



**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

Esperienza CCM in Regione Campania

Antonio D'Onofrio MD, FANMCO, FAIAC, FESC, FEHRA

Director of Electrophysiology and Cardiac Pacing Unit

A.O.R.N. "Dei Colli - V. Monaldi Hospital", Naples, Italy

Esperienza CCM in Regione Campania

Centri con almeno un paziente trattato con terapia CCM

Update 30/11/2023

2019: Pozzuoli, Ariano Irpino, Monaldi, Policlinico Federico II;

2020: Clinica Montevergine, AORN S.Anna e S.Sebastiano, S.Rocco – Sessa Aurunca,
Moscati – Avellino;

2021: Moscati- Aversa, San Giovanni di Dio e Ruggi d’Aragona, Melorio – SMCV;

2022: Castellammare, Nola, AORN Cardarelli, Eboli

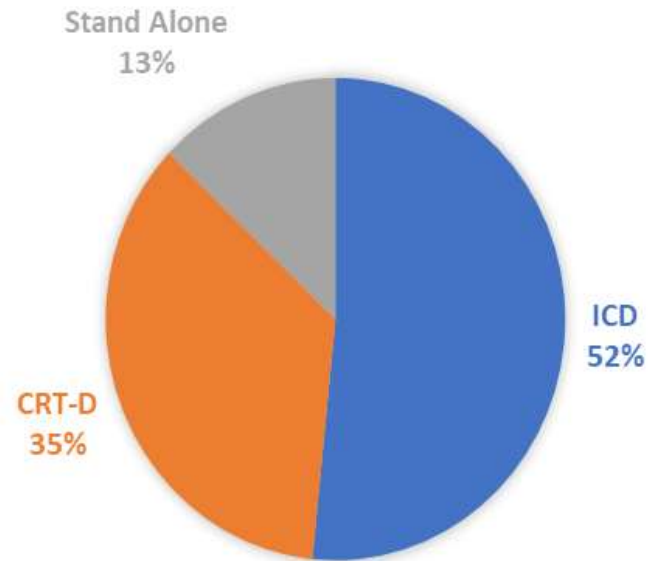
2023: Ospedale del Mare, Anastasia Guerriero – Marcianise

Anno	2018	2019	2020	2021	2022	2023	Total	Centri attivi totali
Numero di pazienti trattati	0	6	8	30	24	25	93	17
Centri attivi	0	4	6	5	9	11		

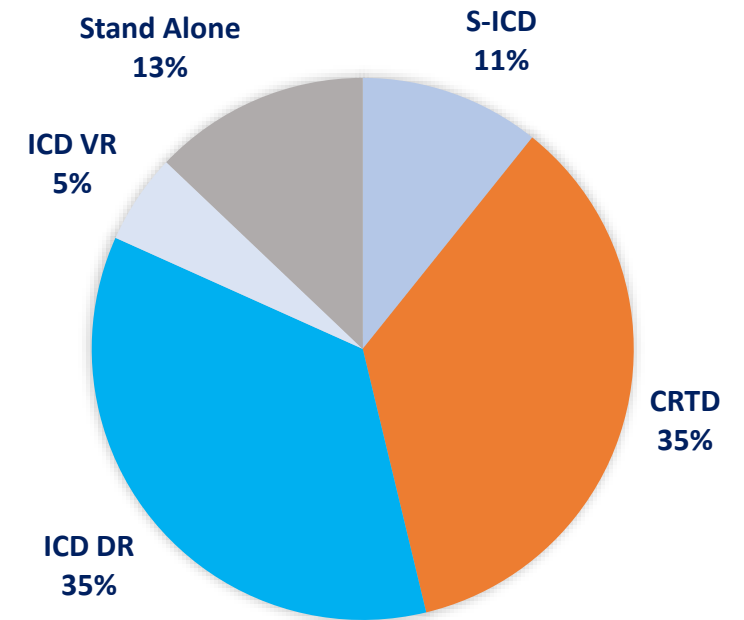
Esperienza CCM in Regione Campania

Tipologia paziente trattato

N =93 PAZIENTI IMPIANTATI CON CCM



N =93 PAZIENTI IMPIANTATI CON CCM



Esperienza CCM in Regione Campania

Follow UP

In assenza di un registro regionale, i dati raccolti sono:

- 93 pazienti impiantati, 74 sono in Follow Up (FU);
- 10/93 di essi hanno un FU di almeno 3 anni (primo impianto nel 05/2019);
- 39/93 hanno un FU di almeno 2 anni;
- 54/93 pazienti hanno un FU meno di 2 anni;
- 9 sono deceduti entro 2 anni
- 84% di sopravvivenza

Esperienza CCM in Regione Campania

Pubblicazioni sulla terapia CCM da centri Campani – Case Reports
Primi casi pubblicati worldwide

- Case report Stand alone CCM in paziente DANISH like – Ariano Irpino
- Case report Bridge to transplant – Monaldi
- Case report in CardioMEMS - Ospedale di Salerno
- Case report in Cardiopatia ipertrofica – Caserta
- Case report LMNA - Monaldi

Use of Cardiac Contractility Modulation in An Older Patient with Non-Ischemic Dilated Cardiomyopathy: A Case Report

Gianvito Manganeli ¹, Antonio Fiorentino ², Gianluca Ceravolo ², Stefana Minichiello ¹, Giuseppe Bianchino ¹, Gennaro Bellizzi ^{1,†}, Giuseppe Pacileo ³ and Daniele Masarone ^{3,*}

- ¹ Cardiology Department, ASL Avellino–Sant’Ottone Frangipane Hospital, 83031 Ariano Irpino, Italy; gianvito.m@teletu.it (G.M.); stefana.minichiello@libero.it (S.M.); giuseppebianchino4@gmail.com (G. Bianchino); gpacileo58@gmail.com (G.P.); gbellizzi58@gmail.com (G. Bellizzi)
- ² Impulse Dynamics Germany, Frankfurt am Main 60487, Germany; afiorentino@impulsedynamics.com (A.F.); gceravolo@impulsedynamics.com (G.C.)
- ³ Department of Cardiology, Heart Failure Unit, A. O. dei Colli, Monaldi Hospital, 80131 Naples, Italy; gpacileo58@gmail.com



Figure 1. The four chambers viewed at admission. Note the severe reduction in systolic function (LVEF 30% using the Simpson biplane method).

