Visceral adiposity and arterial stiffness: echocardiographic epicardial fat thickness reflects, better than waist circumference, carotid arterial stiffness in a large population of hypertensives

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Aims Relationship between obesity and cardiovascular (CV) disease depends not only on the amount of body fat, but also on its distribution. For example, individuals with increased fat accumulation in the abdominal region have atherogenic lipid profiles and are at increased CV risk. The loss of elasticity in medium and large arteries is an early manifestation of atherosclerosis. The aim of this study was to evaluate whether echocardiographic epicardial adipose tissue, an index of cardiac adiposity, is related to carotid stiffness and carotid intima-media thickness (IMT), indexes of subclinical atherosclerosis, better than waist circumference in hypertensive patients.

Methods and results We studied 459 patients with Grade I and II essential hypertension who were referred to our outpatient clinic over a period from May 2007 to March 2008. The population was first sorted by waist circumference and then by epicardial fat thickness ≥ 7 mm or < 7 mm. We measured epicardial fat thickness, waist circumference, carotid artery stiffness, and carotid IMT in all patients. Patients divided according to waist circumference showed no statistical differences in carotid artery stiffness between the two groups. Subjects with epicardial fat thickness ≥ 7 mm were older, had higher systolic, diastolic, and pulse pressure, increased left ventricular mass index, carotid IMT, diastolic parameters, and stiffness parameters compared with those with epicardial fat thickness < 7 mm (P < 0.001). A positive correlation was found between epicardial fat and age, pulse pressure, stiffness parameters, carotid IMT, systolic blood pressure, and duration of hypertension, and a negative correlation was found with diastolic parameters. Age, carotid IMT, and stiffness parameters were independently related to epicardial fat. Conclusion Our findings indicate that epicardial fat reflects carotid artery stiffness in hypertension-induced organ damage.

Key points

- Aims: Relationship between obesity and cardiovascular (CV) disease depends not only on the amount of body fat, but also on its distribution. For example, individuals with increased fat accumulation in the abdominal region have atherogenic lipid profiles and are at increased CV risk.
- Methods and results: We studied 459 patients with Grade I and II essential hypertension who were referred to our outpatient clinic over a period from May 2007 to March 2008. The population was first sorted by waist circumference and then by epicardial fat thickness ≥ 7 mm or < 7 mm. We measured epicardial fat thickness, waist circumference, carotid artery stiffness, and carotid IMT in all patients. Patients divided according to waist circumference showed no statistical differences in carotid artery stiffness between the two groups. Subjects with epicardial fat thickness ≥ 7 mm were older, had higher systolic, diastolic, and pulse pressure, increased left ventricular mass index, carotid IMT, diastolic parameters, and stiffness parameters compared with those with epicardial fat thickness < 7 mm (P < 0.001). A positive correlation was found between epicardial fat and age, pulse pressure, stiffness parameters, carotid IMT, systolic blood pressure, and duration of hypertension, and a negative correlation was found with diastolic parameters. Age, carotid IMT, and stiffness parameters were independently related to epicardial fat.
- Conclusion: Our findings indicate that epicardial fat reflects carotid artery stiffness in hypertension-induced organ damage.

Introduction

Obesity is a major public health issue, with a rapidly increasing prevalence.1 Obese people, defined on the basis of high body mass index (BMI), have a much greater risk of developing myocardial infarction and stroke than subjects with normal levels of total body fatness.2 The relationship between obesity and cardiovascular (CV) disease depends not only on the amount of body fat, but also on its distribution. For example, individuals with increased fat accumulation in the abdominal region have atherogenic lipid profiles and are at increased CV risk.3,4

Epicardial fat thickness (EFT) is clinically related to abdominal visceral adiposity,5 coronary artery disease,6 subclinical atherosclerosis,7 cardiac morphology,8 metabolic syndrome,9 and also visceral fat changes during weight loss intervention.10 Furthermore, epicardial fat is a metabolically active organ and source of several bioactive adipokines.11

The loss of elasticity in medium and large arteries is an early manifestation of atherosclerosis.12–14 Increased stiffness has long been considered intrinsic to the ageing process of the arterial wall.15–17 However, there is evidence...
that, regardless of age, arterial stiffness is associated with a variety of vascular risk factors such as hypertension, diabetes, and cigarette smoking.16–20 Data suggest that arterial stiffness is independently associated with increased risk of ischaemic stroke and CV mortality.12 The relationship of echocardiographic epicardial fat with carotid arterial stiffness is unexplored.

