



The Phenotype of Polycythemia and Hypervolemia in Hospitalized Heart Failure Patients

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ABSTRACT

The Common Phenotype Of Polycythemia And Hypervolemia In Hospitalized Heart Failure Patients

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Abstract:
Background: Heart failure patients have wide variations in intravascular volumes which form the basis for disease initiation and progression and contribute to confusion in treatment strategies. Blood volume analysis (BVA) is a bedside blood test that measures with 98% accuracy intravascular volumes of a HF patient, including plasma and red blood cell volume (RBCV). Extremes in excess of red blood cell volume (polycythemia (P)) in HF patients have been associated with poorer outcomes including mortality. A not uncommon BVA phenotype is that of secondary P, with or without hypervolemia(P/Hypervol). We sought to further clarify the clinical correlates and outcomes associated with this phenotype in a mixed LVEF cohort of hospitalized HF patients and whether this phenotype would be detectable utilizing pHct or Hgb measures.

Methods/Results: In a cohort of 245 consecutively admitted HF patients (142 men/103 women) with mixed EFs who underwent BVA guided care, 25 patients (10.2%) had P/Hypervol and 3 patients (1.2%) had P with normal or low total blood volume. The presence of this phenotype was equal in patients with HFREF and HFpEF (52%/48%). P/Hypervol was observed less frequently in patients over 75 (p=0.03), and among patients with BMI>35 (p=0.07). Despite P, the peripheral Hct (pHct) was either normal (57.1%), or >10% below normal (39.3%), indicating that in a majority of patients excess red cells were accompanied by an excess of plasma and that pHct would not indicate P. The BVA-provided RBCV showed that in 93% of patients with P that diuresis alone would not be able to achieve euvoolemia without extreme hemoconcentration. Patients with P or P/Hypervol were treated with therapeutic phlebotomy or sent for hematology consults to achieve euvoolemia. In terms of outcomes at 30 days post-discharge, 12% of the phenotype were readmitted, similar to those with other phenotypes; no deaths occurred in the P/Hypervol phenotype within 30 days or 365 days. 30-day readmissions did occur (56%) in the phenotype similar to other phenotypes (62.3%).

Conclusions: The P/Hypervol phenotype is common and worrisome for several reasons. Neither the pHct, the BMI or age is sufficient to identify this phenotype. The plasma and red blood cell volume (RBCV) expansion may hasten disease progression accounting for underrepresentation of older patients in this cohort. Further, the discrepancy in the pHct might lead clinicians to suspect that the patient has a dilutionally low pHct, when, in fact, they have an increased RBCV and a diuretic strategy alone will only hemoconcentrate the patient, increasing viscosity and risk of thrombotic events while not achieving euvoolemia. BVA-guided assessment demonstrated the specificity to identify this phenotype, and raise the value of therapeutic phlebotomy to optimize volume and RBCV; this cohort merits improved BVA-guided evaluation to better discern the impact of this phenotype on HF outcomes.

OBJECTIVES

Heart failure patients, regardless of ejection fraction, functional class or stage have wide variations in the components of intravascular volume. Red blood cell volume (RBCV) variations (excess or deficit) impact circulatory integrity and function. Limited information is available on the frequency of RBCV excess, or Polycythemia (P), with or without increased total blood volume in hospitalized heart failure patients. Using direct measurement of blood volume analysis (BVA), we sought to understand the frequency of P in a recent cohort of patients and to further analyze clinical factors that might obscure detection of this important BVA phenotype.

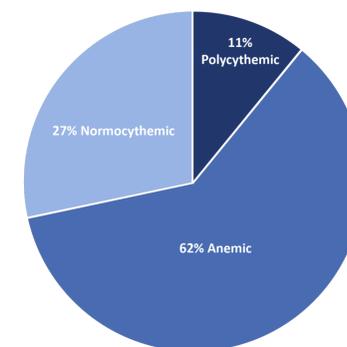
METHODS

245 consecutively admitted patients with heart failure underwent blood volume analysis (BVA, Daxor, Corp., Oak Ridge, TN) to guide hospital care. The report provided personalized measurements of total blood volume, red blood cell volume and plasma volume, as well as percentages of excess or deficit according to patient specific norms. Also, the result included the patient's peripheral hematocrit (pHct). P was an excess of $\geq 10\%$ of the predicted RBCV; hypervolemia (Hypervol) was an excess of $\geq 10\%$ of total blood volume (TBV).

RESULTS

The 245 consecutively admitted HF patients included 142 men and 103 women and included 123 pts with a LVEF <40% and 122 with a LVEF $\geq 40\%$. 25 patients had P/Hypervol and 3 patients had P with normal or low total blood volume. The presence of this phenotype was seen equally in patients with HFREF and HFpEF (52%/48%).

Red Blood Cell Volume Patient Characteristics



P/Hypervol pts tended to be younger, and all had a BMI of 35 or less. When compared to measured RBCV, the pts with P, had a **peripheral Hct** that was normal 57.1% of the time, or >10% below normal 39.3% of the time. (p=0.0015). Conversely, the **BVA provided normalized Hct** was > 45 in 93% of patients with the phenotype. In terms of outcomes at 30 days post discharge 12% of the phenotype were readmitted, similar to other BVA phenotypes; no deaths occurred in the P/Hypervol phenotype within 30 days. Further, there were no deaths in the phenotype in the first year following discharge however readmissions did occur (56%) in the phenotype but similar to those with other BVA phenotypes (62.3%).

CONCLUSIONS

P in heart failure has been thought to occur in 1.2-5.9% of heart failure patients, but has been suspected to be underreported. Using precision BVA measurement of RBCV in patients admitted for heart failure the following guidance has emerged:

- P was present in 11.4% of the admitted patients; equally across LVEFs.
- HYPERvolemia commonly is associated with P with increased risk of expansion of 2 intravascular volumes.
- Patients with P did not have the usual linkages to secondary P risk factors such as older age or an increased BMI.
- Peripheral Hct measurement grossly underestimates the prevalence of P. In 2012 Maurer and colleagues, using BVA, identified “masked polycythemia” in heart failure. This has been also been reported by Miller (2016) and unexpected excesses of RBCV can approach + 100% of patient norms.
- Support and evidence is emerging to measure RBCV when possible rather they rely on a peripheral hematocrit which often over- and under-estimates RBCV.
- While in this cohort managed from the time of admission using BVA guidance did not have increased 30-day readmissions or mortality at one year compared with the rest of the cohort, the discrepancy with the peripheral hematocrit might confound clinicians into thinking the patients with a lower peripheral hematocrit were dilutionally low, and use diuretics with further hemoconcentration risking increased blood viscosity and thrombotic events.
- Without recognizing the P and considering therapeutic phlebotomy, euvoolemia cannot be achieved.
- Further attention to the presence of P in heart failure patients and to consider novel and older approaches to attain euvoolemia-normalization of all intravascular volumes.

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