **reduction in HF hospitalizations** has been observed after **6 and 12 months (p<0.001)**.

## HF-HOSPITALIZATIONS/6M PER PATIENT



**LVEF significantly improved** both at 6 and 12-month follow up ( $p=0.042$  and  $p=0.004$ , respectively), as well as **MLWHFQ score** ( $p=0.001$  and  $p=0.032$ , respectively). **NYHA class improved** significantly both at 6 and 12-months ( $p=0.001$  and  $p=0.012$ ). **LVEF at 12-months improved significantly in non-ischaemic HF ( $p=0.028$ )**, while in patients with ischemic etiology improved significantly at 6-months ( $p=0.0416$ ) but not at 12 ( $p=0.135$ ).



**Conclusion:** **CCM** proved to be **effective in improving symptoms, QoL and in reducing CHF-hospitalizations** in patients with symptomatic **CHF with reduced LVEF**.



### HF-HOSPITALIZATIONS/6M PER PATIENT



IN 12M BEFORE CCM

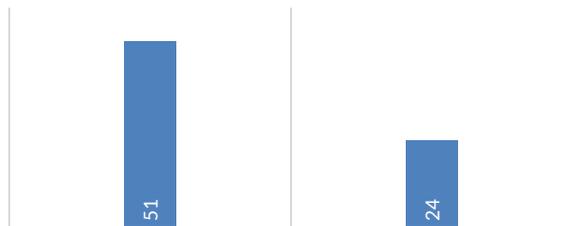
AFTER 6M OF CCM

Data available  
for n. patients

57

39

### MINNESOTA LIVING WITH HEART FAILURE QUESTIONNAIRE



BASELINE

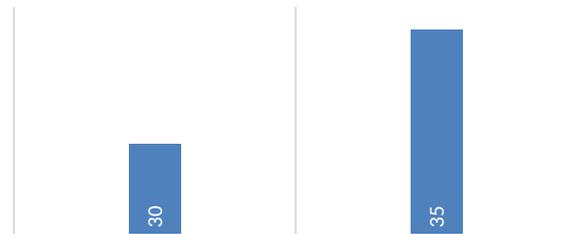
6-M FUP

Data available  
for n. patients

50

29

### EJECTION FRACTION (EF)



BASELINE

6-M FUP

66

37

**68 pz**

### 6-MINUTE WALKING TEST



BASELINE

6-M FUP

Data available  
for n. patients

21

15



# Nuovi e futuri dispositivi CCM

## Optimizer® Smart Mini



- ~23cc IPG con forma fisiologica
- Auto-setup dell'algoritmo CCM
- Telemetria RF
- Longevità >20 anni
- Nuova sezione diagnostica HF
- Certificazione MRI in corso

## Optimizer® Integra



- CCM™ integrata in un ICD con 2 elettrocaterteri
- <50cc
- Telemetria e algoritmo CCM™ come OPTIMIZER SMART-Mini
- Terapia ATP, Shock 36J e pacing post shock
- Longevità di almeno 15 anni
- 2 batterie (1 ricaricabile)

*Sottomissione per approvazione regolatoria in corso in US ed EU.  
Disponibilità commerciale prevista per il 2023.  
Ulteriori valutazione cliniche in corso di definizione.*



# CCM Clinical Trial Support



Optimizer<sup>®</sup> Smart



Optimizer<sup>®</sup> Smart Mini



Optimizer<sup>®</sup> Integra

Clinical Plan

## Post Approval Study

620 subjects  
3-year follow-up  
MLWHFQ, Mortality vs SHFM, Safety

## HFpEF (published 2022) AimHigher

~1,500 subjects, LVEF 40-60%  
Randomized, blinded,  
CCM ON versus OFF, 1-year endpoint

## Safety & Efficacy Protocol in Design



# Problemi aperti..



## **Compliance del paziente**

Impianto di 2 elettrocateri

Rischio infettivo

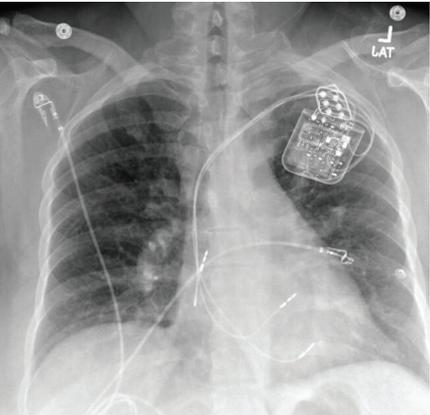
Elettrocateri e TVR

Interferenza tra dispositivi



# Scelta degli elettrocatteteri

- 2 elettrodi su SIV (procedura «standard»)
- Sensing richiesto  $>2\text{mV}$ , ottimale  $5\text{mV}$
- Compatibilità MRI con elettrocatteteri di altra marca MRI conditional (Mini in attesa certificazione)