The aim of this study was to evaluate whether echocardiographic, EEF, an index of cardiac adiposity, is related to carotid stiffness and carotid intima-media thickness (IMT), indexes of subclinical atherosclerosis, better than waist circumference in hypertensive patients.

**Methods**

**Patients**

We studied 459 patients with Grade I and II essential hypertension who were referred to our outpatient clinic over a period from May 2007 to March 2008. Patient histories were taken and each had a complete physical examination. The diagnosis of hypertension was considered when systolic blood pressure (SBP) was >140 mmHg and/or diastolic blood pressure (DBP) >90 mmHg on at least three visits, or when antihypertensive therapy was present. Blood pressure was measured by mercury sphygmomanometer with an appropriate size rubber cuff applied around the non-dominant arm. Readings were based on Korotkoff’s first- and fifth-phase sounds. During each visit, three consecutive BP readings were obtained with the subject in the sitting position after a rest of at least 10 min. The average of the three readings was used for the analyses, rounded to the nearest 2 mm on the scale. Measurements were performed early in the morning and carried out by a trained investigator. We also determined lipid profile, creatinine, and fasting plasma glucose by standard laboratory methods. Moreover, the concentration of hs-C-reactive protein was measured by an ultrasensitive competitive immunoassay. Patients with a diagnosis of secondary hypertension, end-stage renal disease, diabetes mellitus, atrial fibrillation, severe valvular heart disease, or a poor quality of the echocardiographic or carotid ultrasonographic tracing were excluded from the study. Before the investigation, all drugs were discontinued, under medical supervision, for at least 1 week. Of the 459 patients, 30% were previously treated for hypertension and only 5% for dyslipidaemia. The most frequent classes of antihypertensive drugs used were angiotensin-converting enzyme inhibitors, calcium antagonists, and diuretics; for the 23 patients with hypercholesterolaemia, atorvastatin or simvastatin was used. All patients underwent the following clinical and instrumental procedures.

**Anthropometric measurements**

Weight (to the nearest 0.1 kg) and height (to the nearest 0.5 cm) were measured while the subjects were fasting and wearing only their undergarments. Body mass index was calculated as body weight divided by height squared and was used as a marker of obesity degree. Minimum waist circumference (in centimetres) (minimum circumference between the lower rib margin and the iliac crest, midwaist) and maximum hip circumference (in centimetres) (the widest diameter over the greater trochanters) were measured while the subjects were standing with their heels together. We used waist circumference (>88 cm in women and >102 cm in men) as the threshold of predominant truncal/abdominal fat distribution.21 Subjects were subdivided, according to waist circumference, into those with predominant visceral fat accumulation and with predominant peripheral fat accumulation.

**Carotid ultrasonography**

Ultrasound examination of the carotid arteries was performed with a transducer frequency of 7.5 MHz. Measurements involved a primary transverse and longitudinal scanning of the common carotid artery, bifurcation, and internal carotid. The IMT was measured on the far wall at 1 cm from bifurcation of the common carotid artery as the distance between the lumen-intima interface and the media-adventitia interface. All measurements were made at a plaque-free site. Near and far walls of carotid arteries were scanned longitudinally and transversally for plaques. Plaques were defined as a focal echogenic wall thickening that encroached on the arterial lumen, with a minimal IMT > 1.3, or as the presence of calcification.

**Carotid artery stiffness**

Subjects were studied after resting supine for 15 min in a temperature-controlled environment. The stiffness parameter \(\beta\) was calculated according to the formula:

\[
\beta = \ln(Ps/Pd)/(Ds − Dd/Dd);
\]

where Ps and Pd are systolic and diastolic blood pressure in the brachial artery measured by an automated sphygmomanometer (Omron 705CP, Tokyo, Japan), and Ds and Dd are the maximal and minimal diameters of the right common carotid artery measured by e-tracking (ultrasonic high resolution wall tracking Aloka 410, Tokyo, Japan; 7.5 MHz linear array probe).

Adjustable gates were positioned at the junctions of the intima and media, and diameter was calculated and displayed in real time as the difference between the displacement waveforms of the anterior and posterior walls. Measurements were taken as a mean of five beats; \(\beta\) was log transformed for analyses, because its distribution was skewed.

