A novel algorithm for rapid sequence optimization of guideline directed medical therapy for heart failure with reduced ejection fraction

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Introduction: Current guidelines for management of Heart Failure with Reduced Ejection Fraction (HFrEF) recommend Beta-blockers, Angiotensin Receptor Neprilysin Inhibitors (ARNI), Mineralocorticoid Receptor Antagonists (MRA) and SGLT2 inhibitors. However, guideline-directed medical therapies (GDMT) remain underutilized. The 2018 CHAMP-HF registry of HFrEF patients demonstrated that only 1% of patients were treated with target doses of Beta-blockers, MRA and ACE-inhibitors (ACE-I) and Angiotensin Receptor Blocker (ARB) or ARNI. Historically, HFrEF therapies were initiated and up-titrated sequentially. Recent expert commentary has suggested a more aggressive approach of initiating all 4 classes of therapy at low doses after which patients should be up-titrated to target dose

Purpose: This study tested a novel, virtual HFrEF optimization program with the goal of achieving GDMT using a novel “rapid sequence” algorithm.

Methods: We conducted a single center study at a regional cardiovascular centre using a prospective pre-post design. NYHA class II/III HFrEF patients referred from both inpatient and outpatient settings were enrolled in a virtual 3-month HFrEF optimization program. All participants underwent an initial consult with a program nurse and cardiologist. After this, all patients were seen remotely by a nurse every two weeks for adjustment of HFrEF medications. At week 1, patients started on ARNI and SGLT2i. After week 3, Beta-Blocker was initiated. After week 5, MRA was initiated. Following this, medications were up-titrated every two weeks, based on clinical judgement of the overseeing cardiologist. Vital signs and bloodwork were obtained after all medication adjustments. In addition, all patients were seen once weekly by a kinesiologist for lifestyle optimization and counselling.

Results: From April 2020 to January 2021, 297 NYHA class II/III HFrEF patients enrolled in the virtual HFrEF optimization program. Mean age was 69 and 63% were male. Mean ejection fraction was 28% and 54% had ischemic cardiomyopathy. At intake, the proportion of patients prescribed maximally-tolerated dosage was 64% for Beta-Blockers, 7% for MRA, 1% for ARNI and 1% for SGLT2i. At 3-month follow-up, maximally-tolerated dose was prescribed in 84% of patients for beta-blockers (p<0.01), 58% for MRA (p<0.01), 77% for SGLT2i (p<0.01) and 96% for ARNI (p<0.01). 39% of patients achieved maximal doses of all 4 classes of medications at follow-up. No medication-related adverse events were reported and 18 patients were hospitalized for HF exacerbation during study follow-up.

Conclusions: This study demonstrates that a program using aggressive GDMT initiation can safely and effectively improve uptake of therapy in HFrEF patients. Future research should examine HFrEF “rapid sequence” optimization on patient outcomes in a randomized setting.