# Aumento di rischio infettivo?

- **I rischio infettivi relativi al sistema CCM sono analoghi a quelli di un sistema di stimolazione bicamerale (PM convenzionale)**
- La ricaricabilità del sistema garantisce un minor rischio infettivo legato alla sostituzione del dispositivo

Numerosità elettrocateri:

- Le esperienze nei CRT NR non hanno evidenziato un aumento di eventi infettivi legati alla compresenza di 2 dispositivi e 5 elettrocateri
- Lo studio FIX-HF-5C2 (2020 Wiegand) ha rilevato una diminuzione di eventi legati alla presenza di 2 elettrocateri verso il vecchio sistema che ne necessitava 3



# Elettrocateri e rigurgito TV

CRT likely prevents progression of TR by improving LV function

(Prospective Study of TR associated with CRT)

	Baseline	1-year
PM/ICD (247)	4%	10%
	LVEF 53>>51% (p=0.005)	
CRT (43)	14%	11%
	LVEF 30>>38% (p<0.001)	

“RV pacing appears to worsen TR, an effect which might be caused by elevated LV filling pressure due to LV dysfunction”  
 (PROTECT-PACE Investigators, AJC 2015)

Study	# CCM pat	# CCM pat + ICD	% CCM pat + ICD	TR reported
FIX-HF-5	215	208	96%	0
FIX-HF-5C	68	65	96%	0
CCM-REG	503	378	75%	0
<b>Total</b>	<b>786</b>	<b>651</b>	<b>89%</b>	<b>0</b>

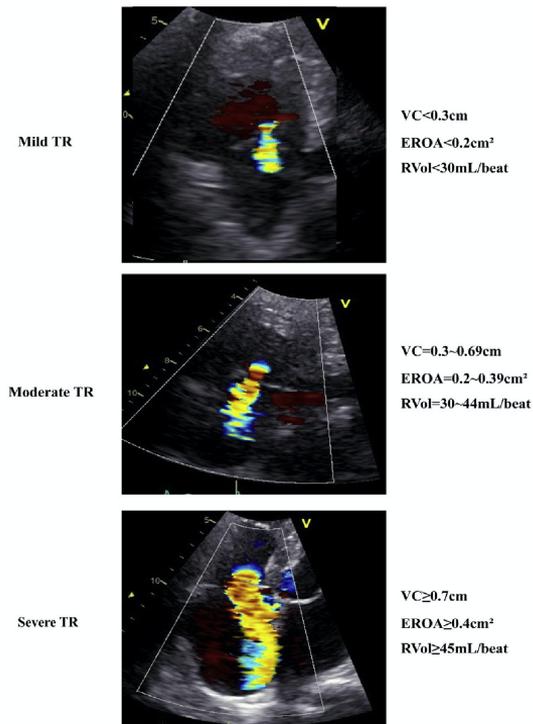
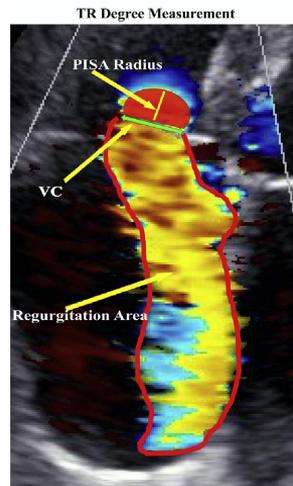
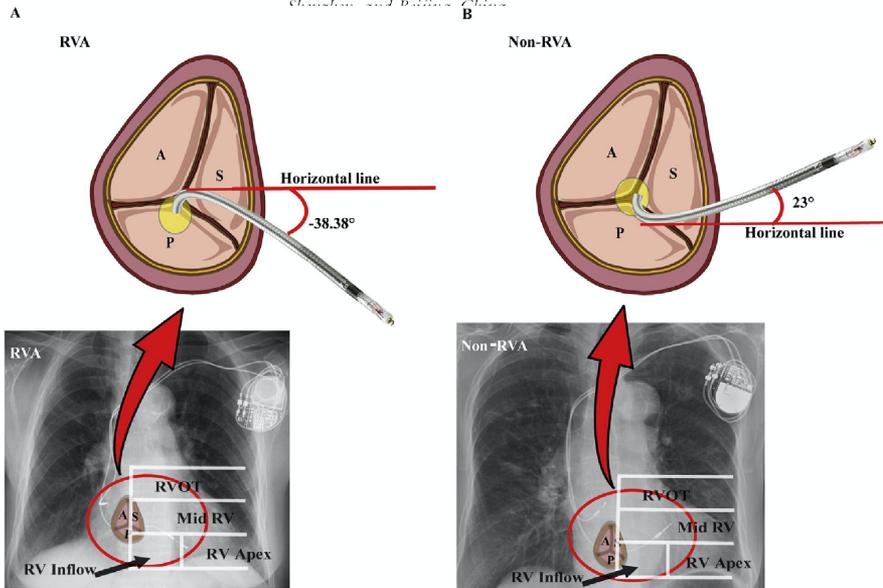
- No reports in 651 patients of TR
- LV improvement has also been observed in CCM patients
- CCM therapy does NOT involve pacing