**Echocardiography**

The M-mode echocardiogram was performed with using 3.5 MHz phased array, placed on the III–IV left intercostal space along the parasternal line, with patients supine, in left lateral decubitus and the head of the bed kept at 30°. The end-diastolic measurements of left ventricular internal dimension, left interventricular septum, and posterior wall thickness at the QRS peak using the Penn convention were measured. The left ventricular mass was calculated according to the Devereux formula. Patients with a left ventricular mass index (LVMI) > 125 g/m² in men, and >110 g/m² in women were classified as having left ventricular hypertrophy. Complete two-dimensional echocardiograms were obtained during normal respiration.

**Epicardial fat measurement**

We measured EEF on the free wall of the right ventricle from the parasternal long-axis views. Epicardial fat was identified as an echo-free space in the pericardial layers on the two-dimensional echocardiography, and its thickness was measured perpendicularly on the free wall of the right ventricle at end-diastole for three cardiac cycles. To standardize the measuring point between different observers, we used the aortic annulus as anatomical reference. The measurement was performed at a point on the free wall of the right ventricle along the midline of the ultrasound beam, perpendicular to the aortic annulus. The average reading from three cardiac cycles for each echocardiographic view was used for the statistical analysis. Echocardiographic images were recorded onto a computerized database. The offline measurement of EEF was performed by two cardiologists who were unaware of the clinical data. The intra- and inter-observer correlation coefficient was 0.96 and 0.93, indicating good reproducibility and reliability.
Based on the mean and distribution of epicardial fat in 50 normal volunteers (mean age 56 ± 10), the normal upper limit was found to be 7 mm.

Diastolic function assessment

The pulsed Doppler sample volume was placed at the mitral valve tips and 5–10 cardiac cycles were recorded from the apical window at a velocity of 100 mm/s. The following measurements of left ventricular diastolic function were determined: early diastolic (E) and late atrial (A) peak velocities (m/s), and their ratio, and E-wave deceleration time (ms). The Doppler tissue imaging (DTI) programme was set to the pulsed-wave Doppler mode. Filters were set to exclude high frequency signals, the Nyquist limit was adjusted to a velocity range of 15–20 cm/s, and gains were minimized to allow for a clear tissue signal with minimal background noise. All DTI recordings were obtained during normal respiration. A 5 mm sample volume was placed at the apical four-chamber view on the lateral corner of the mitral annulus. The resulting velocities were recorded for 5–10 cardiac cycles at a sweep speed of 100 mm/s. The following measurements were determined as diastolic indexes: myocardial early (Eₘ) and atrial (Aₘ) peak velocities (m/s) and their ratio.

Statistical analysis

Continuous variables are expressed as means ± SD and discrete variables as counts and percentages. All statistical analyses were performed using GB-STAT version 6.50 (Dynamic Microsystems, Inc., Silver Spring, MD, USA). Differences between the two groups were assessed using Student’s t-test for unpaired data. Comparison of categorical data were made using Fisher’s exact test. The Pearson correlation coefficient was calculated to investigate the linear relationship between variables. Stepwise forward regression analysis was performed to assess which factors independently influence arterial stiffness, carotid IMT, and epicardial fat. Variables selected for inclusion in the models were those significant at univariate analysis. The P < 0.05 was considered statistically significant. κ-statistic was used to assess inter- and intra-reader variability for echocardiographic and ultrasonographic parameters.

Results

Table 1 shows the demographic and clinical characteristics distinguishing the population studied. Of the 459 subjects studied, 59% (270 patients) were males. Their mean age was 54 ± 11 (range 22–91 years), 24% were current smokers. The population was divided by waist circumference (Table 2). Subjects with abdominal fat were older, had higher systolic and pulse pressure compared with those with peripheral fat (P < 0.001). In these two groups, there were no significant differences in fasting plasma glucose, total cholesterol, HDL cholesterol, serum creatinine, and hs-C-reactive protein. While smoking habit was significantly different between groups (P < 0.05).

The population was divided by EEF (Table 3). The characteristics of patients divided by EEF show a significant difference in stiffness parameters. Subjects with EEF > 7 mm were older, had higher systolic, diastolic, and pulse pressure compared with those with EEF ≤ 7 mm (P < 0.001). In these two groups, there were no significant differences in fasting plasma glucose, total cholesterol, HDL cholesterol, and serum creatinine. While smoking habit was significantly different between groups (P ≤ 0.05), and hs-C-reactive protein had significantly higher concentrations in patients with EEF > 7 mm (P < 0.0001).

