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Central obesity and hypertension: pathophysiologic role of renal haemodynamics and function

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OBJECTIVE: To investigate the role of alterations in renal haemodynamics and function and in plasma renin activity on obesity-induced hypertension.

DESIGN: Renal haemodynamics and function, salt-regulating hormones and structural cardiac parameters were evaluated in 20 lean normotensives and in 64 obese subjects with central or peripheral fat distribution, 43 of them were normotensives and 21 of them were hypertensives. Obesity and central fat distribution were defined according to sex-specific 85th percentile respectively of Body Mass Index (BMI) and Waist to Hip Ratio (WHR).

MEASUREMENTS: Serum immunoreactive insulin (IRI), plasma renin activity (PRA), plasma aldosterone (PA), microalbuminuria (UAE) and 24h urinary excretion of sodium (NaU) were evaluated by current methods. Renal haemodynamics was evaluated by radionuclide study according to Schlegel's and Gate's methods. By radionuclide study, effective renal plasma flow (ERPF), effective renal blood flow (ERBF), glomerular filtration rate (GFR), filtration fraction (FF) and renal vascular resistances (RVR) were measured. Left ventricular mass (LVM) and indexed for body height (LVM/H), cardiac output (CO) and total peripheral resistances (TPR) by ecocardiography were also calculated.

RESULTS: CO, LVM and LVM/H were significantly ($P < 0.05$) higher in all the obese groups than lean controls. In addition, LVM and LVM/H were significantly ($P < 0.05$) higher in obese hypertensives than obese normotensives either with central fat distribution. TPR values were significantly ($P < 0.05$) higher in central obese hypertensives than peripheral obese hypertensives and than central obese normotensives. Moreover, IRI levels were significantly ($P < 0.05$) higher in central normotensive and hypertensive obese subjects than lean subjects.

ERBF and ERPF were significantly ($P < 0.05$) lower and PRA levels were significantly higher only in central obese than lean subjects. On the contrary RVR were significantly ($P < 0.05$) higher in both obese hypertensive groups and in central obese normotensives than lean subjects. Comparisons between peripheral and central obese groups indicated that PRA, RVR and UAE were significantly ($P < 0.05$) higher and ERBF and ERPF values were significantly ($P < 0.05$) lower in both central obese groups than comparable subjects with peripheral obesity.

Multiple regression analysis indicated that RVR increased significantly ($P < 0.05$) with WHR and PRA but not with CO and IRI.

CONCLUSIONS: Our results indicate that obesity with body fat distribution of central type, more than obesity of peripheral type, is associated to abnormalities in renal haemodynamics and function. These data are consistent with the indication that change in renal haemodynamics take place at an early stage in the obesity-induced hypertension.

Keywords: body fat distribution; hypertension; renal haemodynamics; plasma renin activity

Introduction

Hypertension and obesity are disorders that are closely linked, especially when obesity is characterized by a central fat distribution.[1,2] For many years, it has been well demonstrated that obese patients are more likely to be hypertensive than lean subjects and that weight gain is predictive of later onset of hypertension.[3] Although this strong association, the mechanisms of obesity-associated hypertension are still unclear.[4]

Some abnormalities have been reported to explain the higher susceptibility of obese subjects to develop hypertension. They include increased cardiac output and intravascular volumes,[5] sodium retention and dysregulation in salt regulating hormones,[6] hyperinsulinemia and insulin-resistance[7] and enhanced sympathetic nervous system activity.[8] All these abnormalities occurred in subjects with central obesity more than in subjects with peripheral obesity.[9]

On the contrary, few studies have addressed the role of renal haemodynamics on obesity-induced hypertension.[10,11] This is very important since several data indicate that alterations in renal haemodynamics may be early detectable in hypertensive subjects or in prehypertensive conditions.[12-14]

This study was designed to evaluate renal haemodynamics and function in normotensive and hypertensive subjects with central obesity and without the major risk factors for cardiovascular diseases. Our final goal was to analyze the role of renal haemodynmics and plasma renin activity on the obesity-induced hypertension. For this reason data on central obese subjects were compared with those detectable

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in lean controls and in obese subjects with peripheral fat distribution.

Subjects and methods

Study groups

A total of 64 consecutive obese subjects (43 normotensives and 21 hypertensives) with central or peripheral body fat distribution, younger than 40 years, were studied. Twenty lean normotensives matched for age were also included in the study.

