Evaluation of Blood Volume Analysis-Guided Management of Decompensated Heart Failure

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INTRODUCTION

Over 6 million Americans suffer from heart failure (HF). High rates of rehospitalization and mortality and high treatment costs have persisted for decades despite advances in care. Clinical guidelines recommend assessment of congestion and clinical management to euvolemia, but standard methods of diagnosing volume status are unreliable. FDA-cleared Blood Volume Analysis (BVA) [Daxor BVA-100™] is based on the gold standard indicator dilution technique. BVA quantifies otherwise undiagnosed volume derangements. A recent retrospective analysis of BVA-guided HF therapy versus propensity-matched controls (n=245) demonstrated a significant all-cause readmission and mortality benefit to BVA-guided care.[1] An accompanying editorial called for prospective evaluation of the BVA technology.[2]

KEY ELIGIBILITY CRITERIA

Inclusion:

1. Age > 18 years.
2. Admission to the hospital with a primary diagnosis of ADHF, inclusive of all ejection fraction status.
3. Able and willing to provide informed written consent.

Exclusion:

1. Evidence of acute coronary syndrome or myocardial infarction during qualifying ADHF hospitalization.
2. Evidence of hypertensive crisis or acute valvular regurgitation.
3. Revascularization procedure, placement on cardiac transplant list, or other major cardiac or other surgery within 3 months of enrollment.
4. Planned intermittent or continuous intravenous positive inotropic therapy.
5. Severe chronic kidney disease (eGFR<15 ml/min).
6. Evidence of active bleeding or active hemolysis.
7. Hemoglobin measured below 7 g/dl or hematocrit measured below 21%.
8. Receipt of a heart transplant and/or currently treated with mechanical circulatory support.
9. Patients implanted with invasive hemodynamic monitors (e.g. CardioMEMS).
10. Known hypersensitivity to iodine or eggs.

OBJECTIVES

This study's primary objective is to determine if guideline-directed care informed by BVA in addition to usual care results in more appropriate treatment and consistent achievement of euvolemia than usual care alone. This Phase I randomized clinical trial will demonstrate and validate the efficacy of a treatment protocol with decisions informed by BVA.

PROTOCOL

In the BVA-guided-care group, investigators may choose to implement or stop therapies or adjust intensity/dose of therapy to correct Total Blood Volume (TBV) and/or Red Blood Cell Volume (RBCV) in order to target euvolemia, defined as 110% of ideal TBV and within ±10% of ideal RBCV as quantified by BVA. Adjustments in medications will be monitored with serial clinical assessments and laboratory assessments consistent with current usual care.

In the standard-care group, investigators will choose to implement or stop therapies or adjust intensity/dose of therapy as considered appropriate based on usual care clinical assessment and clinical response.

OUTCOME MEASURES

Primary: Quantitative assessment of progress to the BVA euvolemic target (110% of ideal TBV and within ±10% of ideal RBCV) for both subjects and controls.

Secondary: 30-day all-cause readmission and mortality outcomes will be quantified for both treatment arms; Quantitative assessment of continuous outcome metrics (e.g. weight change, net fluid balance, and brain natriuretic peptide [BNP]).

STATISTICAL POWER

32 patients (16 treatment, 16 control) will be needed to support the objectives of validating BVA in a proof-of-concept pilot. The sample size was calculated to observe differences due to treatment between hypervolemic and non-hypervolemic patients, based on data from the earlier retrospective HF outcome study. The results from this Phase I proof of concept study will support the power calculation of a subsequent Phase II randomized controlled trial.

STUDY INFORMATION

Source of support: NHLBI Phase I Small Business Innovation Research (SBIR) award.

ClinicalTrials.gov registration:
https://clinicaltrials.gov/ct2/show/NCT04855097

Trial design: Prospective, two-center, parallel design, interventional, single-blinded, randomized pilot study of the potential for BVA to positively impact acute decompensated HF treatment decisions.

Leadership: Jacob Joseph (Clinical and Site PI) , Bradley Bart (Site co-PI), Orly Vardeny (Site co-PI), Jonathan Feldschuh (PI), Inder Anand (Steering Committee), Wayne L. Miller (Steering Committee), John Strobeck (Steering Committee), Richard Nelson (Steering Committee), Ankeet S. Bhatt (Steering Committee).

Participating centers: VA Boston Health Care System, 150 S Huntington Ave., Boston, MA 02130; Minneapolis VA Health Care System, One Veterans Dr., Minneapolis, MN 55417.

Estimated study duration: August 1, 2021 – May 31, 2022.

Contact information: For information about research opportunities with Daxor, contact Soren Thompson, Vice President, sthompson@daxor.com.

REFERENCES

1. J. E. Strobeck, J. Feldschuh, and W. L. Miller, "Heart Failure Outcomes With Volume-Guided Management," *JACC Hear. Fail.*, vol. 6, no. 11, pp. 940–948, 2018, doi: 10.1016/j.jchf.2018.06.017.
2. Tang WHW, Telukuntla KS, Mayuga KA. "Can Blood Volume Analysis–Guided Acute Heart Failure Therapy Improve Clinical Outcomes?" *JACC Hear. Fail.*, vol. 6, no. 11, pp. 949-950. doi:10.1016/j.jchf.2018.08.003.

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