Patients with EEF > 7 mm showed a significantly increased LVMI and carotid IMT (P < 0.001). Moreover, there were significant differences in all diastolic and stiffness parameters (Table 3). These parameters showed a high stiffness and left ventricular diastolic dysfunction in patients with EEF > 7. A strong positive correlation was found (Figures 1 and 2) between EEF and β stiffness parameter (r = 0.59, P < 0.0001) and carotid IMT (r = 0.44, P < 0.0001). A weak positive correlation was found between EEF and Ep (r = 0.37, P < 0.0001), SBP (r = 0.35, P < 0.0001), and duration of hypertension (r = 0.33, P < 0.001). Furthermore, EEF was negatively correlated with diastolic parameters (E/A: r = −0.29, Eₘ/Aₘ; r = −0.32, P < 0.0001) and AC (r = 0.33, P < 0.001). A low positive correlation was found between EEF and E-wave deceleration time (r = 0.17, P < 0.01), and a low negative correlation with DBP (r = −0.13, P < 0.01). Stepwise forward regression analysis was performed with EEF as a dependent variable and with age, SBP, DBP, pulse pressure, carotid IMT, LVMI, E-wave deceleration time, E/A and Eₘ/Aₘ ratios, and stiffness parameters as independent variables. As shown in Table 4, carotid IMT, age, pulse pressure, and β stiffness parameter were independently related to EEF. Moreover, stepwise forward regression analysis was performed with carotid IMT as a dependent variable and with age, SBP, DBP, pulse pressure, EEF, LVMI, E-wave deceleration time, E/A and Eₘ/Aₘ ratios, and stiffness parameters as independent variables; only age, β stiffness parameter, and pulse pressure were independently related to carotid IMT. Stepwise forward regression analysis was performed with β stiffness parameter as a dependent variable and with age, SBP, DBP, pulse pressure, EEF, LVMI, E-wave deceleration time, E/A and Eₘ/Aₘ ratios, and stiffness parameters as independent variables; only age, EEF, and carotid IMT were independently related to β stiffness parameter. The inter- and intra-reader variability was good (κ > 0.75).

Table 1 Characteristics of patients at admission (n = 459)

| Characteristic                  | Mean ± SD  |
|--------------------------------|------------|
| Age (years)                    | 54 ± 11    |
| Male (%)                       | 59         |
| Body mass index (kg/m²)        | 28 ± 4     |
| Smokers (%)                    | 24         |
| Duration of hypertension (years)| 7 ± 6    |
| Systolic blood pressure (mmHg) | 148 ± 14   |
| Diastolic blood pressure (mmHg)| 95 ± 7     |
| Pulse pressure (mmHg)          | 55 ± 5     |
| Heart rate (bpm)               | 73 ± 11    |
| Fasting plasma glucose (mg/dL) | 95 ± 12    |
| Total cholesterol (mg/dL)      | 204 ± 35   |
| HDL cholesterol (mg/dL)        | 49 ± 12    |
| Triglycerides (mg/dL)          | 131 ± 57   |
| Serum creatinine (mg/dL)       | 0.93 ± 0.2 |
| hs-C-reactive protein (mg/L)   | 2.0 ± 1.9  |
| β                              | 9.4 ± 2    |
| Pressure-strain elasticity modulus (kPa) | 112 ± 25  |
| Arterial compliance (mm²/kPa)  | 0.9 ± 0.05 |
| Left ventricular mass index (g/m²) | 110 ± 22 |
| Carotid intima-media thickness (mm) | 0.74 ± 0.2 |
| E/A ratio                      | 0.88 ± 0.41|
| Eₘ/Aₘ ratio                    | 0.98 ± 0.35|
Discussion

Cardiovascular risk assessment is a fundamental step in the management of hypertensive patients, while it is not difficult to determine the degree of hypertension and co-existing risk factors. This is not the same for target organ damage (TOD). In fact, TOD is a debated issue, since it strongly influences the clinical assessment, but is difficult to detect and classify. It also depends on the diagnostic test chosen. Our study showed that patients with EEF > 7 mm exhibited higher LVMI, diastolic dysfunction, and increased carotid stiffness and IMT, which correlated with the severity of EEF; whereas no significant differences were found when patients were divided according to waist circumference value. These results raise the question of the most sensitive and reliable indicator of TOD. The development of new, non-invasive tools for the detection of subclinical atherosclerosis, e.g. carotid IMT and measurement of carotid stiffness,