Obese subjects were recruited from the obese population attending the obesity center of the Internal Medicine Department at the University of Palermo (Italy). Obese subjects were totally unselected as far as degree of obesity, body fat distribution, glucose tolerance, blood pressure, and other cardiovascular risk factors were evaluated.[15]

Lean normotensives were volunteer subjects by us recruited to undergo a clinical checkup and found to be healthy.

The subjects were defined as obese on the basis of sex specific 85th percentile of BMI values as reported in the Italian Consensus Conference on Obesity.[16] In view of this, the men with BMI higher than 30.5 kg/m^2 and the women with BMI higher than 27.3 kg/m^2 were considered obese. On the contrary, the men with BMI less than 25 kg/m^2 and the women with BMI less than 24.7 kg/m^2 were considered lean.

Central fat distribution was defined on the basis of sex-specific 85th percentile of waist to hip ratio (WHR). The cut-off value of central obesity was considered ≥ 0.81 for women and ≥ 0.92 for men.[16]

Exclusion criteria included severe hypertension, cardiovascular diseases, left ventricular hypertrophy, renal disease and renal failure (serum creatinine >110 μmol/L), insulin dependent or independent diabetes mellitus, hyperlipoproteinemia, electrolyte imbalances, smoking habit and alcoholism or psychiatric problems. In addition, to eliminate the known influence of family history of hypertension on renal hemodynamics and function, lean and obese normotensives with positive family history of hypertension were also excluded.

All the subjects included in this study were subdivided as follows:

Lean normotensives: This group consisted of subjects (ten males and ten females) aged 27 to 38 years (mean age 35 ± 6) with BMI mean value of 22 ± 2 kg/m^2 and WHR mean value of 0.87 ± 0.007 (males 0.91 ± 0.01; females 0.80 ± 0.01).

Obese subjects with peripheral fat distribution: This group consisted of 18 normotensive subjects (eight males and ten females) aged 31–39 years (mean age 35 ± 4) with BMI mean value of 34 ± 4 kg/m^2 and WHR mean value of 0.85 ± 0.04 (males 0.89 ± 0.03, females 0.80 ± 0.02), and ten hypertensive subjects (four males and six females) aged 31 to 38 years (mean age 35 ± 3) with BMI mean value of 34 ± 3 kg/m^2 and WHR mean value of 0.84 ± 0.05 (males 0.99 ± 0.03; females 0.79 ± 0.02).

Obese subjects with central fat distribution: This group consisted of 25 normotensive subjects (11 males and 14 females) aged 29 to 39 years (mean age 33 ± 6) with BMI mean value of 34 ± 4 kg/m^2 and WHR mean value of 0.95 ± 0.01 (males 0.99 ± 0.01; females 0.89 ± 0.02), and 11 hypertensive subjects (five men and six women) aged 25 to 39 years (mean age 37 ± 2) with BMI mean value of 34 ± 6 kg/m^2 and WHR mean value of 0.94 ± 0.05 (males 1.00 ± 0.04; females 0.88 ± 0.05). Hypertension was defined as blood pressure consistently higher than 140/90 mmHg, according to indications of JNC.[17]

Arterial blood pressure was measured with an appropriate large cuff in obese subjects.[15] Mean blood pressure (MBP) was calculated by the sum of diastolic blood pressure plus one third of pulse pressure.

All the patients were untreated for at least 4 weeks before the study and they maintained a normal sodium intake (120 mEq/day). In view of this all the subjects were advised to follow a computerized and no-added-salt diet. The good adhesion to dietetic regimen was controlled through periodical and randomized examination of urinary excretion of sodium. During this withdrawal period no significant changes in body weight were observed. Each patient gave informed consent after receiving a detailed description of the study procedure and the study was also approved by the Ethics Committee of our Institution.

Preliminary investigations included measurements of blood and urinary electrolytes, creatinine clearance, fasting blood sugar and oral glucose tolerance test, serum cholesterol, triglyceride levels and liver function tests.

Laboratory methods

Venous blood samples were drawn after an overnight fast to measure immunoreactive insulin (IRI), plasma renin activity (PRA) and plasma aldosterone (PA).

Insulin Immunoreactive insulin levels were determined by the radioimmunoassay double antibody method using a commercial kit (Sorin, Saluggia — Italy). Intraassay variation was 7.5% and interassay variation was 8%. Sensitivity for detection of insulin was 17 pmol/L.

