



Racial Differences in Blood Volumes in Patients with Heart Failure and a Preserved Ejection Fraction (HFPEF): Implications for Diagnosing Anemia.

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Background

- Anemia is common in subjects with HFPEF but the diagnosis can be confounded by the concomitant expansion of plasma volume (PV) that occurs in volume overloaded states such as heart failure.
- Additionally, the chronic use of medications such as diuretics that act by contracting plasma volume could result in an under-diagnosis of anemia based on standard hemoglobin measures
- The contracted red blood cell volume (RBCV) that characterizes anemia induces a physiologic compensatory expansion of PV in order to maintain the overall blood volume (BV) at a constant level.
- Since the prevalence of anemia differs by race in the general population, we analyzed blood volume in subjects with HFPEF to determine if racial differences were present.

Methods

Study Subjects.

- Subjects were outpatients referred for evaluation and treatment to the Columbia University Medical Center Heart Failure Center.
- Subjects aged >21 years with HF with a preserved ejection fraction (e.g. $\geq 45\%$) and stable symptoms were studied.
- Subjects with acute decompensated HF, severe renal dysfunction (serum creatinine >3.0 mg/dl or history of nephrotic syndrome), and severe hepatic dysfunction (serum liver enzymes >3 times the upper limits of normal or history of cirrhosis) were excluded.
- Cardiac medications included diuretics, digoxin, renin-angiotensin system inhibitors, and/or beta-adrenergic receptor antagonists that were stable before the measurement of blood volume.

Hemoglobin:

- Hemoglobin was measured as part of a routine complete blood count from the hospital core laboratory (Sysmex XE 2100; Sysmex Corporation, Kobe, Japan).
- Anemia was defined according to WHO criteria as a hemoglobin <12 gm/dl in women and <13 gm/dl in men

Blood volume measurements:

- Plasma volume was determined after the intravenous administration of iodine-131-labeled albumin.
- Blood volume and red blood cell volume were calculated from the plasma volume measurement, the measured hematocrit corrected for trapped plasma, and mean body hematocrit.
- Blood volume components (plasma, red cell and total volume) were determined and compared to normal values adjusted for age, gender and weight on the basis of the ideal weight system to yield % deviations from normal.
- Anemia, based on blood volume analysis, was defined by RBCV $<10\%$ below ideal.
- To determine if PV compensation in patients with RBCV deficits was appropriate, the absolute PV compensation in response to RBCV deficit was calculated as deviation from ideal PV – RBCV deficit and the % compensation was calculated as (deviation from ideal PV - RBCV deficit)/ideal PV.

Results

- Anemia, as defined by WHO criteria, was present in 42 (68%) of subjects and did not differ by gender or race.
- However, anemia as defined by measured RBCV deficit was present in just 22 (34%) of subjects.
- Using RBCV deficit as the basis to diagnose anemia led to a reclassification of anemic patients in 33% of Whites, 80% of Hispanics and 53% of Blacks as compared to hemoglobin.
- These differences in the prevalence of anemia as determined by hemoglobin level versus measured RBCV deficit are in part attributable to greater absolute PV compensation (average=476 ml) and per cent compensation (16.2%) of PV in response to RBCV deficit as found in Hispanics more commonly than African-Americans, $p < 0.05$.