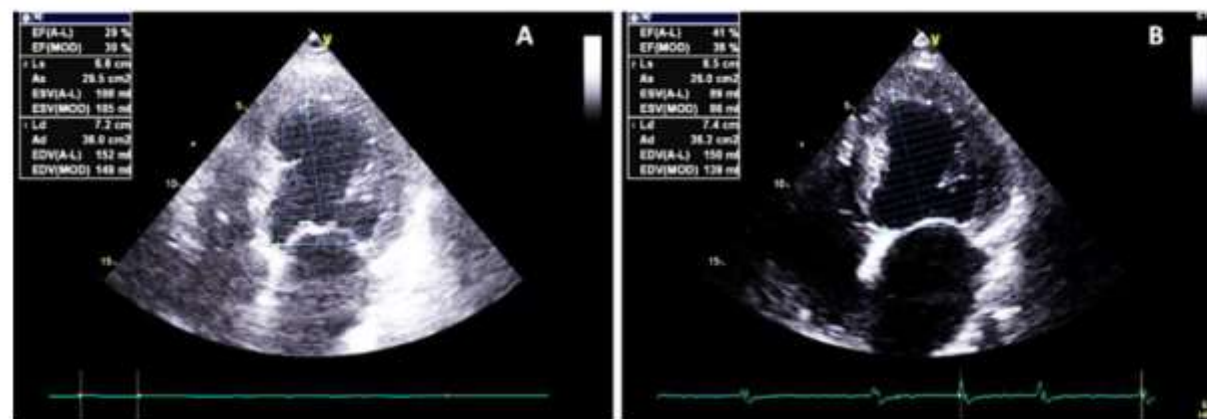


Figure 4. The four chambers viewed at baseline (Panel A) and at 18-month follow-up (Panel B). Note the reverse remodelling of the left ventricle with an increase in systolic function of the left ventricle (LVEF 41% using the Simpson biplane method).

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

Daniele Masarone^{1*}, Andrea Petraio², Antonio Fiorentino³, Santo Dellegrottaglie^{4,5}, Fabio Valente¹, Ernesto Ammendola¹, Gerardo Nigro⁶ and Giuseppe Pacileo¹

TABLE 3 | Comparison on cardiopulmonary exercise test derived data between baseline and 6 months follow-up.

Parameter	Baseline	6 months follow-up
RER	1.07	1.12
HR	155 b/m	166 b/m
Work	88 watts	112 watts
VO ₂ peak	13.8 ml/kg/min	16.7 ml/kg/min
Oxygen pulse (VO ₂ peak/HR)	8.9 ml/beat	10 ml/beat
VE/VCO ₂	34	25

RER, respiratory exchange ratio; HR, heart rate; VCO₂, carbon dioxide output; VE, ventilation; VO₂, oxygen uptake.

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 ²	2.36 m ²
BP	130/80 mmHg	120/70 mmHg
HR	105 b/m	88 b/m
LVEDVI	123.9 ml/m ²	119.8 ml/m ²
LVESVI	99.1 ml/m ²	85.3 ml/m ²
EF (Simplon biplane)	20%	28%
E/e' average	14	9
LAVI	47 ml/m ²	43 ml/m ²
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

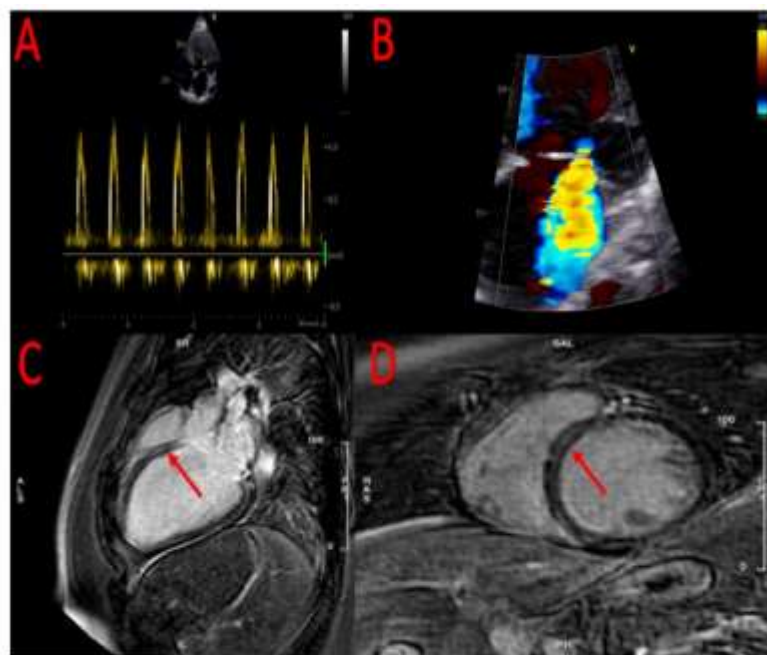


FIGURE 1 | Echocardiographic evidence of severe diastolic dysfunction (A) and severe mitral regurgitation (B). At cardiac magnetic resonance, evidence of small area of fibrosis at the basal level of the interventricular septum (C,D).

BMI, body mass index; BSA, body surface area; BP, Blood pressure; HR, heart rate; LVEDVI, left ventricular end diastolic volume index; LVESVI, left ventricular end systolic volume index; EF, ejection fraction; E/e' average, ratio between Peak velocity of early diastolic transmitral flow and peak velocity of early diastolic mitral septal and lateral annular motion; LAVI, left atrium volume index; PASP, Pulmonary Artery Systolic Pressure; IVC, inferior vena cava; NT-proBNP, N terminal pro Brian Natriuretic Peptide; MLWHFQ, Minnesota Living With Heart Failure Questionnaire.