Plasma renin activity and plasma aldosterone PRA and PA were measured by the radioimmunoassay (RIA) using a commercial kit (Sorin, Saluggia — Italy).

Intraassay variations were 5% for PRA and 9.5% for PA, whereas interassay variations were 7% for PRA and 11.2% for PA. Sensitivity of methods were 0.03 ng/(L·s) for PRA and 40 pmol/L for PA.

Urinary excretion of sodium and microalbuminuria To evaluate urinary excretion of sodium (NaU) and albumin (UAE) three consecutive 24h urine collections were used. NaU and UAE values were expressed as the mean value of the three determinations. Sodium levels in urine were measured by current ion selective electrode method (Beckman).

Microalbuminuria was measured through a double anti-

body radioimmunoassay method, using a commercial kit (Sclavo, Siena; Italy).

Renal haemodynamics Renal haemodynamics was evaluated by radionuclide study according to methods described by Schlegel[18] and by Gates and their colleagues.[19]

The methods utilized respectively for the measurement of effective renal plasma flow and glomerular filtration rate were based on the determination by scintillation Camera of the fraction of the injected dose of Tc–99m DTPA and ^{131}I Hippuran present in the kidneys 1–3 min after its administration according to the following procedure.

All the patients were well hydrated orally (10 ml/Kg, 1–2 h before the study). An 18 gauge cannula was placed into a right or left antecubital vein and 3 mCi of Tc-99m DTPA (freshly prepared from a constant source) followed at 15-min intervals by 250 μCi of ^{131}I-labelled sodium iodohippurate were injected. The injected dose was measured by counting the syringe on the gamma camera under standardized geometry (at 20 cm). Renal data acquisition was also performed with the computerized large field scintillation Camera (General Electric) with high resolution 1.5 inch parallel-hole collimator, with the patient in supine position over the camera. The data were recorded in computer memory every 15 sec during 10 min for Tc-99m DTPA and 20 min for ^{131}I hippuran. Data acquisition was initiated at the moment of injection and was analyzed at the end of the study, after outlining each kidney in a region of interest.

In practice, 3–4 min for each measurement is sufficient as described by Schlegel *et al.*[18] To calculate effective renal plasma flow and glomerular filtration rate the relative and fractional uptake were first determined by the computer then related to the clearance values; relative and fractional uptake were related to clearance value by the empiric regression equations previously reported.[18,19]

Using radionuclide techniques effective renal plasma flow (ERPF; ml/min), effective renal blood flow [ERBF = ERPF (1-haematocrit); ml/min], glomerular filtration rate (GFR; ml/min) and filtration fraction (FF = GFR/ERPF; %) were calculated. Renal vascular resistance (RVR) was also measured by the formula RVR = (MBP.60.1332)/ERBF (dynes.sec.cm^{-5}).

Noninvasive radionuclide technique gives a certain advantage in comparison with traditional method utilized in evaluating the ERPF or GFR. In fact, the isotopic methods can estimate GFR or ERPF without blood or urine sampling. These methods allow determination of these measurements separately for each kidney and derive values for global renal function.[20]

The accuracy and reliability of this technique in the evaluation of global renal function or unilateral kidney function have been well reported.[20] This method was currently utilized and validated in our laboratory.[21,22] In particular inulin clearance correlated with fractional uptake of 99m-Tc DTPA measured between 2 and 3 minutes after renal tracer appearance ($r = 0.89$; $P < 0.0001$); PAH clearance correlated with fractional kidney uptake of 131-I-Hippuran measured between 2 and 3 min after renal tracer appearance for both global and unilateral renal function ($r = 0.81$; $P < 0.0001$). Both correlations were found in 45 subjects with various levels of renal function, ranging from normal to anuric conditions. A good correlation was observed between inuline clearance and GFR calculated by Gate's formula ($r = 0.85$; $P < 0.0001$) for global renal function and between PAH clearance and ERPF measured by Schelegel's formula ($r = 0.83$; $P < 0.0001$) for global renal function.

The reproducibility of isotopic GFR ($r = 0.90$) and ERPF ($r = 0.92$) determination was excellent. No significant differences between the calculated lines and line of identity were observed. Finally, the reproducibility of the processing (kidney outlining and creation of background region of interest) by successive analysis of renal function was good ($r = 0.97$ for GFR and 0.94 for ERPF).

