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Editorial

How Deep Is My Ocean? Defining Decongestion for Patients and Trialists

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It is estimated that approximately 6.2 million Americans over the age of 20 years suffer from heart failure (HF).[1] Some patients have a slow functional decline, but a significant proportion present with new or sudden worsening of signs and symptoms of HF, manifesting as acute decompensated heart failure (ADHF). ADHF is not only associated with a considerable economic and social burden but also with significant mortality among patients with chronic HF. For instance, in the Atherosclerosis Risk in Communities study, the age-adjusted mortality following ADHF hospitalization at 28 days and 1 year were around 10% and 30%, respectively.[2]

Prompt assessment of fluid and perfusion status with the institution of decongestive therapies remains the cornerstone for management of ADHF. Contrary to the significant advances in medical therapy for chronic HF, the treatment options for ADHF remain limited, with loop diuretics remaining the hallmark of decongestive therapy for many decades.[3] The goal of management in ADHF is to achieve complete decongestion and achieve a euvolemic state since residual congestion is being increasingly recognized as a marker of worse clinical outcomes.[4,5]

The clinical questions that arise in the care of ADHF patients are "how to identify patients at high risk of adverse events?" and "how to identify if effective decongestion has been achieved?" While numerous congestion scoring scales are available, significant variability exists when defining optimal/adequate decongestion.[6–9] This issue becomes important as clinical trials seek to incorporate decongestion as one of the clinical end points in addition to hard end points such as mortality, and lack of standardized definition may hinder data aggregation and comparative analysis across various studies. For example, in the Diuretic Optimization Strategies Evaluation trial, freedom from congestion was a prespecified secondary outcome that was defined as jugular venous pressure of <8 cm, with no orthopnea and with trace peripheral edema or no edema.[10] On the contrary, the recently published Acetazolamide in Decompensated Heart Failure with Volume Overload trial used successful decongestion as a primary end point which was defined as the absence of volume overload (no more than trace edema, no residual pleural effusion, and no residual ascites).[11]

In the 2-part review series on patient selection and end point definitions for decongestion studies in ADHF, Georges et al[12] describe a novel approach to identify patients with ADHF who are at risk of residual congestion based on prior clinical course, severity of congestion, diuretic resistance, and renal dysfunction. A grading system for baseline evaluation of congestion is reported and, using various subjective and objective parameters, decongestion end points are defined on a spectrum ranging from unsatisfactory to optimal decongestion following initiation of decongestive therapies.[13] Additionally, a granular staging system for decongestive treatment failure is proposed for use in future ADHF trials.

Who is at high risk of residual congestion?

In the first part of the review series, the authors describe a novel approach to identify high-risk patients based on 4 different factors. First, based on prior clinical course, patients with an ADHF hospitalization in the past 6 months or 2 or more hospitalizations in the past 12 months are deemed to be at high risk. Second, severity of congestion based on objective parameters such as central venous pressure ≥16 mm Hg obtained by invasive measurement, elevated natriuretic peptides (brain natriuretic peptide [BNP] >500 pg/mL or NT-proBNP >3000 pg/mL), hemodilution (hemoglobin <11 g/L) with absolute expansion of plasma volume by ≥30%, and elevated high sensitivity troponins (>40 ng/L) in the absence of acute coronary syndromes are identified as high risk. Third, diuretic resistance with spot urine sodium <50 mmol/L at 2 hours with urine output of <600 mL over 6 hours following an appropriate dose of intravenous diuretic has been reported to be linked with poor outcomes. Finally, renal dysfunction based on blood urea nitrogen levels, presence of acute kidney injury on admission, and worsening renal function are some of the other identified high-risk features.

While most of these parameters have been validated in prior studies, comprehensive assessment based on these cut-off values might be critical in recognizing patients who are at high risk and may benefit from inclusion in clinical trials of adjunctive decongestive medical and device-based therapies.

What is effective decongestion?

The goal of treatment in ADHF should be a patient with no residual congestion. In the second part of the review series, the authors propose

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decongestion end point definitions based on degree of residual congestion using various objective and subjective parameters such as severe, moderate, mild, and no residual congestion. Optimal decongestion (or no residual congestion) is achieved when there is improvement in self-reported New York Heart Association functional class symptoms to 1 without any evidence of orthopnea, pedal edema, hepatomegaly, and ascites. Furthermore, improvement in central venous pressure to $\leq$5 mm Hg, pulmonary capillary wedge pressure $\leq$12 mm Hg, hemoconcentration ($<$10% expansion of blood volume), and NT-proBNP levels of $\leq$400 pg/mL are some of the objective measurements associated with optimal decongestion.

What are the implications?

To make significant progress, it is necessary to have a standardization of decongestion end points for ADHF patients. Currently, HF intervention trials have not adopted standardized definitions and have not had a meaningful impact on this problem. In this regard, the authors are commended for taking the lead on this initiative. Standardized decongestion end points may not only improve care by serving as optimum clinical targets for ADHF patients but may also serve as performance indicators of high-quality care from an administrative perspective.[14] Indeed, standardized grading of congestion severity and residual decongestion will be of critical importance when reporting outcomes of clinical trials that look at various medical and device-related therapies for decongestion. However, given inherent complexities of these grading systems, utilization in day-to-day clinical practice may be limited, and further studies are needed to provide better insight and validation.

The work by Georges and colleagues will hopefully stimulate standardization but will need to be streamlined and simplified as well as validated. When developing new frameworks for assessment, there is a conflict between complexity/completeness and simplicity. In the area of cardiogenic shock, a multitude of risk scores had been developed,[15–18] but none were widely utilized until the Society for Cardiovascular Angiography & Interventions (SCAI) Consensus Statement,[19] which proposed a simple system based on clinical, hemodynamic, and laboratory findings. With subsequent validation of SCAI stages,[20] it has become the common language for cardiogenic shock. The hope is that a variation of the currently presented work will follow a similar path.

Modern science has allowed us to map the seas and know the depth of every location on our planet, as well as explore the Moon and beyond. It is puzzling that we know the depth of the Mariana Trench (36,201 feet below sea level) but cannot be precise about the degree of congestion in our patients. Invasive measurements provide great insight but remain underutilized as they carry cost, discomfort, and procedural and infectious risk, which is a barrier to their standard use in trials or clinical care. Hopefully, future work will allow us to all know the depth of our patients' HF "ocean" and lead to improved outcomes.

Declaration of competing interest

David A. Baran has previously consulted for Abiomed, Abbott, LivaNova, Getinge, and Teleflex. He is on the steering committees for Procyrion, CareDx, and Natera. Aravdeep Jhand has no disclosures. None of these are relevant to this editorial.

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