Table 2 Characteristics of patients divided by waist circumference

|                        | Peripheral fat (n = 270) | Visceral fat (n = 189) | P-value |
|------------------------|--------------------------|------------------------|---------|
| Age (years)            | 54 ± 12                  | 59 ± 9                 | 0.001   |
| Male (%)               | 65                       | 50                     | NS      |
| Body mass index (kg/m²) | 28 ± 4                   | 28 ± 3                 | NS      |
| Smokers (%)            | 30                       | 15                     | 0.05    |
| Duration of hypertension (years) | 6 ± 6                  | 7 ± 5                  | NS      |
| Systolic blood pressure (mmHg) | 146 ± 14               | 149 ± 14               | 0.02    |
| Diastolic blood pressure (mmHg) | 95 ± 7                | 96 ± 8                 | 0.005   |
| Pulse pressure (mmHg)  | 53 ± 5                   | 52 ± 7                 | NS      |
| Heart rate (bpm)       | 74 ± 11                  | 73 ± 10                | NS      |
| Fasting plasma glucose (mg/dL) | 94 ± 12                | 95 ± 11                | NS      |
| Total cholesterol (mg/dL) | 204 ± 36               | 206 ± 33               | NS      |
| HDL cholesterol (mg/dL) | 49 ± 11                 | 48 ± 12                | NS      |
| Triglycerides (mg/dL)  | 126 ± 59                 | 132 ± 56               | NS      |
| Serum creatinine (mg/dL) | 0.93 ± 0.2              | 0.92 ± 0.2             | NS      |
| hs-C-reactive protein (mg/L) | 1.8 ± 1.14            | 2.0 ± 1.84             | NS      |
| β                      | 9.5 ± 2                  | 9.2 ± 2                | NS      |
| Pressure-strain elasticity modulus (kPa) | 111 ± 26              | 114 ± 22               | NS      |
| Arterial compliance (mm²/kPa) | 0.9 ± 0.04             | 0.9 ± 0.03             | NS      |
| Left ventricular mass index (g/m²) | 109 ± 22               | 111 ± 22               | NS      |
| Carotid intima-media thickness (mm) | 0.75 ± 0.2            | 0.73 ± 0.2             | NS      |
| E/A ratio              | 0.89 ± 0.38              | 0.87 ± 0.28            | NS      |
| Eₘ/Aₘ ratio           | 0.99 ± 0.42              | 0.97 ± 0.38            | NS      |

Table 3 Characteristics of patients divided by epicardial fat

|                        | Epicardial fat (n = 360) ≤ 7 | Epicardial fat (n = 99) > 7 | P-value |
|------------------------|-------------------------------|----------------------------|---------|
| Age (years)            | 52 ± 10                       | 63 ± 8                     | 0.001   |
| Male (%)               | 64                            | 40                         | 0.03    |
| Body mass index (kg/m²) | 28 ± 0.3                     | 28 ± 4                     | NS      |
| Smokers (%)            | 28                            | 10                         | 0.05    |
| Duration of hypertension (years) | 6 ± 5                       | 8 ± 7                      | 0.01    |
| Systolic blood pressure (mmHg) | 146 ± 13                    | 150 ± 15                   | 0.01    |
| Diastolic blood pressure (mmHg) | 95 ± 7                     | 93 ± 7                     | 0.01    |
| Pulse pressure (mmHg)  | 51 ± 6                       | 57 ± 8                     | 0.001   |
| Heart rate (bpm)       | 73 ± 11                      | 72 ± 10                    | NS      |
| Fasting plasma glucose (mg/dL) | 93 ± 11                   | 94 ± 10                    | NS      |
| Total cholesterol (mg/dL) | 202 ± 35                    | 209 ± 36                   | NS      |
| HDL cholesterol (mg/dL) | 49 ± 11                      | 48 ± 11                    | NS      |
| Triglycerides (mg/dL)  | 127 ± 57                     | 139 ± 59                   | NS      |
| Serum creatinine (mg/dL) | 0.92 ± 0.2                 | 0.93 ± 0.2                 | NS      |
| hs-C-reactive protein (mg/L) | 1.7 ± 1.15                 | 2.2 ± 1.64                 | 0.0001  |
| β                      | 8.3 ± 2                      | 10.3 ± 2                   | 0.0001  |
| Pressure-strain elasticity modulus (kPa) | 108 ± 25                | 118 ± 25                   | 0.001   |
| Arterial compliance (mm²/kPa) | 0.8 ± 0.05                 | 0.9 ± 0.02                 | 0.001   |
| Left ventricular mass index (g/m²) | 107 ± 21                   | 119 ± 24                   | 0.001   |
| Carotid intima-media thickness (mm) | 0.70 ± 0.2                | 0.84 ± 0.2                 | 0.001   |
| E/A ratio              | 0.98 ± 0.37                  | 0.85 ± 0.22                | 0.001   |
| Eₘ/Aₘ ratio           | 0.99 ± 0.43                  | 0.86 ± 0.31                | 0.005   |
has opened up a new avenue for CV research and clinical cardiology practice. Our findings confirm, in part, observations, obtained in different clinical settings. To the best of our knowledge, this is the first evaluation of the influence of epicardial fat on carotid stiffness in patients with essential hypertension. Our study is the first to identify a strong association between EEF and carotid stiffness in a group of hypertensive patients.

