Anemic Patients with HFNEF Have a Reduced Red Cell Volume, True Anemia and Concomitant Plasma Volume Expansion.

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Background

- Anemia is a significant co-morbidity among patients with heart failure and a normal ejection fraction (HFNEF), commonly called "diastolic heart failure" (DHF).
- Data in subjects with HFNEF are emerging to suggest a significant relationship between anemia, clinical symptoms, left ventricular (LV) structure, hemodynamics, morbidity, and renal function and adverse outcomes including increased morbidity and mortality.
- Standard laboratory testing to diagnose anemia relies on hemoglobin and hematocrit levels below a particular threshold.
- However, such testing is unable to distinguish anemia that is secondary to plasma volume expansion (i.e. dilutional) from anemia that is characterized by a red cell deficit.
- In subjects with systolic heart failure, a significant percentage of anemic patients were found to be hemodiluted and not have a true red cell deficit (e.g. true anemia) as assessed by blood volume analysis. (*Circulation*. 2003; 107:226-229)
- We sought to determine whether HFNEF patients with anemia defined by WHO criteria had a true anemia or were simply hemodiluted.

Methods

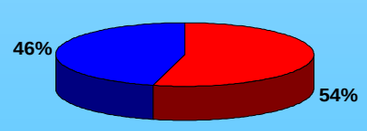
- ***Study Design***
  - Cohort descriptive study
- ***Study Subjects (n=25)***
  - All patients in the HFNEF group met criteria for *diastolic heart failure* as defined by the European Society of Cardiology: signs and symptoms of congestive heart failure, a normal LV ejection fraction (we specifically required ejection fraction ≥50% by three dimensional echocardiography) and evidence of abnormal diastolic function.
  - We employed the NHANES criteria for define the signs and symptoms of heart failure which include symptoms of dyspnea, resting heart rate, rales, JVD, and evidence of fluid on chest x-ray.
    - An NHANES score of ≥ 3 was required.
- ***Anemia***
  - All patients met WHO criteria for anemia defined by hemoglobin < 12 g/dL in women and hemoglobin < 13 g/dL for men.
- ***Blood Volume Analysis (BVA)***
  - Blood volume, red cell volume, and plasma volume can be determined from serial samples of the concentration of a tracer (10-25 microcuries of ^{131}Iodine tagged albumin) after allowing for complete mixing of the tracer in the circulation (12 minutes). Five cc blood samples are collected before isotope injection and at 12, 18, 24, 30 and 36 minutes after isotope injection.
  - Specimens collected were analyzed with an automated system (BVA-100 Blood Volume Analyzer, Daxor Corp., NY).
- Mean values of total blood volume, plasma volume and red cell volume were calculated, as well as compared to ideal volume based on the indexed values accounting for the study subject's gender as well as height and weight (*Circulation*. 1977; 56: 605-612), in order to determine a blood volume deficit or excess.
- Anemia was defined as having <95% predicted RBC volume.

Results

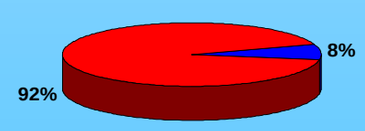
Demographic and Clinical Characteristics of Study Subjects (n=25)

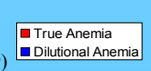
Age (years)	71 ± 14
Race (W, B, H, O)	8/9/8/0
Gender (% female)	76%
Height (cm)	161 ± 10
Weight (kg)	84 ± 21
BSA	1.88 ± 0.21
Hemoglobin (g/dL)	11 ± 1
Thiazide Diuretic	
# of Subjects	4 (16%)
Mean daily dose (mg)	28 ± 16
Loop Diuretic	
# of Subjects	19 (76%)
Mean daily dose (mg)	95 ± 90
BUN (mg/dL)	37± 23
Creatinine (mg/dL)	1.7 ± 0.9
Estimated GFR (mL/minute)	55 ± 31

Systolic Heart Failure

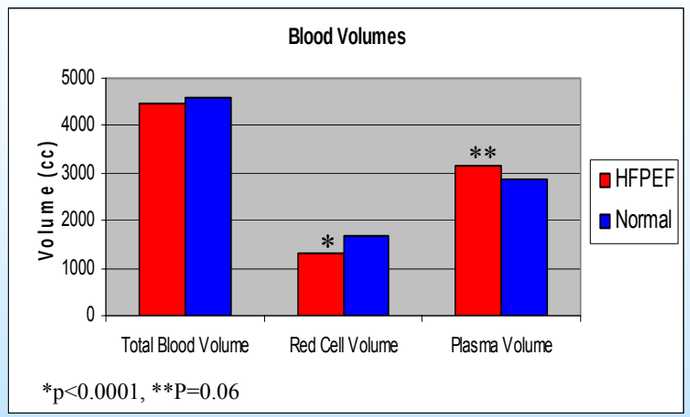


Heart Failure with a Preserved Ejection Fraction





(*Circulation*. 2003; 107:226-229)



*p<0.0001, **P=0.06

BVA Derived Parameters	Mean Values (N=25)
Blood Volume Deficit (mL)	119 ± 1070
Red Cell Deficit (mL)	387 ± 319
Excess Plasma Volume (mL)	268 ± 825

Study Limitations

- This was a single center study.
- Patients studied while clinically stable as outpatients and not during an acute decompensation, therefore relevance to inpatient population unclear.
- While shown to be concordant with other measures of red cell mass that utilize chromium labeled red blood cells, the red cell volume was estimated from spun hematocrits and measures of plasma volume.

Conclusions

- Patients with HFNEF and low hemoglobin often have a true anemia characterized by, on average, a greater than one unit decrement in red cell volume.
- Accompanying the deficit in red cell volume in these patients is a plasma volume expansion suggesting that impaired renal function may be the underlying mechanism of both anemia and volume overload in these subjects. .