# Nonapical Right Ventricular Pacing Is Associated with Less Tricuspid Valve Interference and Long-Term Progress of Tricuspid Regurgitation

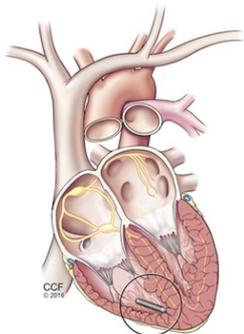


Yu-Juan Yu, MD, PhD, Yan Chen, MD, PhD, Chu-Pak Lau, MD, Ying-Xian Liu, MD, Mei-Zhen Wu, MD, Ying-Ying Chen, MD, Lai-Ming Ho, PhD, Hung-Fat Tse, MD, PhD, and Kai-Hang Yiu, MD, PhD, *Hong Kong, Shenzhen and Beijing, China*





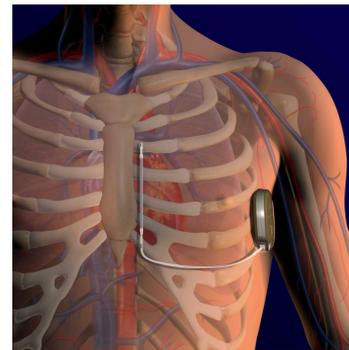
# CCM ed altri dispositivi



**PM leadless**  
Indicazione al  
pacing



**LifeVest**  
Prevenzione  
rischio aritmico



**S-ICD**  
Prevenzione  
rischio aritmico



**CCM**  
Trattamento HF

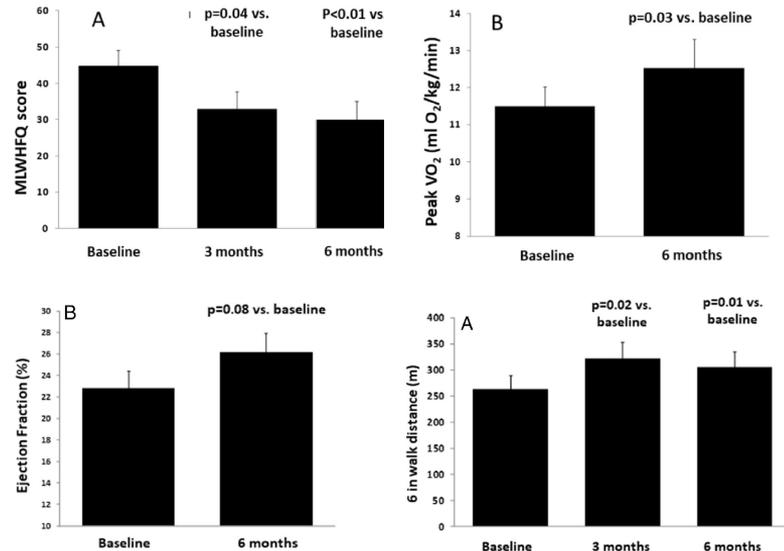


# FIX-CHF-12: CCM in CRT non responders

Following 3–6 months of CCM added to OMT and CRT, patients showed **improvements in exercise tolerance (peak VO<sub>2</sub>), and quality of life (MLWHFQ), as well as 6 minute walk distance, and NYHA classification, with a trend toward improvement in LVEF.**

