1142-179 Body Fat Distribution Influences Cardiac Output in Normotensive and Hypertensive Overweight Individuals: The HyperGEN Study

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Background: We have shown that in obesity increased cardiac output is related to fat-free mass but also to adipose mass. Whether these relations are present in milder overweight and similar with central (CFD) or peripheral fat distribution (PFD) has never been explored in population studies. **Method:** 522 overweight, non-obese participants (NIH 1998) in the *HyperGEN* study, without diabetes or known cardiovascular disease, and with normal LV function were studied (262 with CFD, by waist girth>88/102 cm in women/men). Fat-free and adipose mass were measured by bioelectric impedance and body composition was estimated as the ratio of adipose to fat-free mass (A/FFMr). Stroke volume (SV) and cardiac output (CO) were measured by echocardiography. **Results**: Hypertension was present in 73% of PFD and 78% of CFD. Table shows that overweight with CFD was associated with greater adiposity, similar in normotensive and hypertensive participants. At comparable fat-free mass, CO was higher in overweight with CFD than in PFD, whereas peripheral resistance was similar. CO was related to adipose mass (beta=0.13, p<0.01), independently of fat-free mass (beta=0.30, both p<0.0001) and African-American ethnicity (beta=0.10, p<0.03); no independent relations were found with age, sex or hypertension. **Conclusions**: in overweight, non obese subjects, central fat distribution is associated with more severe degree of abnormalities in body composition and influences magnitude of cardiac output independently of fat-free mass.

2-way ANCOVA adjusting for age, sex and race

	Normotensive		Hypertensive	
	PFD (n=71)	*CFD (n=87)*	*PFD (n=189)*	*CFD (n=205)*
BMI (kg/m^2)	27	28	27	28*
Fat-free mass (kg)	49	52	48	51*
Adipose mass (kg)	26	32	26	31*
A/FFMr	0.59	0.67	0.60	0.68*
Cardiac output (l/min)	4.73	4.98	4.75	5.12*
Peripheral resistance	1638	1630	1779	1694#
Mean BP (mmHg)	94	98	103	104#

*effect of fat distribution; #effect of hypertension: 0.04<p<0.0001

1142-180 Peroxisome Proliferator-Activated Receptor-Alpha Intron 7 Polymorphism Exhibits Racial Dimorphism and Is Associated With Increased Left Ventricular Mass

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Background: Peroxisome proliferator-activated receptor-alpha (PPARα) is a key transcription regulator of myocardial fatty acid metabolism. Recently an intron 7 G>C polymorphism in the PPARα gene was associated with pathologic left ventricular (LV) hypertrophy in Caucasian men, but not in women. The frequency of the polymorphism and its influence on measures of myocardial LV mass (LVM) has not been well evaluated in a racially mixed population.
Methods and Results: The PPARα intron 7 G>C polymorphism was genotyped in 107 subjects to investigate a relationship with LVM. There was no significant difference in systolic BP, LV ejection fraction (LVEF) or history of HTN between the 4 groups, or within the groups between genotypes. The allelic frequencies were racially dimorphic [C allele frequency =0.22 in Non-African Americans (NAA) and 0.52 in African Americans (AA)]. Among NAA women, the intron 7 CC genotype was significantly associated with increased LVM (LVM/Ht$^{2.7}$, p<0.001 vs. GG and GC); a similar association was found among NAA men (p=0.048 GG vs. CC). No association of intron 7 genotypes and LVM were found among AA women or men, albiet this subgroup had a smaller sample size.
Conclusions: 1) The PPARα intron 7 G>C polymorphism is racially dimorphic and 2) this study confirms the influence of the PPARα intron 7 CC genotype on LVH in NAA men, and extends this to NAA women. Given the racial dimorphism in allelic frequencies further investigation is warranted to evaluate whether the C allele is associated with LVM in AA.

