Contractility Modulation in Patients on Ambulatory Milrinone, A Cautionary Tale

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Background

- Cardiac Contractility Modulation (CCM) is an approved adjunct therapy in patients with medically refractory Class III congestive heart failure (CHF) with ejection fraction (EF) 25-45% and not indicated for biventricular pacing. Previous trials did not include patients with class IV CHF on intravenous ionotropic therapy. We sought to evaluate outcomes in a cohort of patients with both CCM and IV ambulatory milrinone.

Methods

- Six patients met inclusion criteria (NYHA Class IV, EF 25-45%, on ambulatory milrinone, and prior subcutaneous or transvenous defibrillator), were offered a 2-lead Impulse Dynamics Optimizer system. Consents were obtained for 5 of the 6 patients, with subsequent CCM implantation between April 2020 and June 2021.

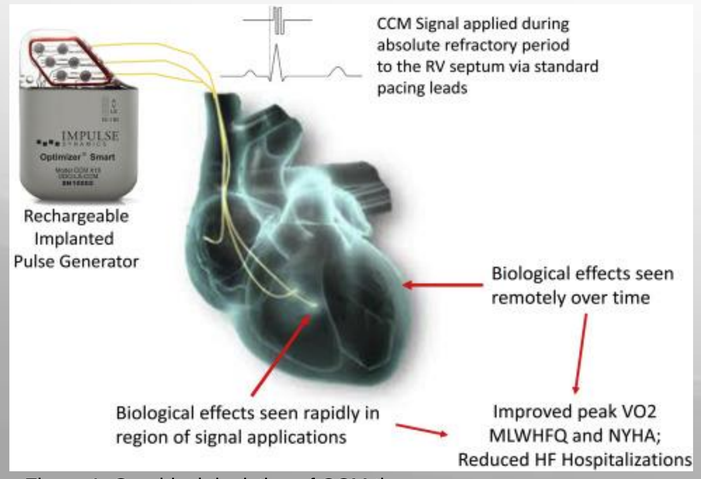

Figure 1: Graphical depiction of CCM therapy

Results

Patient	Age	Type	Left Ventricular EF	CO/CI	Milrinone (mcg/kg/min)
1	48	Ischemic	25%	4.3/2/1	0.25
2	43	Non-ischemic	38%	3.3/1.4	N/A
3	55	Ischemic	25-35%	3.6/2.1	0.25
4	45	Non-ischemic	35-40%	4.2/1.6	0.375
5	53	Non-ischemic	25-30%	4.3/1.9	0.25

Table 1: Patient characteristics at the time of CCM initiation.

- Patient 1 had significant improvement with rise in EF/CO/CI to 40%/5.4/2.4 respectively with termination of milrinone and subsequent removal from the transplant list by 6 months post implantation. Patient 2, who had concomitant end stage renal disease on hemodialysis, died suddenly 2 months post procedure of unclear causes. Patient 3, who was not a candidate for advanced therapies, symptomatically improved to NYHA Class II at follow up 3 months post implantation, however EF had mildly decreased to 20-25% and milrinone rate has been stable. Patient 4 received an LVAD due to worsening symptomatic and hemodynamic status. Patient 5 had mild improvement in EF to 34% and is pending further hemodvnamic evaluation.

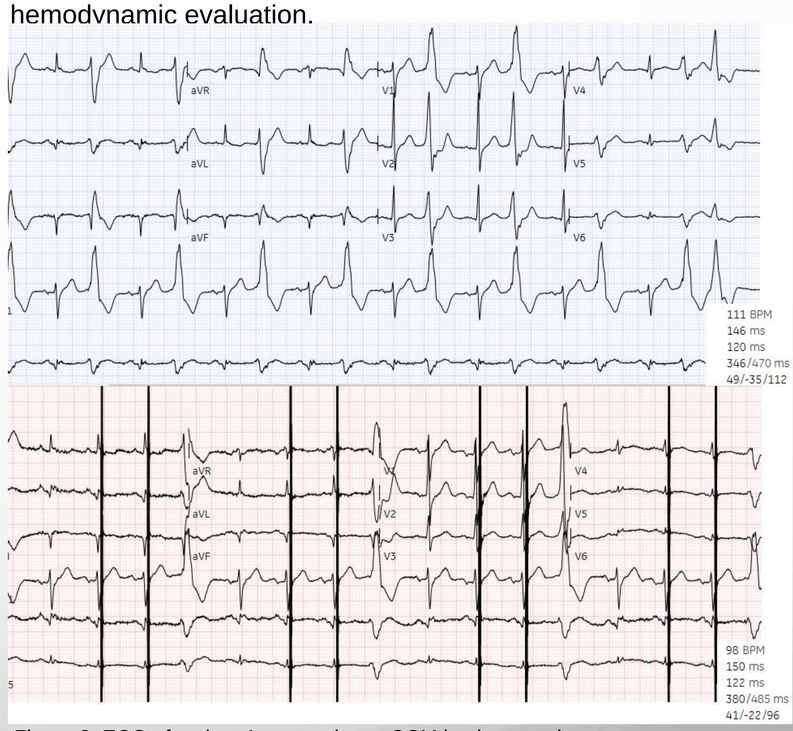

Figure 2: ECG of patient 1, pre and post CCM implementation.

Conclusion

- CCM may be beneficial in severe forms of CHF requiring IV milrinone. Identifying the appropriate patient population requires further study. Individualized shared decision-making is critical prior to its application in this patient cohort.

Discussion

- CCM functions by applying biphasic high voltage bipolar signals to the right ventricular septum during the absolute refractory period (Fig 1), thereby improve calcium handling and bring about a reverse remodeling effect (2). In animal models, use of CCM has also been shown to decrease fibrosis and sympathetic tone, as well as improve systolic reserve and diastolic filling. (2). The FIX-HF-5C trial has shown a significant reduction in the 6-month composite rate of cardiac mortality and HF hospitalizations (4). Long term mortality up to 3 years post CCM was also shown to improve with this therapy, particularly in the 35-45% group, and hospitalization were decreased by 75% compared to non CCM patients (3). A further study supports the cost effectiveness of this therapy, assuming its benefits will continue to apply beyond the 3-year mark (5).

References

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