Echocardiography Two-dimensional and M-mode echocardiography examination was performed by an Esaote Biomedica computer-aided ultrasound system equipped with 2.5 and 3.5 MHz phased array transducers and a standard VHS video format was used to record it. Echocardiograms were analyzed by one reader without knowledge of both clinical data and the study group of each subject.

Left ventricular mass (LVM) and LVM indexed for body height (LVM/H) was calculated by echocardiographic findings, according to the Devereux method from necropsy validation studies.[23] Left ventricular hypertrophy (LVH) was assumed in the presence of LVM/H > 2 standard deviations of the sex specific mean of a group of 110 normotensive subjects without family history of hypertension providing the normal values for our laboratory (88 ± 16 g/m for men and 75 ± 14 g/m for women). Accordingly, patients were considered to have LVM when the LVM/H values were > 120 g/m for men and > 105 g/m for women.[24,25] Cardiac output (CO) was calculated by the formula stroke volume (SV) × HR. SV was automatically calculated by the formula CSA × FVI where CSA was aortic cross sectional area and FVI was flow velocity integral.[25]

Total peripheral resistances (TPR) were calculated by the formula MBP × 80 × 1332/CO and expressed as dynes × sec × cm^{-5}. Since cardiac output, TPR and RVR become expanded when corrected for body height and contracted when corrected for weight,[15,16] absolute values only were used in the present study.

Statistical analysis

Data are presented as mean value ± standard deviation. Differences between lean and obese groups were analyzed by one way analysis of variance and Student-Newman-Keuls post hoc test. Linear and multiple regression analyses were used to determine coefficients of correlation among BMI, WHR, cardiac output and measurements of renal haemodynamics.

In multiple regression analysis WHR, cardiac output, plasma renin activity and plasma insulin were independent variables. A P value lower than 0.05 was considered statistically significant.

Table 1 Details of obese and lean subjects

	Normotensives			*Hypertensives*	
	Lean	*OB–C*	*OB–P*	*OB–C*	*OB–P*
Cases n.	20	25	18	11	10
Gender (M/F)	10/10	11/14	8/10	5/6	4/6
Age (years)	35 ± 6	33 ± 6	35 ± 4	37 ± 2	35 ± 3
Height (cm)	166 ± 9	162 ± 8	163 ± 8	162 ± 9	162 ± 7
BMI (Kg/m^2)	22 ± 2	34 ± 4*	34 ± 4*	34 ± 6*	34 ± 3*
WHR (%)	0.87 ± 0.07	0.95 ± 0.01*a	0.85 ± 0.04	0.94 ± 0.05*a	0.84 ± 0.05
SBP (mmHg)	124 ± 4	126 ± 10	125 ± 8	160 ± 5*b	159 ± 4*b
DBP (mmHg)	78 ± 8	79 ± 9	78 ± 5	102 ± 5*b	100 ± 5*b
MBP (mmHg)	92.7 ± 6.9	94.9 ± 5.7	94 ± 6	121 ± 11*b	120 ± 7*b
HR (beats/min)	70 ± 4	72 ± 4	74 ± 4	76 ± 5	75 ± 3
CO (ml/min)	6792 ± 1050	7910 ± 1386*	8050 ± 800*	7874 ± 1076*	7950 ± 910*
TPR (dynes sec cm^{-5})	1093 ± 207	1012 ± 215	965 ± 100	1278 ± 300*ab	1005 ± 150*
LVM (g)	145 ± 32	171 ± 35*	170 ± 26*	217 ± 51*b	190 ± 30*
LVM/H (g)	87 ± 20	105 ± 21*	106 ± 21*	130 ± 33*b	117 ± 30*
IRI (pmol/l)	71 ± 22	120 ± 64*	105 ± 58	115 ± 70*	110 ± 44

OB -C = central obesity; OB-P = peripheral obesity; BMI = Body mass index; WHR = waist hip ratio; MBP = mean blood presszure; HR = heart rate; CO = cardiac output; TPR = total peripheral resistances; LVM = left ventricular mass; LVM/H = left ventricular mass/height; IRI = immunoreactive fasting insulin.
One way analysis of variance and Student-Newman-Keuls post-hoc test
** $P < 0.05$ vs lean;*
[a] $P < 0.05$ vs peripheral obese;
[b] $P < 0.05$ obese hypertensives vs obese normotensives.