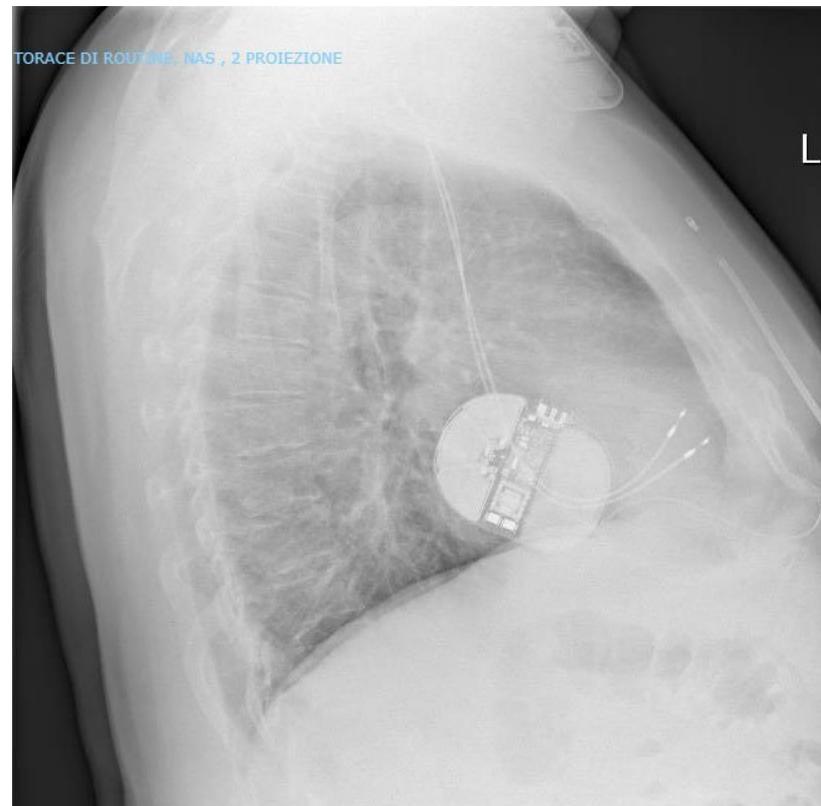
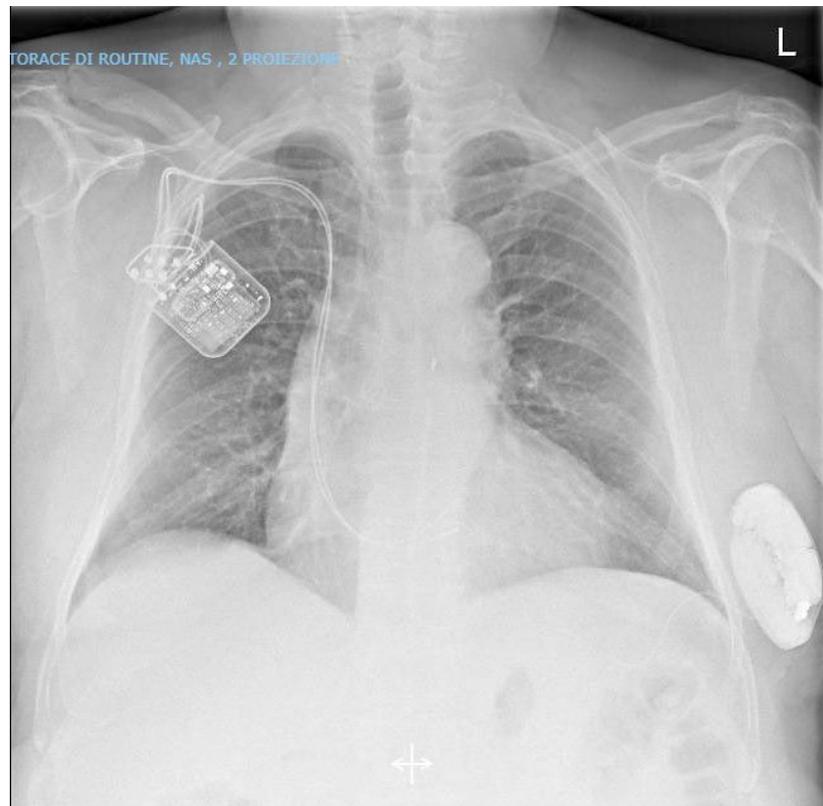
*“The existence of two implantable devices, each with its own set of electrodes raises general questions about the number of leads required.*