Table 1: Demographic and Clinical Characteristics

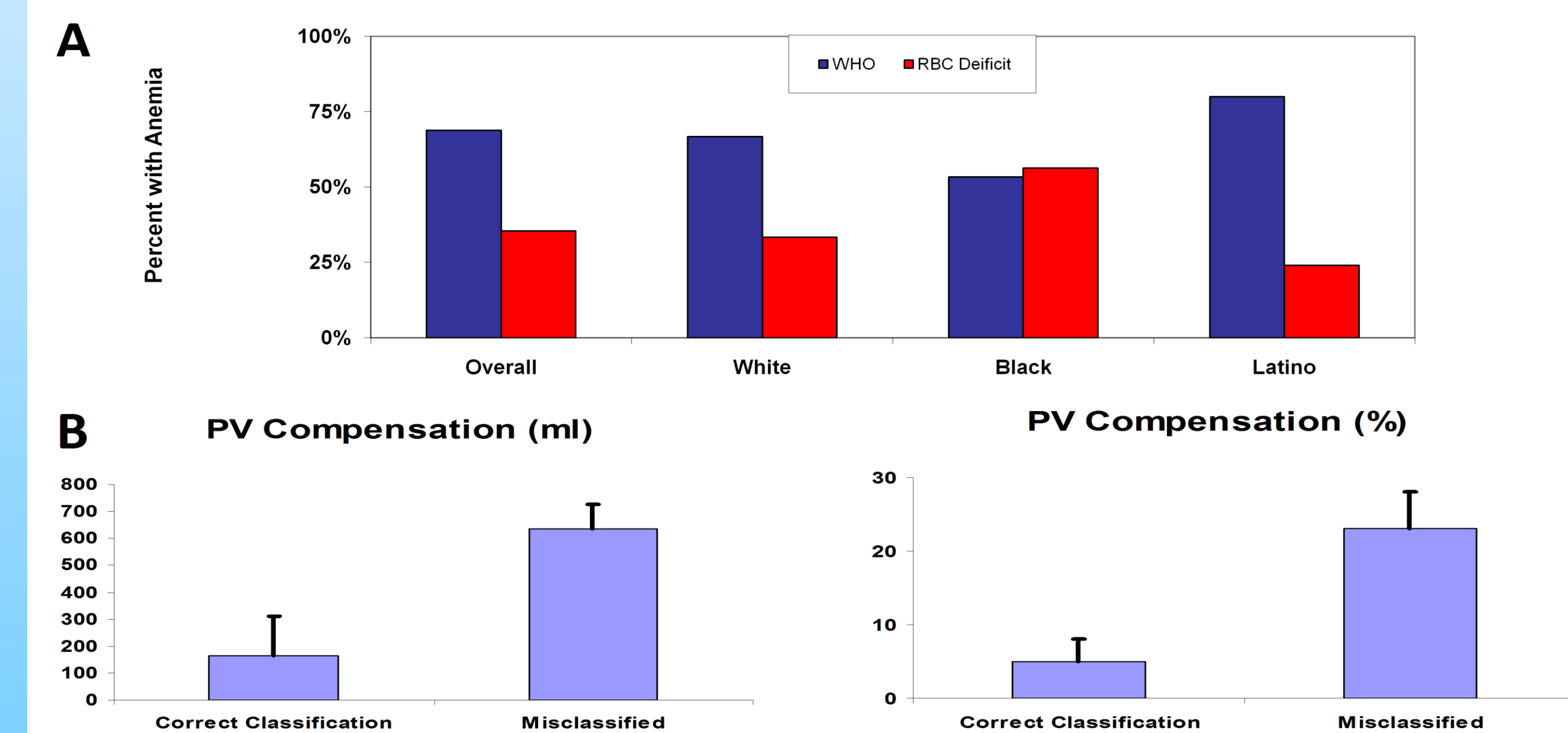
	Overall (n=62)	Whites (n=20)	Blacks (n=16)	Hispanics (n=24)	P value
Demographics					
Age (years)	70± 12.7	75± 12	68± 15	67± 11	NS
Gender (% female)	61	38	81	68	0.02
Body Size					
Weight (kg)	80± 14	86± 18	81± 15	74±7*	0.01
BMI	30± 4.3	31± 4	31± 5.8	29± 3	NS
BSA (m2)	1.89± 0.2	1.98± 0.3	1.9± 0.2	1.8± 0.1*	0.01
Anemic (%)	67	67	53	80	NS
Three dimensional Echocardiography					
EDVI (ml/m2)	60±13	62±13	62±16	56± 10	NS
SVI (ml/m2)	32±7	33± 7	34± 8	31± 6	NS
EF (%)	54± 6	54± 5	54± 6	55± 6	NS
LV mass (grams/m2)	78±22	78±16	85±22	74±25	NS
EDV/Mass ratio	0.81±0.24	0.83±0.2	0.77±0.24	0.83±0.26	NS
Laboratory Results					
Hemoglobin (gm/dl)	11.6± 2.1	12± 2.2	12± 2	11± 2	NS
BUN (mg/dl)	33± 18.9	38± 19	31± 22	31± 17	NS
Creatinine (mg/dl)	1.6± 0.8	1.6± 0.7	1.6± 0.7	1.5± 0.9	NS
eGFR (ml/min)	51± 21	48± 16	53± 24	51± 23	NS

* $p < 0.05$ versus Whites by ANOVA with post hoc Bonferonni correction

Table 2: Blood Volume in HFPEF stratified by Racial Groups

	Overall (n=62)	Whites (n=21)	Blacks (n=16)	Hispanics (n=25)	P value
Blood Volume (ml)	4728± 1135	5342± 1264	4214± 783*	4541± 1009*	0.0048
Ideal Blood volume (ml)	4570± 687	4820± 800	4472± 583	4423± 609	NS
Excess/Deficit Blood volume (ml)	438± 599	606± 667	373± 621	339± 514	NS
BV Deviation (%)	9±13	12± 14	8± 13	7±11	NS
Red Cell Volume (ml)	1473± 471	1741± 599	1298± 218*	1360± 372*	0.0039
Ideal Red Cell volume (ml)	1739± 336	1883± 390	1652± 250	1674± 306	NS
Excess/Deficit Red Cell volume (ml)	48± 469	138± 452	198± 558	-123± 376	NS
RBC Deviation (%)	3±27	-1.7± 25.9	11± 30	-7 ± 22	NS
Plasma Volume (ml)	3254± 768	3601± 781	2915± 686*	3180± 713	0.02
Ideal Plasma volume (ml)	2830± 371	2937± 423	2820± 357	2749± 322	NS
Excess/Deficit Plasma volume (ml)	532± 474	664± 514	370± 474	525± 424	NS
Plasma Deviation (%)	18± 15	22 ± 16	13±16	19± 14	NS

* $p < 0.05$ versus Whites



Conclusion

- In patients with HFPEF, the diagnosis of anemia based on hemoglobin levels is confounded by plasma volume derangements resulting in an almost two-fold over-diagnosis of anemia in this overall population.
- Such data could have important implications for the diagnosis and management of anemia in ethnic minorities with HFPEF.