Results

Characteristics of lean and obese groups

All the groups were comparable with regard to sex, age and height. Lean and obese normotensives and both obese hypertensive groups were also comparable with regard to systolic, diastolic and mean blood pressure. Central and peripheral obese groups were also comparable with regard to BMI. In addition WHR values were similar in normotensive and hypertensive obese groups with the same type of body fat distribution (Table 1).

CO, LVM and LVM/H were significantly ($P < 0.05$) higher in all the obese groups than lean controls. In addition, LVM and LVM/H were significantly ($P < 0.05$) higher in obese hypertensives than obese normotensives, either with central fat distribution. TPR values were significantly ($P < 0.05$) higher in central obese hypertensives than peripheral obese hypertensives and than central obese normotensives. Moreover, IRI levels were significantly higher in central obese subjects, both normotensives and hypertensives, than lean subjects (Table 1).

Renal haemodynamics and function

(1) *Obese vs lean subjects* ERBF and ERPF were significantly ($P < 0.05$) lower and PRA levels were significantly ($P < 0.05$) higher only in central obese subjects, both normotensives and hypertensives, than lean subjects. On the contrary, RVR were significantly ($P < 0.05$) higher in both obese hypertensives, and in central obese normotensives than lean normotensives. UAE were significantly ($P < 0.05$) higher in central normotensive and hypertensive obese groups than lean subjects. No significant change between normotensive obese subjects with peripheral fat distribution and lean controls were found (Table 2).

(2) *Obese hypertensives vs obese normotensives* RVR values were significantly ($P < 0.05$) higher in both obese hypertensive groups than comparable obese normotensives. The remaining renal haemodynamics parameters and BUN, creatinine, PRA and NaU/24h did not differ significantly between the two hypertensive obese groups and the two comparable normotensive obese groups (Table 2).

(3) *Central obese vs peripheral obese* PRA, RVR and UAE values were significantly ($P < 0.05$) higher and ERBF and ERPF were significantly lower ($P < 0.05$) in both central obese groups than comparable normotensive and hypertensive obese with peripheral fat distribution. BUN, Creatinine and NaU/24h did not differ between central and comparable peripheral obese groups (Table 2).

Correlations

In all the obese subjects, BMI and WHR correlated directly with CO (respectively, $r = 0.63$, $P < 0.001$; $r = 0.69$, $P < 0.001$). Moreover, in obese subjects with central fat distribution RVR correlated directly with PRA ($r = 0.60$; $P < 0.02$) and WHR ($r = 0.57$; $P < 0.02$).

Multiple regression analysis indicated that RVR increased significantly ($P < 0.05$) with WHR, and PRA but not with CO and IRI.

Table 2 Measurements of renal haemodynamics and function in obese and lean subjects

	Normotensives			*Hypertensives*	
	Lean	*OB–C*	*OB–P*	*OB–C*	*OB–P*
Cases n.	20	25	18	11	10
BUN (mmol/l)	12.2 ± 2.9	12.1 ± 2.5	12 ± 2.3	12.3 ± 2.2	12.1 ± 2
Creatinine (μmol/l)	72 ± 6	74 ± 5	75 ± 6	74 ± 4	75 ± 3
PRA (ng/[1.s])	0.42 ± 0.2	0.70 ± 0.2*a	0.50 ± 0.1	0.72 ± 0.1*a	0.45 ± 0.2
PA (pmol/l)	220 ± 26	232 ± 62	225 ± 40	240 ± 58	230 ± 50
GFR (ml/min)	120 ± 30	113 ± 20	110 ± 15	109 ± 14	110 ± 12
ERBF (ml/min)	1032 ± 145	906 ± 150*a	990 ± 120	833 ± 64*a	930 ± 44
ERPF (ml/min)	585 ± 108	507 ± 97*a	580 ± 90	474 ± 80*a	540 ± 30
RVR (dynes sec cm^{-5})	7468 ± 1782	8839 ± 1520*a	7588 ± 1430	12626 ± 3367*ab	10312 ± 1380 *b
FF (%)	22.4 ± 5.6	21.7 ± 4.5	19 ± 4.5	23.5 ± 3	20 ± 3
UAE (mg/24h)	19 ± 13	33 ± 18*a	20 ± 12	36 ± 14*a	22 ± 15
NaU/24h (mmol/24h)	127 ± 39	134 ± 10	130 ± 8	125 ± 31	131 ± 7

OB -C = central obesity; OB-P = peripheral obesity; BUN = blood urea nitrogen; PRA = plasma renin activity; PA = plasma aldosterone; GFR = glomerular filtration rate; ERBF = effective renal blood flow; ERPF = effective renal plasma flow; RVR = renal vascular resistances; FF = filtration fraction; UAE = urinary albumin excretion; NaU/24h = 24 hours urinary excretion of sodium.
One way analysis of variance and Student-Newman-Keuls post-hoc test
**P < 0.05 vs lean;*
[a]P < 0.05 vs peripheral obese;
[b]P < 0.05 obese hypertensives vs obese normotensives.