A Multistep Approach to Deal With Advanced Heart Failure: A Case Report on the Positive Effect of Cardiac Contractility Modulation Therapy on Pulmonary Pressure Measured by CardioMEMS

Valeria Visco¹, Cristina Esposito², Michele Manzo², Antonio Fiorentino³, Gennaro Galasso¹, Carmine Vecchione^{1,4} and Michele Ciccarelli^{1*}

¹ Department of Medicine, Surgery and Dentistry, University of Salerno, Fisciano, Italy, ² Cardiology Unit, University Hospital "San Giovanni di Dio e Ruggi D'Aragona", Salerno, Italy, ³ Impulse Dynamics Germany GmbH, Frankfurt Am Main, Germany, ⁴ Vascular Physiopathology Unit, IRCCS Neuromed, Pozzilli, Italy

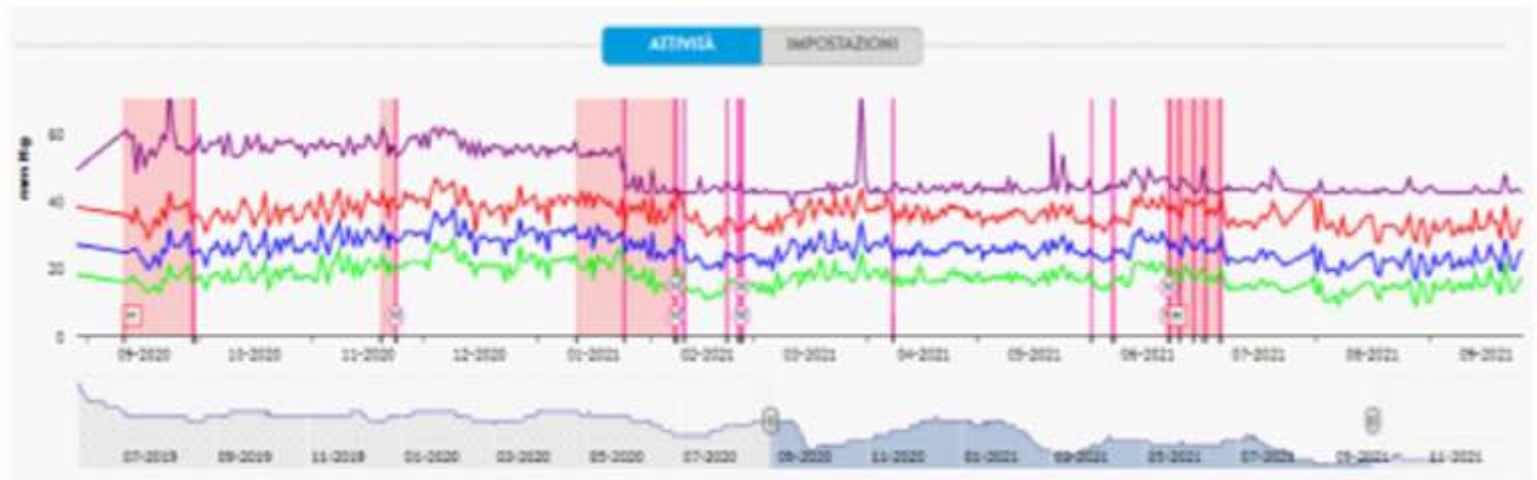
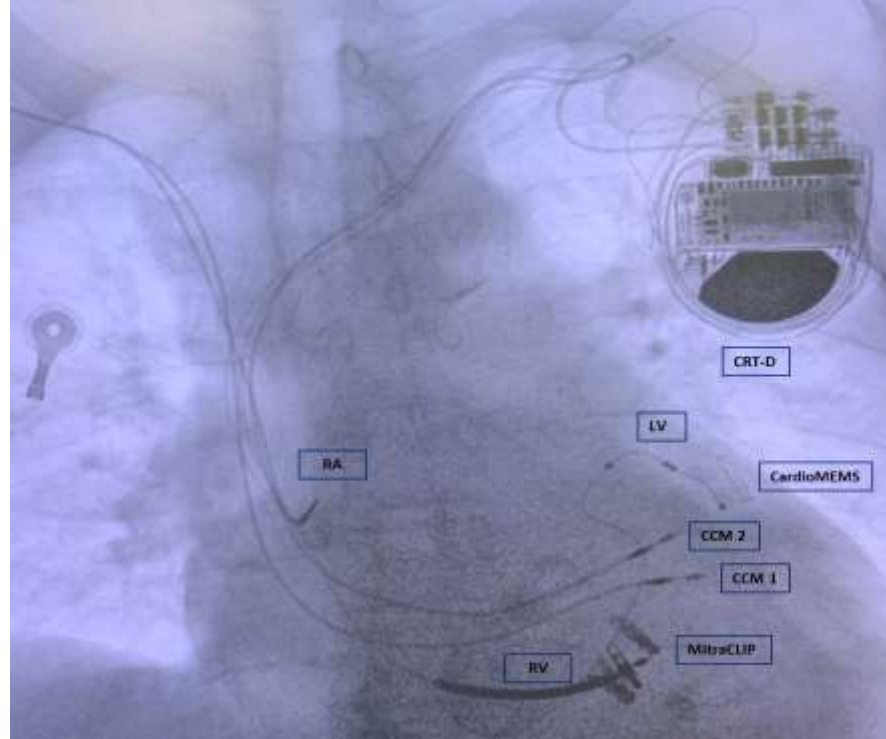


FIGURE 4 | Pulmonary artery pressure tracing detected by CardioMEMS. Starting from September 2020, there was a progressive shortening of the time between hospitalizations (pink squares) for levosimendan infusions. Pulmonary artery pressure tracing showing a mean diastolic PA drop after Optimizer Smart[®] implantation (January 2021), M and/or purple lines, remote therapy modifications; H, hospitalization.