	NAA Women (n=44)	NAA Men (n=35)	AA Women (n=22)	AA Men (n=6)
Age (yrs)	48±9	48±13	53±14	52±13
LV Ejection Fraction (%)	66±5	66±6	67±6	65±4
Systolic BP (mmHg)	121±18	125±18	128±18	131±13
History of Hypertension (%)	32	49	59	33
LVM/Ht$^{2.7}$ (g/m$^{2.7}$)	39±10	45±11	45±11	33±10
Frequency C Allele	.18	.26	.52	.50

1142-181 Does Indexation to Fat-Free Mass Eliminate or Reverse Gender Differences in Left Ventricular Mass?

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Mean left ventricular mass (LVM) is greater in men than women, regardless of indexation to height (Ht) or body surface area (BSA). Indexation to fat-free body mass (FFM) may better reflect metabolic demand, potentially allowing improved identification of inappropriately elevated LVM, but the gender-differential effect of indexation to FFM on LVM by cardiovascular magnetic resonance (CMR) is unknown.
Methods: Clinically healthy adults (144 women and 135 men, aged 59±9 years) from the Framingham Offspring cohort underwent volumetric FFE-EPI CMR (1.5T, Philips) to determine LVM. FFM was determined using two gender-specific methods: Kvist formula FFM=Wt-(0.923*(1.36*Wt/Ht-42.0)), men, FFM=Wt-(0.923*(1.61*Wt/Ht-38.3)), women, Wt=weight. Kuch FFM= 5.1*Ht^1.14*Wt^0.41, men; FFM=5.34*Ht^1.47*Wt^0.33, women. LVM was indexed to Ht, Wt, BSA, Ht^2.7 and Kvist and Kuch FFM. Gender differences were assessed by Student's t test.
Results: Men had significantly greater LVM (Table) before and after indexation to Ht, Ht^2.7, BSA and Wt. Indexation to Kuch-FFM eliminated gender differences in LVM, while Kvist-FFM gave significantly greater adjusted LVM in women.
Conclusion: Men have greater LVM than women and this gender difference persists after traditional indexation methods. However, indexation to FFM eliminates LVM gender differences (Kuch) or gives greater indexed LVM in women (Kvist). Further work is needed to determine the prognostic value of volumetric LVM indexed to FFM.

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LVM by Gender (mean±SD)

Index	None	Ht	Ht^2.7	BSA	Wt	Kvist	Kuch
Men	156±29	88±16	33±6.5	76±14	1.8±0.36	2.42±0.43	2.55±0.46
Women	110±20	62±14	30±6.4	63±10	1.6±0.29	2.68±0.51	2.51±0.44
p-value	<0.001	<0.001	<0.001	<0.001	<0.005	<0.005	0.45, *NS

1142-182 Differences in Brain-Natriuretic Peptide and Left Ventricular Dimensions and Mass in Normotension, Prehypertension and Hypertension

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Background: BNP and increase in left ventricular mass (LVM) are associated with increased cardiovascular risk. The JNC VII guidelines for hypertension considernormotension, prehypertension and hypertension. Surrogate end-markers for cardiovascular damage in prehypertension are not known.
Objective: To study the significance of BNP and LVM as well as left ventricular enddiastolic diameter (LVIDD) in prehypertension versus normotension and hypertension.
Methods:
A total number of 159 subjects with normotension (BP < 120/80 mm Hg); 243 subjects with prehypertension (BP 120-139/80-89 mm Hg) and 143 subjects with hypertension (BP ≥ 140/90 mm Hg) underwent an echocardiographic exam and a blood sampling for BNP.
Results: Data are expressed as mean ± s.e.m. in Table 1. Statistical significance between prehypertension and normotension and hypertension between prehypertension and normotension has been calculated.
*P < 0.05; ** P < 0.01
Conclusions:
Prehypertension is characterized by a significantly higher LVIDD and LVM in comparison with normotension and a lower LVIDD and LVM in comparison with hypertension. BNP is not elevated in prehypertension, but is in hypertensive subjects. Thus prehypertension is characterized by structural changes in the left ventricle not detectable by increases in BNP.