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SHORT COMMUNICATION

Sex differences in the relationships of abdominal fat to cardiovascular disease risk among normal-weight white subjects

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The objectives of this study are to investigate the relationships between abdominal fat and risk factors for cardiovascular disease (CVD) among normal-weight (NW) white subjects and to determine how these relationships differ by sex. NW adults (177 males and 258 females) and overweight adults (133 males and 111 females) from the Québec Family Study and the HERITAGE Family Study were retained for this study. Risk factors included systolic and diastolic blood pressures, low-density lipoprotein and high-density lipoprotein cholesterols, triglycerides, and fasting glucose. Only in NW female adults, abdominal visceral fat (AVF) area assessed by computed tomography was significantly correlated with all risk factors, except for fasting glucose, even after age, study cohort, and fat mass were taken into account. NW female subjects with at least one risk factor had a significantly higher AVF than those without risk factors, although the difference was small. Thus, only NW female adults with more AVF tended to have a more adverse CVD risk factor profile.
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Introduction

Ruderman *et al*[1] proposed the concept of a 'metabolically obese, normal-weight' (NW) individual and suggested that central obesity (especially elevated abdominal visceral fat, AVF) may be responsible for this clinical profile. Several studies on abdominal fat in NW people have found relationships between abdominal fat levels and cardiovascular disease (CVD) or CVD risk factors in NW male subjects[2–4] and in some groups of NW female subjects,[5–7] but not in others.[8] However, abdominal fat has been suggested to have a greater role in CVD risk in obese female subjects than in obese male subjects.[9–11] Hence, some controversy exists regarding sex differences in the role of abdominal fat among NW people. The present study investigated the relationships between indicators of abdominal fat and CVD risk factors in NW individuals and whether there were sex differences in the relationships.

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Subjects and methods

Subjects were Whites, aged 17–60 years, from Phase 2 of the Québec Family Study (QFS) and from the baseline cohort of the HERITAGE Family Study. Detailed information about the subjects is available in prior publications.[12–14] The sample of the present study included NW subjects (177 males and 258 females) and overweight (OW) subjects (133 males and 111 females) using the cut-offs proposed by WHO[15] and NIH.[16] More details about the samples and the methods can be found in a recent paper.[14] Informed consent was obtained and the study protocols were approved by the Institutional Review Boards of QFS and HERITAGE Family Study centers.

Methods

Body density was measured by the underwater weighing method in the post-absorptive state. Abdominal subcutaneous fat (ASF) and AVF levels were assessed as described elsewhere.[17] The CT scan was performed between the fourth and fifth lumbar vertebrae (L4–L5) with subjects in a supine position and arms stretched above the head. Plasma cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, fasting glucose levels, and systolic and diastolic blood pressure were determined as described previously.[14]

Statistical analysis

The NW subjects were divided into quintiles of AVF and ASF. The OW group and each quintile in the NW group were then evaluated for the presence of risk factors. The risk factor classification was based on the same criteria as in a prior publication.[14] Logistic regression analysis was used to estimate the odds ratios (OR) for prevalence of risk factors across abdominal fat quintiles, adjusting for age, study cohort, and fat mass (FM). The lowest (first) quintile of each abdominal fat area in the NW group was used as a reference group (OR = 1). The OR was thus determined for each of the other four quintiles in the NW group and for the OW group relative to the first quintile of the NW group for each variable within each gender.

Results

AVF and ASF in NW male subjects were $63.3 \pm 33.7\,cm^2$ ($13.0–224.0\,cm^2$) and $118.7 \pm 58.4\,cm^2$ ($21.0–295.9\,cm^2$), and those in NW female subjects were $54.3 \pm 29.5\,cm^2$ ($13.1–205.0\,cm^2$) and $198.4 \pm 72.6\,cm^2$ ($13.1–205.0\,cm^2$), respectively.

Table 1 shows partial correlation coefficients between AVF and ASF and CVD risk factors. In NW male individuals, a significant correlation was observed only between AVF and triglycerides after FM was taken into account, while similar coefficients with diastolic blood pressure, low-density lipoprotein (LDL) cholesterol, and triglycerides remained significant in OW male individuals. In NW female subjects, AVF significantly correlated with all risk factor variables except for fasting glucose even after FM was taken into account. In contrast, ASF negatively correlated with HDL cholesterol when age and study cohort were adjusted for, and significantly correlated with systolic blood pressure when FM was also controlled for in NW female subjects.

The quintiles of AVF and ASF among NW subjects were evaluated for the presence of CVD risk factors (Table 2). More than half of the male subjects in the fifth quintiles of AVF and ASF exhibited CVD risk factors. Although no OR for the quintiles among NW group and OW groups was significantly different from 1 in male subjects and female subjects, the fourth quintile of AVF in NW female subjects had a significantly lower OR than the fifth quintile ($P = 0.03$), and the second quintile had a marginally significant lower OR ($P = 0.053$).