Device therapy nello scompenso cardiaco cronico: un caso di cardiomiopatia ipertrofica trattato con terapia di modulazione della contrattilità cardiaca

Felice Gragnano^{1,2}, Orlando Munciguerra^{1,2}, Agostino Mattera Iacono², Marcello Brignoli²,
Raffaele Chianese², Giuseppe Limongelli³, Miguel Viscusi², Paolo Calabrò^{1,2}

¹Dipartimento di Scienze Mediche Traslazionali, Università degli Studi della Campania "Luigi Vanvitelli", Napoli

²Divisione di Cardiologia, Dipartimento Cardio-Vascolare, AORN Sant'Anna e San Sebastiano, Caserta

³Malattie Rare Cardiovascolari, Dipartimento di Scienze Mediche Traslazionali, Università degli Studi della Campania "Luigi Vanvitelli",
AORN Ospedali dei Colli-Ospedale Monaldi, Napoli

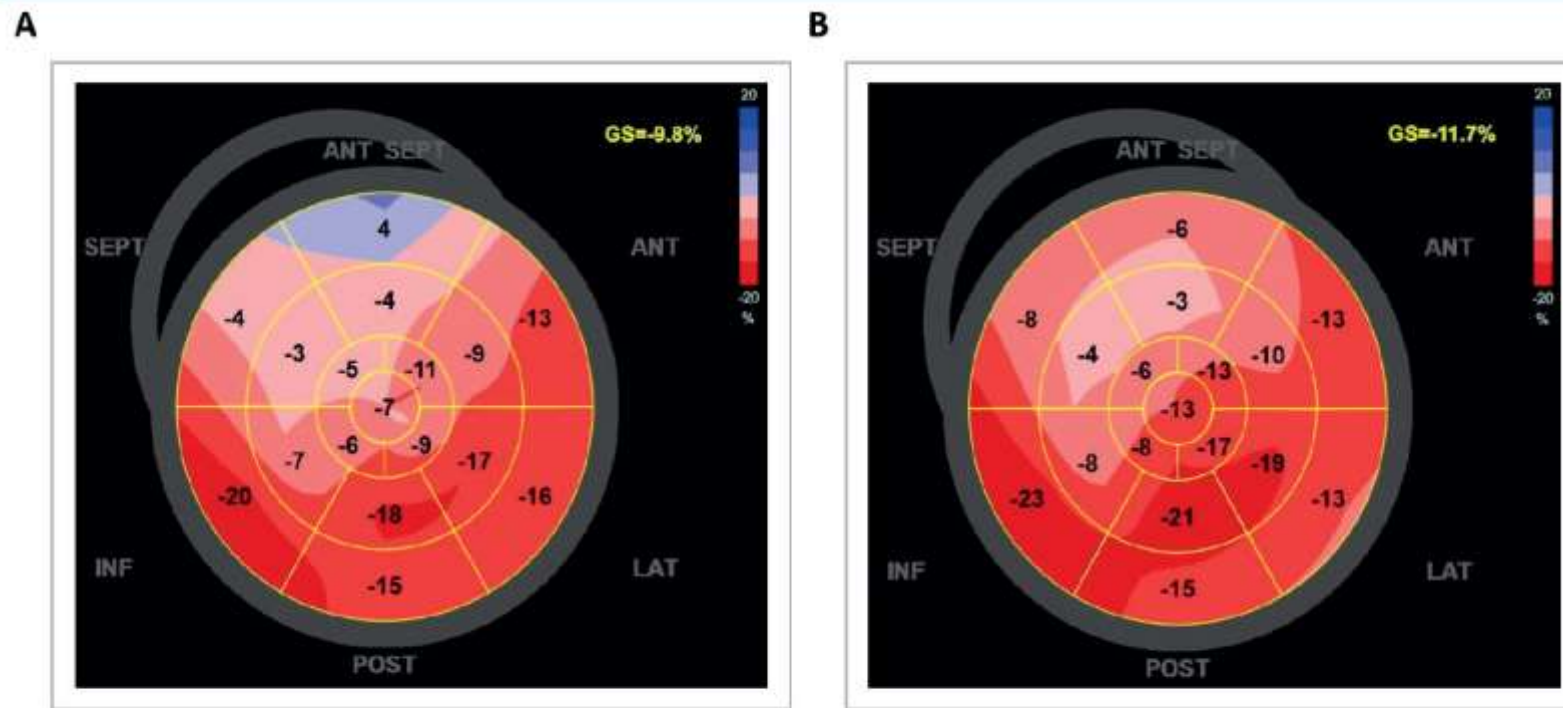


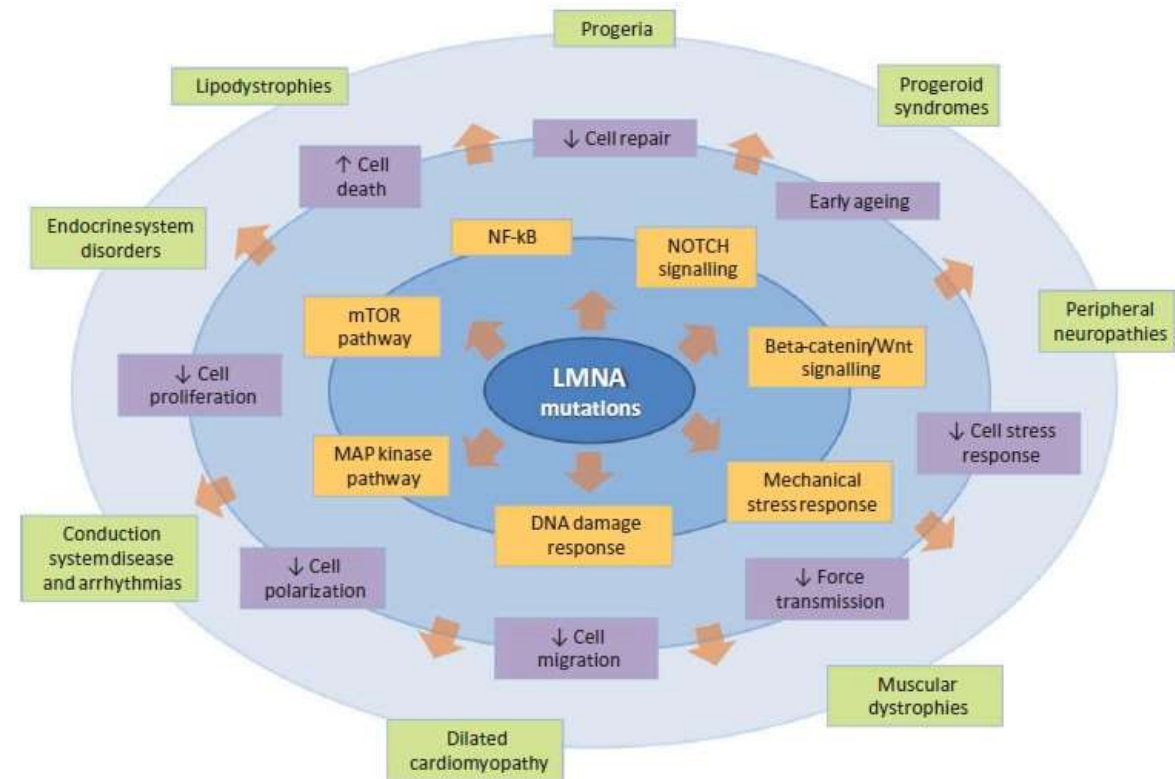
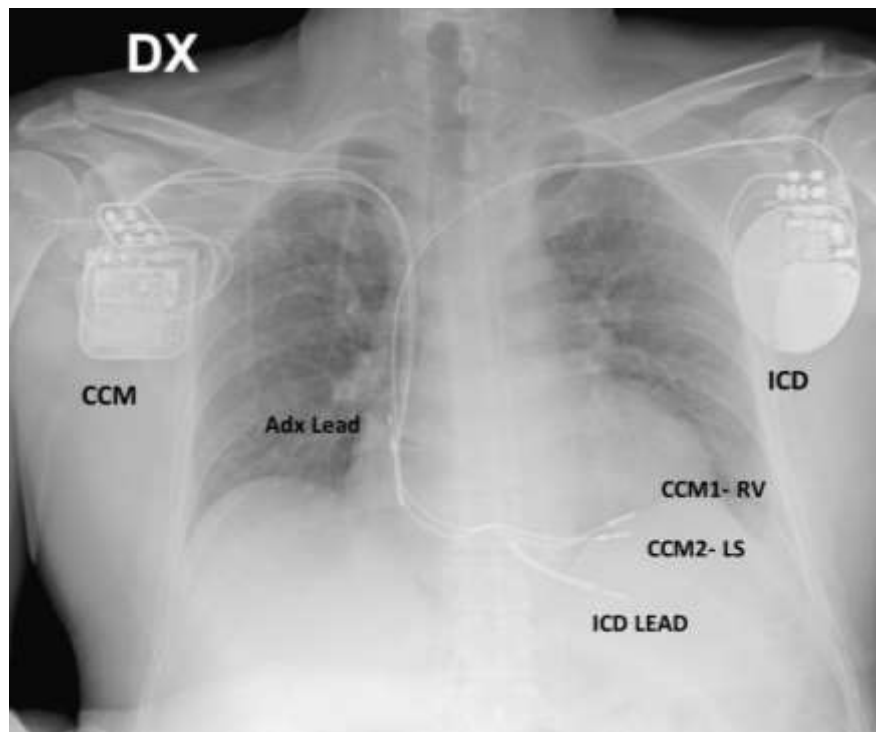


Figura 3. Strain globale (GS) del ventricolo sinistro in paziente con cardiomiopatia ipertrofica e scompenso cardiaco cronico pre- (A) e post-terapia di modulazione della contrattilità cardiaca con impianto di OPTIMIZER® Smart (B).

CASE REPORT | VOLUME 9, ISSUE 6, P381-385, JUNE 2023

First human implant of the cardiac contractility modulation in patient with dilated cardiomyopathy–related laminopathy