*However current experience with CCM combined with ICD or CRT devices has not identified a correspondingly larger number of complications.”*





# S-ICD e CCM



# CCM + S-ICD



Received: 21 November 2017 | Revised: 28 January 2018 | Accepted: 4 February 2018  
 DOI: 10.1002/dic.22919



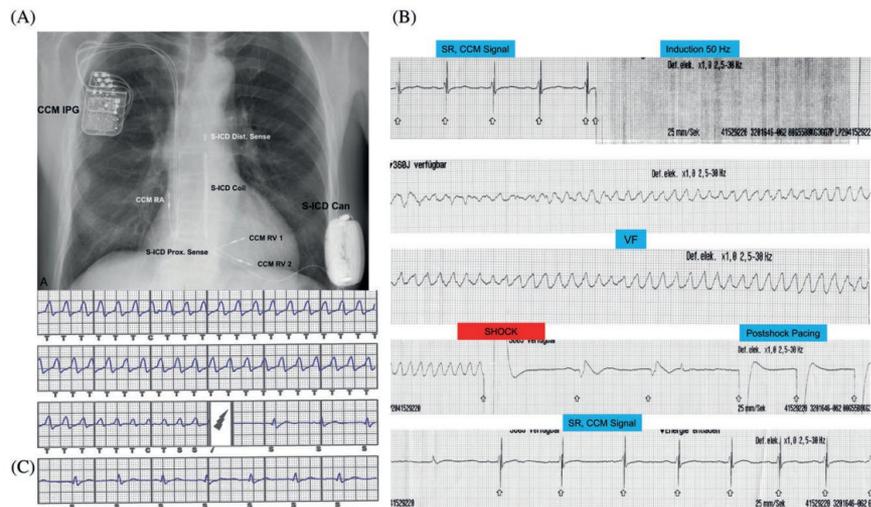
## CLINICAL INVESTIGATIONS



### Long-term results of combined cardiac contractility modulation and subcutaneous defibrillator therapy in patients with heart failure and reduced ejection fraction

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- 20 patients with CCM + S-ICD
- Mean fup 34,3 months
- CCM and S-ICD can be successfully combined in patients with HFrEF. S-ICD and CCM remain efficacious when used together, with no interference affecting their function.

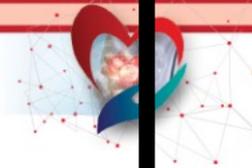


**FIGURE 1** (A) Chest x-ray of patient with CCM and S-ICD. (B) Intraoperative S-ICD testing with activated CCM: rhythm strip ECG. (C) S-ICD report of the same test from the same patient. Abbreviations: CCM, cardiac contractility modulation; ECG, electrocardiogram; IPG, implantable pulse generator; RA, right atrium; RV, right ventricle; S-ICD, subcutaneous implantable cardioverter-defibrillator; VF, ventricular fibrillation

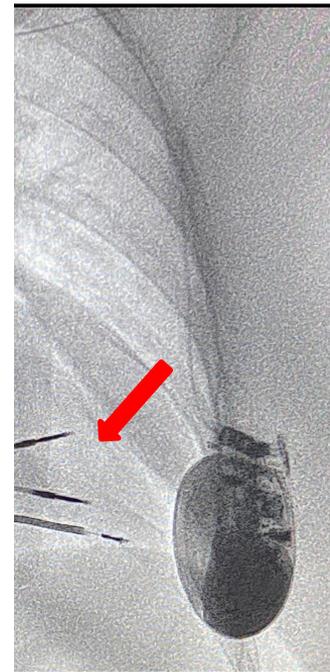


# CCM, ICD ed estetica

- 55 year-old woman
- non-ischemic dilated cardiomyopathy
- submammary ICD 2y/a for primary prevention
- recurrences of acutely decompensated heart
- LVEF 37%, NYHA III
- OMT (betablocker, sacubitril/valsartan, empagliflozin, mineralcorticoid-receptor antagonist and loop diuretics)
- Narrow QRS



*submammary technique was safe and feasible. Patient' cosmetic needs and concerns were addressed and resolved, with no issues in the device inductive recharging process, as optimal connection was obtained. CCM therapy can therefore be correctly delivered allowing the patient to benefit from it with greater comfort, cosmesis and better overall device acceptance.*