Discussion and conclusions

Analysis of renal haemodynamics change

This study indicates that changes in renal haemodynamics may be detectable in central and peripheral obese subjects compared to lean control group. They included reduced renal plasma and blood flow and increased renal vascular resistances. All these abnormalities were more evident in central than peripheral obese subjects and were detectable both in normotensive and in hypertensive subjects with body fat distribution of central type. They were associated with greater left ventricular mass, that however remained in the normal range, and with higher cardiac output.

These last three alterations have been well reported both in normotensive and hypertensive obese subjects.[5,10,11,15,25,26]

Few studies have addressed the relationship between obesity and regional haemodynamics.[10,11]

In the current study, decreases in renal plasma and blood flow and increases in renal vascular resistances occurred in normotensive and hypertensive subjects with central obesity, despite cardiac output was higher in obese than lean subjects. This has not been considered a surprising datum but it is possible to indicate that changes in renal haemodynamics differ from those occurring in central haemodynamics in obese humans with central body fat distribution. This study was not designed to explain the mechanisms responsible of this difference. Further investigations have to be pointed to analyze the influence of body fat distribution on regional haemodynamics in other vascular districts.

The detection of increased renal resistances and PRA values and decreased renal flow both in central obese hypertensives and in central obese normotensives might explain the higher susceptibility of these subjects to develop hypertension.

In fact, changes in renal blood flow have been recently reported in pre-hypertensive conditions. Studies of normotensive relatives of patients with essential hypertension indicated an increased renal vasoconstriction in response to mental stress and postural changes.[27,28] Moreover, an important recent European study of normotensive children of parents both of whom had well-established essential hypertension, in comparison with children with matched normotensive parents, showed reduced renal blood flow in the children of the hypertensive parents.[14] Reduced regional blood flow and enhanced responsiveness to angiotensin II have also been found in pre-hypertensive rat models.[29] In established hypertension, renal blood flow has long been known to be reduced with a relative preservation of glomerular filtration rate.[30,31]

Moreover, Hall *et al.*[10] have recently reported that marked sodium and water retention associated to obesity-induced hypertension are due to increased tubular reabsorption rather than renal vasoconstriction in dogs after 5 weeks of high-fat diet. Despite they found higher levels of PRA comparable to those reported in our central obese humans, renal flow increased in obese hypertensive dogs,[10] whereas it decreased in our obese population with central body fat distribution. It is possible to hypothesize that these differences might be related to the different experimental model. In fact the dogs studied by Hall developed acutely both obesity and hypertension and cannot be considered comparable with humans characterized by chronic obesity. This indication could also explain conflicting data reported on the renin levels in obese animals or in obese humans. In fact, Rocchini *et al.*[32] found no change in plasma renin activity in obese dogs, whereas Tuck *et al.*[33] reported that plasma renin activity was higher in obese than lean humans.

In addition, other data recently reported by Schmieder *et al.*[11] suggested no effect of obesity on the renal circulation in normotensive or hypertensive obese subjects, but they did not consider the influence of body fat distribution in their obese population.[11] This is a very important finding since it has been well demonstrated that central obesity is associated with hypertension, cardiovascular diseases, or with haemodynamic and metabolic disorders.[9,26]

Accordingly, it is hard to indicate that renal haemodynamics is not influenced by obesity unless body fat distribution is also measured.

Analysis of renal function

In this study indications of renal vasoconstriction associated to a maintained GFR may be recognized in normotensive and hypertensive obese subjects with central fat distribution. On the other hand, FF and UAE levels were higher, indicating an early impaired renal function in these subjects. On the contrary, these alterations were not detectable in obese normotensives and hypertensives with peripheral fat distribution.

The association of changes in renal haemodynamics and central obesity is further supported by multiple regression analysis, indicating that WHR and plasma renin activity remained the best predictors of RVR in central hypertensive and normotensive obese subjects even when fasting plasma insulin and cardiac output were considered. This finding might indicate that the kidney, more than central haemodynamics, has a pathophysiologic role in the developing of hypertension in the obese subjects with central fat distribution.