Antonio D’Onofrio, MD   • Giuseppe Palmiero, MD • Giuliano D’Alterio, MD • Stefano De Vivo, MD •
Benedicta Maione, Biol • Silvia Leonardi, Biol



First human implant of the cardiac contractility modulation in patient with dilated cardiomyopathy–related laminopathy

Antonio D’Onofrio, MD   • Giuseppe Palmiero, MD • Giuliano D’Alterio, MD • Stefano De Vivo, MD •

Benedicta Maione, Biol • Silvia Leonardi, Biol

Table 1 Data collected at baseline, 6 months follow-up, and 12 months follow-up

Parameter	Baseline	6 months	12 months	Normal values
KCCQ	75.5	87.3	93.6	75–100
LVEDV [mL]	133	81	125	106 ± 22
LVESV [mL]	80	50	64	41 ± 10
LVEF [%]	40	50	50	62 ± 5
GLS [%]	-11.3	-13	-12.8	-18 ± 2
RVD1 [mm]	46	39	39	33 ± 4
RVD2 [mm]	42	42	42	27 ± 4
RVD3 [mm]	75	69	69	71 ± 6
NT-proBNP [pg/mL]	1520	801	675	0–125
Laminin [ng/mL]	34	28.13	13	0–50
Collagen 4 [ng/mL]	33	15.6	21	0–30
Collagen 3 [ng/mL]	18.1	16.5	21.3	0–30
Copeptin [pmol/L]	17.54	14.92	11.32	<17
C-cystatin [mg/L]	1.14	1.01	1.12	0.47–1.09
Lp-PLA2 [ng/mL]	1628	26.57	201.5	1–200
Interleukin-6 [pg/mL]	5.1	3.6	< 2	0–5

GLS = global longitudinal strain; KCCQ = Kansas City Cardiomyopathy Questionnaire.