NW female subjects with at least one risk factor had a significantly higher AVF ($58.2 \pm 17.6\,cm^2$) than those without risk factors ($52.2 \pm 16.8\,cm^2$) even after adjustment for age, study cohort, and FM. In NW male subjects, no

Table 1 Partial correlation coefficients between abdominal fat areas and risk factors in each sex

	NW group controlling for				*OW group controlling for*			
	Age and cohort		*Age, cohort and FM*		*Age and cohort*		*Age, cohort and FM*	
Risk factors	*AVF*	*ASF*	*AVF*	*ASF*	*AVF*	*ASF*	*AVF*	*ASF*
Males								
Systolic blood pressure	0.03	0.02	0.02	−0.01	0.06	−0.03	0.06	−0.09
Diastolic blood pressure	0.12	0.13	0.05	0.05	0.20*	−0.09	0.25**	−0.09
LDL cholesterol	0.15*	0.15	0.07	0.03	−0.03	0.26**	−0.17*	0.12
HDL cholesterol	−0.19*	−0.25***	−0.04	−0.07	−0.15	−0.20*	−0.12	−0.20*
Triglycerides	0.33***	0.30***	0.19*	0.10	0.24**	0.17	0.19*	0.07
Fasting glucose	0.19*	0.20**	0.09	0.07	0.33***	0.11	0.31***	0.00
Females								
Systolic blood pressure	0.24***	−0.04	0.25***	−0.15*	0.16	0.24*	0.14	0.28**
Diastolic blood pressure	0.22***	0.04	0.19**	−0.07	0.17	0.20*	0.16	0.25*
LDL cholesterol	0.22***	−0.05	0.24***	−0.11	0.32***	0.18	0.30**	0.13
HDL cholesterol	−0.24***	−0.19**	−0.16*	−0.07	−0.23*	0.02	−0.22*	0.12
Triglycerides	0.25***	0.05	0.25***	−0.00	0.21*	−0.04	0.24*	0.02
Fasting glucose	0.10	0.06	0.05	−0.04	0.10	−0.13	0.11	−0.14

NW, normal-weight; OW, overweight; FM, fat mass; AVF, abdominal visceral fat; ASF, abdominal subcutaneous fat.*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Table 2 ORs of prevalence of subjects with risk factors in each sex

	NW group					*OW group*
	Quintiles					
	Q1	*Q2*	*Q3*	*Q4*	*Q5*	
Males						
Quintiles of AVF						
Range of AVF	13.0–36.8	37.4–49.4	49.4–66.4	66.5–83.1	83.3–224.0	38.1–260.0
Number of subjects[a]	10/35	9/36	8/35	16/36	18/35	77/133
OR (95% CI)	1	0.76 (0.26–2.22)	0.46 (0.15–1.44)	0.94 (0.31–2.85)	1.00 (0.30–3.30)	1.09 (0.35–3.47)
Quintiles of ASF						
Range of ASF	21.0–64.8	65.8–95.2	95.3–127.7	127.8–172.0	173.1–295.9	69.6–446.0
Number of subjects[a]	11/35	11/36	7/35	11/36	21/35	77/133
OR (95% CI)	1	0.72 (0.25–2.07)	0.34 (0.11–1.09)	0.58 (0.19–1.77)	1.37 (0.41–4.63)	1.07 (0.33–3.41)
Females						
Quintiles of AVF						
Range of AVF	13.1–30.6	30.8–40.5	40.5–52.6	53.0–74.8	75.0–205.0	34.2–212.0
Number of subjects[a]	5/51	5/52	11/52	5/52	14/51	35/111
OR (95% CI)	1	0.82 (0.23–2.92)	2.09 (0.69–6.31)	0.81 (0.21–3.05)	2.81 (0.78–10.19)	3.66 (0.95–14.14)
Quintiles of ASF						
Range of ASF	50.2–131.0	131.9–167.6	168.0–210.9	211.6–267.6	268.2–514.9	216.8–513.2
Number of subjects[a]	6/51	6/52	12/51	7/53	9/51	35/111
OR (95% confidence interval)	1	0.77 (0.24–2.48)	1.78 (0.62–5.10)	0.76 (0.22–2.59)	1.05 (0.29–3.78)	2.03 (0.52–7.88)

OR (odds ratio), relative to the first quintile in NW group, obtained by logistic regression analysis adjusting for age, study cohort, and FM. NW, normal-weight; OW, overweight; FM, fat mass; AVF, abdominal visceral fat; ASF, abdominal subcutaneous fat. [a]Number of subjects with at least one risk factor / total number of subjects in each quintile. No OR was significantly different from 1.

significant difference in AVF was observed between these two groups ($60.8 \pm 22.0\,cm^2$ *vs* $62.7 \pm 20.7\,cm^2$).

Discussion

Despite similar standard deviations and ranges for both FM and AVF, a sex difference remained after adjusting for FM. In male subjects but not in female subjects, adjustment for FM eliminated the associations between abdominal fat variables and CVD risk factors, except for plasma triglycerides.

Some previous studies have, however, obtained different results, indicating that AVF area was higher in NW male subjects with CVD risk factors than NW subjects without risk factors.[3,4] These discrepancies may arise from differences in sample size or the more accurate measurement methods (FM from underwater weighing and AVF from CT) used in the present study. Also, ethnicity may contribute to the heterogeneous results. Some of the previous studies in NW people were performed with Asians, whose body composition and fat distribution characteristics differ from Caucasians.[18,19]

In conclusion, only NW female subjects with an elevated AVF level tend to have a more adverse CVD risk factor profile, independent of total adiposity. It should be emphasized that these findings are based on cross-sectional observations. A prospective design would provide a better quantification of the contributions of total fatness and AVF to the metabolic profile.

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