Central obesity as a prehypertensive condition

The mechanisms responsible for the decrease in renal blood flow and the increase in renal vascular resistance and PRA in normotensive and hypertensive subjects with central obesity are unknown, but some proves suggest that they may be genetically determined.[6,9,26,29,34]

In the present study, some characteristics of the normotensive subjects with central obesity i.e. greater left ventricular mass, higher PRA levels, renal vascular resistances and cardiac output and lower renal plasma and blood flow may be likewise to those found in normotensive sons of hypertensive parents that are well considered in a prehypertensive condition.[14,27,28,29] Our previous data indicated that altered responses of sodium regulating hormones to saline load may be detectable in normotensive obese subjects. They included delayed and reduced suppressions in PRA and plasma aldosterone and a lack of increase in ANF.[6] In addition these altered responses were not influenced by the presence of insulin resistance in obese subjects.[34] The inability to suppress angiotensin II levels appropriately during volume expansion may cause blood pressure to be very sodium sensitive, leading to a decreased slope of pressure natriuresis.[10] This observation is consistent with the finding that blood pressure is salt sensitive in obese subjects.[35]

Our results indicate that body fat distribution of central type, more than obesity of peripheral type, is associated to abnormalities in renal haemodynamics and function. Finally, these data are consistent with the indication that changes in renal haemodynamics take place at an early stage in obesity-associated hypertension. The mechanisms responsible of these changes have to be further investigated.

References

1 Chang BN, Perlman LV, Epstein FH. Overweight and hypertension: A review. *Circulation* 1969; **39**: 403–421.
2 Licata G, Corrao S, Parrinello G, Scaglione R. Obesity and cardiovascular disease. *Ann It Med Int* 1994; **9**: 29–32.
3 Kannel WB, Brand N, Skinner JJ, Dawber T, McNamara P. The relation of adiposity to blood pressure and development of hypertension. *Ann Int Med* 1967; **67**: 48–59.
4 Dustan HP. Mechanism of hypertension associated with obesity. *Ann Int Med* 1983; **98 (part II)**: 860–864.
5 Licata G, Scaglione R, Capuana G, Parrinello G, Di Vincenzo D, Mazzola G. Hypertension in obese subjects: distinct hypertensive subgroup. *J Hum Hypertens* 1990; **4**: 37–41.
6 Licata G, Volpe M, Scaglione R, Rubattu S. Salt regulating hormones in young obese subjects. Effects of saline load. *Hypertension* 1994; **23 (suppl. 1)**: 20–24.
7 Rocchini AP. Insulin resistance and blood pressure regulation in obese and non obese subjects. *Hypertension* 1991; **17**: 837–842.
8 Landsberg L, Young JB. The role of sympathoadrenal system in modulating energy expenditure. *Metabolism* 1984; **13**: 475–479.
9 Licata G, Scaglione R, Ganguzza A, Corrao S, Donatelli M, Parrinello G, *et al.* Central obesity and hypertension: relationship between fasting serum insulin, plasma renin activity and diastolic blood pressure in young obese subjects. *Am J Hypertens* 1994; **7**: 314–320.
10 Hall JE, Brands MW, Dixon WN, Smith MJ. Obesity-induced hypertension: renal function and systemic hemodynamics. *Hypertension* 1993; **22**: 292–299.
11 Schmieder RE, Messerli FH. Does obesity influence early target organ damage in hypertensive patients. *Circulation* 1993; **87**: 1482–1488.
12 Bianchi G, Cusi P, Gatti M, Lupi G, Ferrari P, Barlassina C *et al.* A renal abnormality as a possible cause of essential hypertension. *Lancet* 1979; **1**: 173–177.
13 Luke RG. Essential hypertension: a renal disease ? A review and update of the evidence. *Hypertension* 1993; **21**; 380–390.
14 Van Hooft IM, Grabbee DE, Derkx FHM, deLeeuw PW, Schalekamp MADG, Hofman A. Renal hemodynamics and the renin-angiotensin-aldosterone system in normotensive subjects with hypertensive and normotensive parents. *N Engl J Med* 1991; **324**: 1305–1311.
15 Licata G, Scaglione R, Barbagallo M, Parrinello G, Capuana G, Lipari R, *et al.* Effect of obesity on left ventricular function studied by radionuclide angiocardiography. *Int J Obesity* 1991; **15**: 295–302.
16 Crepaldi G, Belfiore S, Bosello O, Caviezzel F, Contaldo F, Enzi G, *et al.* Special report: Italian Consensus Conference-Overweight, Obesity and Health. *Int J Obesity* 1991; **15** 781–790.
17 The fifth report of the Joint National Committee on detection evaluation, and treatment of high blood pressure. *Arch In Med* 1993; **153**: 154–183.
18 Schlegel JU, Haway SA. Individual renal plasma flow determinations in two minutes. *J Urol* 1976; **III**: 282–288.
19 Gates GE. Glomerular filtration rate: estimation from fractional renal accumulation of ^{99m}Tc DTPA. *Am J Radiol* 1981; **138** 565–570.