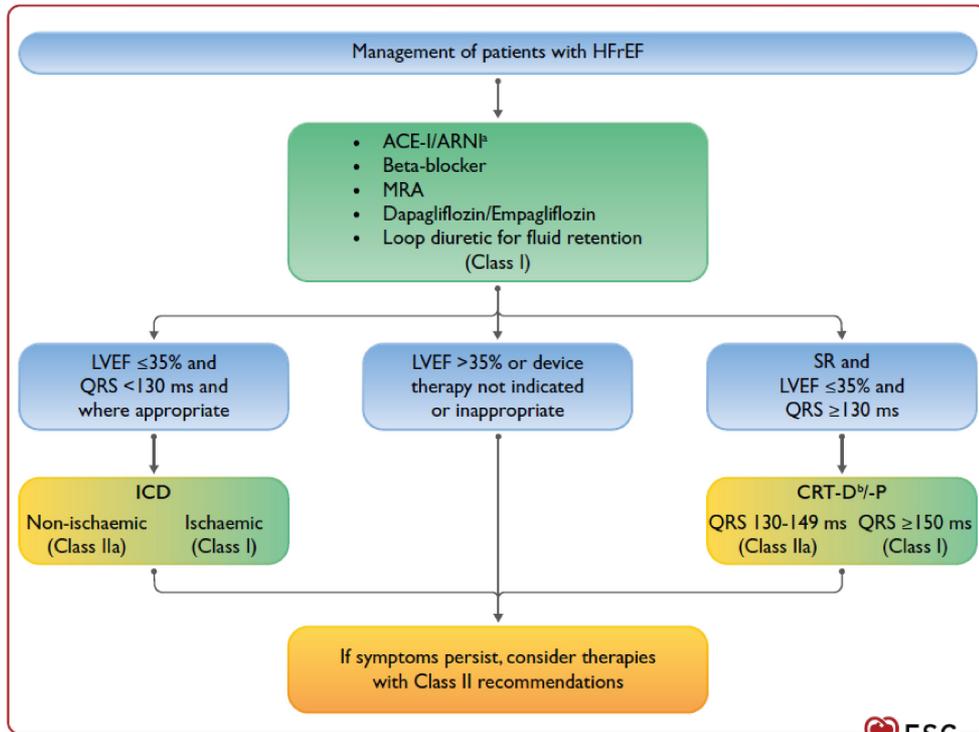
# Grazie a tutti!



# Quali prospettive per i pazienti se non



## a Cura



### Recommendations for the treatment of patients with advanced heart failure

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Patients being considered for long-term MCS must have good compliance, appropriate capacity for device handling and psychosocial support. <sup>414–416</sup>	I	C
Heart transplantation is recommended for patients with advanced HF, refractory to medical/device therapy and who do not have absolute contraindications.	I	C
Long-term MCS should be considered in patients with advanced HFrEF despite optimal medical and device therapy, not eligible for heart transplantation or other surgical options, and without severe right ventricular dysfunction, to reduce the risk of death and improve symptoms. <sup>378,396,397,401,402,404,417</sup>	IIa	A
Long-term MCS should be considered in patients with advanced HFrEF refractory to optimal medical and device therapy as a bridge to cardiac transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death. <sup>398–400,402,404</sup>	IIa	B
Renal replacement therapy should be considered in patients with refractory volume overload and end-stage kidney failure.	IIa	C
Continuous inotropes and/or vasopressors may be considered in patients with low cardiac output and evidence of organ hypoperfusion as bridge to MCS or heart transplantation. <sup>389,390</sup>	IIb	C
Ultrafiltration may be considered in refractory volume overload unresponsive to diuretic treatment. <sup>391,392</sup>	IIb	C

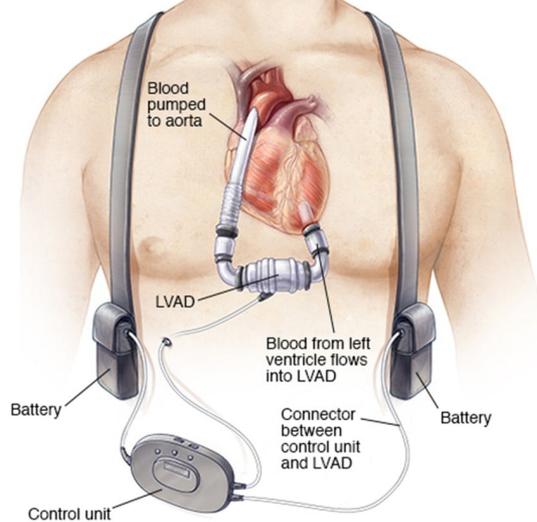
**LVAD**

HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MCS = mechanical circulatory support.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