Better QoL

Reverse remodeling & improved LV systolic function

Improved hemodynamics

Reduced fibrosis, maladaptive hypertrophy, activity of disease

Quality of Life

Morpho-functional LV

Disease severity

Myocardial fibrosis

Neurohormonal activation

Disease activity

Inflammatory activity

Esperienza CCM in Regione Campania

Registri e Case Series

Registri

- Report CCM;
- CARDILAM;
- Italian Registry

Case series

- Impatto su funzione RV (Contaldi et al)
- Impatto su TR (Masarone et al)
- Impatto su meccano-energetica (Masarone et al)

Il REPORT CCM (REGistro Prospettico Osservazionale sulla Terapia CCM, inserito su clinicaltrials.gov NCT 04902079 approvato dal CE Università degli studi della Regione Campania - Vanvitelli ed autorizzato con delibera dirigenziale n°903 del 17.11.2020) ha lo scopo di valutare gli effetti durante un FU di 12 mesi:

- Clinici e strumentali (parametri ecocardiografici);
- laboratoristici (laminina, interleuchina 6, Cystatina C, copeptina, collagene 3 e collagene 4 oltre all'NT-proBNP);
- nonché l'impatto sulla qualità della vita (valutazione score questionario MLWHFQ).

	Totale pazienti impiantati (n= 45)
Età	66 [51-74]
Maschi	89% (40/45)
Ischemici	58% (n 26)
Altro device impiantato	93% (42/45)
- ICD	59,5% (25/42)
- CRTD	40,5% (17/42)
NYHA III	87% (n 39/45)
NYHA II	13% (n 6/45)
Lista Trapianto	9% (n 4/45)
FA permanente	47% (n 21/45)
QRS (ms)	120 [100-146]
FE (%)	30 [25-35]
MLWHFQ	51 [42-66]
NT-ProBNP	2580 [1081-4003]

Terapia Farmacologica basale	Totale pazienti impiantati (n= 45)
Ace Inibitori	22% (10/45)
Beta-Bloccanti	82% (37/45)
Glifozine*	27% (12/45)
Allopurinolo	33% (15/45)
Sacubritil/Valsartan	69% (31/45)
Antagonisti Aldosterone	60% (27/45)
Diuretici Ansa	91% (41/45)

*introdotti dal 1/2022

Monaldi Experience Follow-up

Parameters	Baseline 45 pts	3-Mo 43 pts	6-Mo 39 pts	12-Mo 38 pts
MLWHFQ score	51 [42-66]	31 [14-58]	38 [24-60]	17 [9-50]
EF (%)	30 [25-35]	33 [30-38]	34 [30-40]	39 [33,5-44]
NT-proBNP (pg/ml)	2580 [1081-4003]	2030 [989-8812]	1842 [974-2507]	1406 [709-2712]

REPORT CCM - Marker Biochimici

29 pazienti

Parameters	Baseline	3-Mo	6-Mo	12-Mo	Normal range
Co-peptina [pmol/mL]	25,1 [13,6-54,2]	17,4 [13,2-23,03]	14,9 [9,6-26,1]	9,5 [6,15-11]	<17
Collagene 3 [ng/mL]	80,85 [29,8-145]	54,25 [27,8-119,5]	68,2 [35,2-174]	44 [32,25-134,9]	0-30
Collagene 4 [ng/mL]	50 [24,3-67,1]	27,5 [17,4-50,8]	30,45 [17-48]	24,6 [20,5-43,8]	0-30
Laminina 4 [ng/mL]	16 [15-18]	25 [21-56]	17 [5,5-26,5]	16 [15-17]	0-50
Interleuchina 6 [pg/mL]	4,8 [3,6-6,8]	4,8 [2,9-8,3]	4,3 [3,6-5,9]	3,7 [3,2-4,8]	0-5
Cystatina C [mg/mL]	1,9 [1,5-2,3]	1,4 [1,2-2]	1,4 [1,3-2,1]	1,2 [1,1-1,3]	0,47-1,09
LP-PLA2 [ng/mL]	139 [101-165]	134 [86-147]	131 [99,9-144]	130 [98-142]	1-200
Amiloide [µg/mL]	9,8 [2,8-14,1]	5,4 [3-13,5]	6,9 [1,6-48,7]	5,7 [4,9-6,4]	< 10
Adrenomedullina	1,7 [1,3-2,1]	1,5 [1-2,2]	1,8 [1,7-2]	1,2 [0,9-1,3]	0-1

CARDILAM CCM-Protocol

CARDILAM-CCM *ClinicalTrials.gov* Identifier: NCT04904393

Study Type : Observational; Prospective Estimated Enrollment : 20 participants;

- **Primary Outcome Measures:**

- ***1. Improvement of QoL [Time Frame: 12 months]***

- ✓ Evaluation of the effect of CCM therapy on Quality of Life evaluated from the reduction of MLWHFQ score at FU post implant of CCM device compared to baseline.

- ***2. Reduction of HF Hospitalizations and Emergency Ward accesses [Time Frame: 12 months]***

- ✓ Reduction of HF Hospitalizations and Emergency Ward accesses collected during the FU post implant of CCM device compared to number of Hospitalizations and Emergency Ward accesses collected 1 year before the implant of CCM therapy device

- ***3. Improvement of Functional Capacity [Time Frame: 12 months]***

- ✓ Evaluation of the impact of CCM therapy on Functional Capacity evaluated from the gain of the distance travelled in the 6MWT at FU post implant of CCM therapy device compared to baseline

- **Secondary Outcome Measures :**

- ***1. Assess of HF biomarkers trends [Time Frame: 12 months]***

- ✓ Assess of HF biomarkers trends (lamini, NT-ProBNP, copeptin) during the FU compared to baseline

Italian Registry



Bologna
18-17 settembre 2021

EHRA 2022
Copenhagen,
April 3-5

A.S.L. VC Cardiac Contractility Modulation (CCM) Italian Registry: preliminary analysis

M. Matta¹, C. Devecchi¹, R. Troccoli², A. Lupi³, P. Paffoni⁴, P. Nocerino⁵, G. Dell'Era⁶, G. Manganelli⁷,
N. Di Belardino⁸, A. Lucifero⁹, V. Giudici¹⁰, C. D'Agostino², E. Occhetta¹, F. Rametta¹

- (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 Calbita Fatebenefratelli Hospital, Rome, Italy. (10) Bolognini Hospital, Seriate, Italy.