20 Chachati A, Meyers A, Gordon JP, Rigo P. Rapid method for measurement of differential renal function: validation. *J Nucl Med* 1987; **28**: 829–836.
21 Scaglione R, Indovina A, Parrinello G, Lipari R, Mu-le' LG *et al.* Antihypertensive efficacy and effects of nitrendipine on cardiac and renal haemodynamics in mild to moderate hypertensive patients: randomized controlled study versus hydrochlorothiazide. *Cardiovasc Drugs Ther* 1992; **6**: 141–146.
22 Licata G, Scaglione R, Ganguzza A, Parrinello G, Costa R, Merlino G, *et al.* Effect of amlodipine on renal haemodynamics in mild to moderate hypertensive patients. A randomized controlled study versus placebo. *Eur J Clin Pharmacol* 1993; **45**: 307–311.
23 Devereux RB, Alonso DR, Lutes EM, Gottlieb GJ, Campo E, Sach I. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986; **57**: 450–458.
24 Licata G, Scaglione R, Parrinello G, Corrao S. Rapid left ventricular filling in untreated hypertensive subjects with or without left ventricular hypertrophy. *Chest* 1992; **102**: 1507–1511.
25 Corrao S, Parrinello G, Arnone S, Indovina A, Scaglione R, Licata G. Influence of obesity on the echocardiographic evaluation of left ventricular ejection fraction by area-length method: comparison with radionuclide angiography. *J Cardiovasc Diagn Proc* 1993; **11**: 127–134.
26 Jern S, Bergbrant A, Bjorntorp P, Hanson L. Relation of central haemodynamics to obesity and body fat distribution. *Hypertension* 1992; **19**: 520–527.
27 Hollenberg NK, Williams GH, Adams DF. Essential hypertension abnormal renal vascular and endocrine responses to a mild psychological stimulus. *Hypertension* 1981; **3**: 11–17.
28 Lawton WJ, Sinkey CA, Fitz AE, Mark AL: Dietary salt produces abnormal renal vasoconstrictor responses to upright posture in borderline hypertensive subjects. *Hypertension* 1988; **11**: 529–536.
29 Arendshorst WJ, Chatziantoniou C, Daniels F. Role of angiotensin in the renal vasoconstriction observed during the development of genetic hypertension. *Kidney Int* 1990; **38 (suppl. 30)**: s92–s96.
30 Hollemberg NK, Boruchi LJ, Adams DF. The renal vasculature in early essential hypertension: evidence for a pathogenetic role. *Medicine* 1978; **57**: 167–178.
31 Guyton AC: Circulatory Physiology III: arterial pressure and hypertension. Philadelphia, Pa, WB Saunders Co, 1980, pp 1–553.
32 Rocchini AP, Moorehead CP, DeRemer S, Bondi D. Pathogenesis of weight related changes in blood pressure in dogs. *Hypertension* 1989; **13**: 922–928.
33 Tuck ML, Sowers J, Dornfield L, Kledzik G, Maxwell M. The effect of weight reduction on blood pressure, plasma renin activity, and plasma aldosterone levels in obese patients. *N Engl J Med* 1981; **304**: 930–933.
34 Scaglione R, Corrao S, Amato P, Parrinello G, Ganguzza A. Dichiara MA, *et al.* Effects of insulin resistance on salt regulating hormone responses to saline load in young obese subjects (abs). *Am J Hypertens* 1994; **7**: 75A.
35 Rocchini AP, Key J, Bondi D, Chico R, Moorehead C, Katch V *et al.* Effect of weight loss on the sensitivity of blood pressure to sodium in obese adolescents. *N Engl J Med* 1989; **321**: 580–585.