# Quali prospettive per i pazienti se non consideriamo la CCM?



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300 impianti/anno in Italia di dispositivi LVAD

## Table 16 Patients potentially eligible for implantation of a left ventricular assist device

Patients with persistence of severe symptoms despite optimal medical and device therapy, without severe right ventricular dysfunction and/or severe TR, with a stable psychosocial background and absence of major contraindications\*, and who have at least one of the following:

- LVEF <25% and unable to exercise for HF or, if able to perform cardiopulmonary exercise testing, with peak  $\text{VO}_2 < 12 \text{ mL/kg/min}$  and/or <50% predicted value.
- $\geq 3$  HF hospitalizations in previous 12 months without an obvious precipitating cause.
- Dependence on i.v. inotropic therapy or temporary MCS.
- Progressive end-organ dysfunction (worsening renal and/or hepatic function, type II pulmonary hypertension, cardiac cachexia) due to reduced perfusion and not to inadequately low ventricular filling pressure ( $\text{PCWP} \geq 20 \text{ mmHg}$  and  $\text{SBP} \leq 90 \text{ mmHg}$  or cardiac index  $\leq 2 \text{ L/min/m}^2$ ).



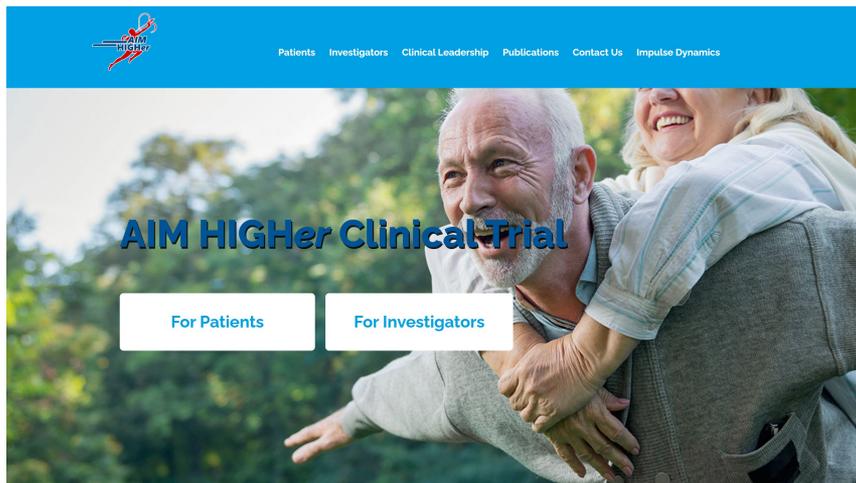
# Post Approval Study (PAS) of the OPTIMIZER Smart and CCM Therapy

## (PAS)

- The OPTIMIZER Smart Post-Approval Study is a **prospective, multi-center, non-randomized, single arm open label** study of **620 subjects** receiving an OPTIMIZER implant as standard of care. Patients to be included will have NYHA functional class III symptoms and a left ventricular ejection fraction of 25-45%
- **Primary endpoint:**
  - **Incidence of procedure and device-related complications [ Time Frame: 1 year ]**  
 Demonstrate, in the post-approval setting, that the OPTIMIZER Smart is safe to use, by assessing the rate of procedure related complications (30 days) and device related complications (1-year)
  - **All-cause mortality [ Time Frame: 3 years ]**  
 Observed mortality will be compared to the predicted mortality according to the Seattle Heart Failure Model (SHFM) at 1 year and 3 years post-implant
- **Conducted in US**
- **Study Directors:**
  - Rami Kahwash, MD      The Ohio State University Wexner Medical Center
  - Raul Weiss, MD      The Ohio State University Wexner Medical Center



# AIM HIGHer trial



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

**Ongoing enrolment in US**  
**Not started in EU**

AIM HIGHer trial:

the largest randomized, sham-controlled, device-based interventional heart failure trial that will evaluate the efficacy of CCM therapy in 1,500 patients with EFs between 40% and 60%

CCM therapy for HFpEF has already received the FDA's breakthrough device designation