HT.4.02

CARDIAC CONTRACTILITY MODULATION (CCM) ITALIAN REGISTRY: A PRELIMINARY ANALYSIS

M. Matta¹, C. Devecchi¹, F. De Vecchi¹, A. Lupi¹, P. Nocerino¹, G. Dell'Era¹, G. Manganelli¹, N. Di Belardino¹, A. Lucifero¹, A. Schaffer¹, G. Patti¹,
E. Occhetta¹, F. Rametta¹
¹ Divisione di Cardiologia, Ospedale Sant'Andrea, Vercelli, ITALY
² Divisione di Cardiologia, ASL Verbania-Cusio-Ossola, Domodossola, ITALY
³ Divisione di Cardiologia, Ospedale Santa Maria delle Grazie, Pozzuoli, ITALY
⁴ Divisione di Cardiologia, Azienda Ospedaliera-Universitaria Maggiore della Carità, Novara, ITALY
⁵ Divisione di Cardiologia, Ospedale Sant'Obbano Frangipane, Ariano Irpino, ITALY
⁶ Divisione di Cardiologia, Ospedale Riuniti Anzio-Nettuno, Anzio, ITALY
⁷ Divisione di Cardiologia, Ospedale Fatebenefratelli Isola Tiberina, Roma, ITALY

Introduction: Cardiac contractility modulation (CCM) therapy is indicated for patients suffering symptomatic congestive Heart Failure (CHF) with reduced left ventricular ejection fraction (LVEF). CCM therapy increases the activity of proteins involved in intracellular calcium handling by delivering high-output non-excitatory electrical impulses during ventricular absolute refractory period. This therapy has been associated with improvement of quality of life (QoL) and reduction of hospitalizations in patients with CHF, but data are limited to short-term registries and small trials. The aim of this registry is to assess the long-term outcome of CCM therapy in a large cohort of patients, and the preliminary results are presented in this study.

Methods: The CCM Italian Registry is a prospective, observational multicenter study investigating the long-term impact of CCM therapy in CHF patients on LVEF, hospitalizations, QoL and functional class assessed by the Minnesota Living With HF Questionnaire (MLWHFQ) and 6-minutes walking test (6MWT). Preliminary results after one year of enrollment have been analyzed in this study. Data are expressed as median and interquartile range. Changes from baseline have been tested with Wilcoxon signed-rank test.

Results: A total of 28 patients suffering symptomatic CHF, with LVEF < 45% and NYHA class > II despite optimal medical therapy, have been enrolled and implanted with CCM device (Optimizer Smart, Impulse Dynamics) in 8 participating sites. Most patients were male (27 patients, 96%), with a median age of 74 (70-77) years. The most frequent aetiology was ischemic (18 patients, 65%) and 22 (80%) of them had another implanted device (15 ICD, 7 CRT-D). Eight (29%) patients presented chronic atrial fibrillation. Twenty-five (89%) patients were treated with beta-blockers and 23 (82%) received sacubitril/valsartan (11) or ACE-inhibitors/angiotensin-receptor blockers (12). A significant reduction in CHF-related hospitalization has been observed after 6 months and 12 months of CCM implantation (Figure 1), with a relative risk reduction around 80% at 12 months (p<0.001). As shown in Figure 2, LVEF significantly improved both at 6 and 12-month follow up (p=0.020 and p=0.022, respectively), while MLWHFQ score significantly improved at 6-month (p=0.004), but not reaching the significance at 12-month (p=0.140). The 6MWT distance did not show significant changes (p=0.470), mainly due to physical non-cardiovascular limitations in some of the enrolled patients. NYHA class improved significantly both at 6-month (p=0.002) and 12-months (p=0.001), with overall 80% of patients showing an improvement of at least 1 class compared to baseline.

Conclusion: CCM proved to be effective in improving symptoms, QoL and in reducing CHF-related hospitalizations in patients with symptomatic CHF with reduced LVEF despite optimal medical therapy as tolerated. This prospective Italian Registry will be fundamental to gather more evidence on the long-term outcome of CCM therapy in the Italian clinical practice.

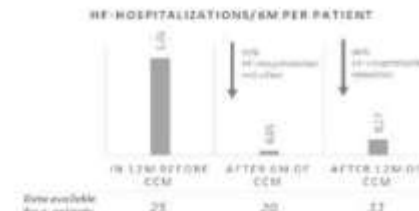


Figure 1. Occurrence of heart failure-related hospitalizations per patient at 6-months and 12-months follow-up compared to the last 12 months before CCM implantation.

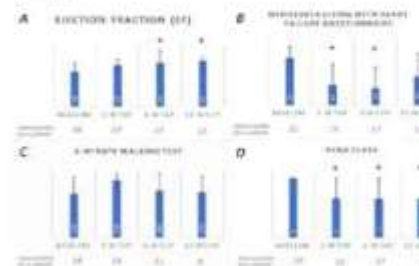
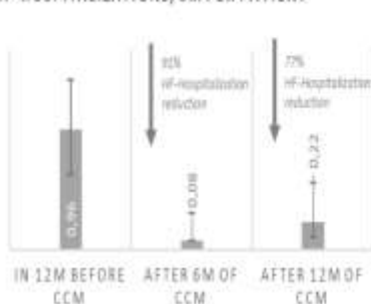


Figure 2. Variation between baseline and 6, 6 and 12 months follow-up after CCM implantation in the following parameters: A) Left Ventricular Ejection Fraction, B) MLWHFQ score, C) 6-Minutes Walking test distance, D) NYHA class. * p-value<0.05 by Wilcoxon signed-rank test.

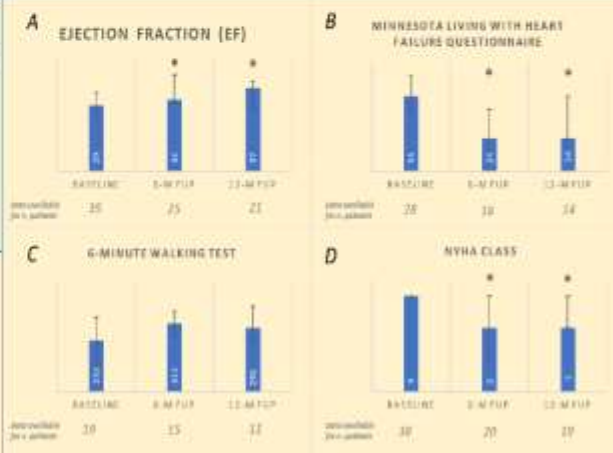
Purpose and Methods: Cardiac contractility modulation (CCM) is a treatment option for improvement in quality of life (QoL) and reduction of HF-hospitalizations in patients suffering symptomatic **Chronic Heart Failure (HF) with reduced left ventricular ejection fraction (LVEF)** despite optimal medical 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**.



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

Matteo Ziacchi^a, Alberto Spadotto^b, Stefano Ghio^b, Marta Pellegrino^c, Luciano Potena^a, Daniele Masarone^d, Marco Merlo^e, Davide Stolfo^e, Maria Michela Caracciolo^f, Corinna Inserra^g, Fabrizio Ammirati^h, Michele Ciccarelliⁱ, Furio Colivicchi^j, Stefano Bianchi^k, Giuseppe Patti^l, Fabrizio Oliva^m, Giuseppe Arcidiaconoⁿ, Roberto Rordorf^b, Daniela Pini^c, Giuseppe Pacileo^d, Antonio D'Onofrio^d, Giovanni Battista Forleo^f, Matteo Mariani^g, Francesco Adamo^h, Alessandro Alonzoⁱ, Matteo Ruzzolini^k, Chiara Ghiglieno^l, Manlio Cipriani^m, Giorgio Firettoⁿ, Nadia Aspromonte^{o,p}, Francesco Clemenza^q, Gaetano Maria De Ferrari^q, Michele Senni^r, Maria Grazia Bongioni^s, Claudio Tondo^t, Massimo Grimaldi^u, Francesco Giallauria^v, Francesco Rametta^w, Procolo Marchese^x, Mauro Biffi^a and Gianfranco Sinagra^e

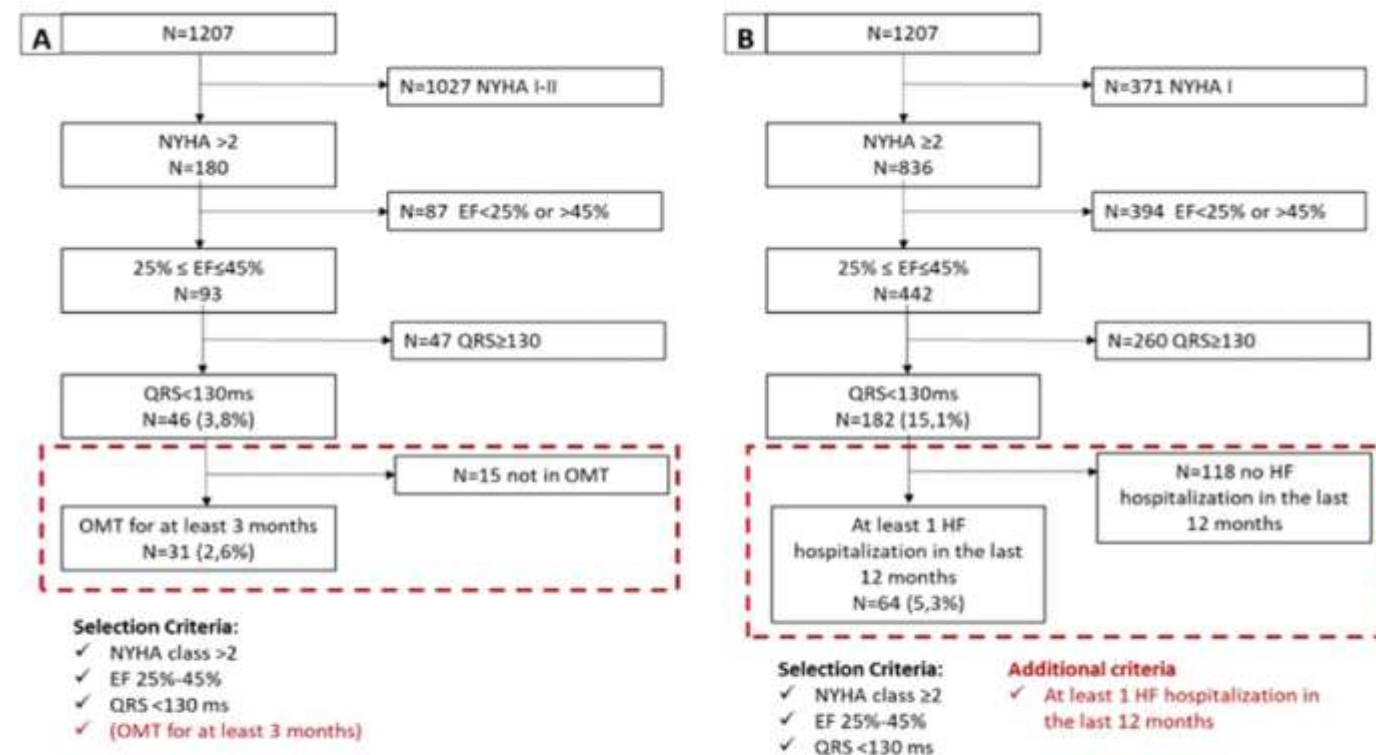


Figure 4. Patients eligible to CCM implant according to different selection criteria. A: patients selection according to FDA selection criteria. B: patients selection according to CCM Italian registry criteria (NYHA>3 or NYHA 2 + HF hospitalization in the last year).

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](#)

REVIEW ARTICLE | ARTICLES IN PRESS

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



Thank You for your attention