Various methods to quantify visceral adipose tissue directly by expensive magnetic resonance imaging and radiation-exposing computed tomography, as well as indirectly by anthropometric measures (e.g. waist circumference, BMI), exist. Magnetic resonance imaging is the gold standard technique to accurately measure visceral adiposity, although there is some concern about the accuracy of actual visceral adiposity content based on single slice sampling (i.e. whole body magnetic resonance imaging scan is the true gold standard). Waist circumference as a measure of visceral obesity may be less reliable in older persons. Body mass index, an anthropometric measure of visceral adiposity is considered a poorer indicator of CV risk than waist circumference across ethnicities, suggesting that BMI may not be a very good measure of visceral obesity. In light of the limitations, lack of practicality of existing methods and the recognition that more reliable measures of visceral adiposity are needed, and Iacobellis et al. proposed the direct measurement of epicardial adipose tissue thickness via echocardiography as a marker for visceral adiposity.

Increased aortic stiffness has been shown to be more related to body fat repartition (assessed by waist circumference) and visceral adiposity than to increased BMI. The pathophysiology that links abdominal adiposity to stiffening is still largely unknown. Visceral adipocytes have an elevated lipolytic activity that results in increased free fatty acid release in the portal vein with an accumulation (liver, pancreas, and muscles) that contributes to insulin resistance. Furthermore, other mechanisms could be involved, such as increases in circulating proinflammatory cytokines or leptin. In the present study, hypertensive patients with EEF presented higher serum hs-C-reactive protein levels than hypertensive patients with lower EEF. It has also been proposed that an increase in circulating proinflammatory cytokines may contribute to the development of CV disease in obese individuals. Furthermore, a recent study supported the hypothesis that epicardial adipose tissue, expression of adiponectin, is actively implicated in global CV risk, describing its association with hypertension.

The pathophysiology that links aortic stiffness to CV morbidity and mortality in hypertensive subjects may be associated with the reduced compliance of the large arteries that modifies the timing of wave reflections and thus determines ventricular load. The net effect of these hemodynamic changes may be ischaemia, particularly in the subendocardium, which, if chronic, is associated with interstitial fibrosis and the development of heart failure. Because atherosclerosis is characterized by a long asymptomatic phase, therapy initiated before complications could effectively reduce the risk of a first event such as a cerebro-CV disturbance. The aim of preventive medicine must be to optimize the detection and treatment of individuals who are clearly at risk from a myocardial infarction or other CV complication. Since hypertension and other traditional risk factors have limited predictive value, recent technologic progress now allows the diagnosis of early disease. A two-stage preventive strategy can be proposed: screening for traditional risk factors, followed by investigation of pre-clinical atherosclerosis. In fact, the traditional primary preventive screening for risk factors discovers many individuals who have no vascular precursors of atherosclerosis and excludes many individuals destined to develop progressive atherosclerosis. In this context, our method
could be a good start for the very first selection of those patients with CV risk factors to be sent to more complex tests. It provides an opportunity to evaluate large patient populations in a non-invasive fashion and may be useful in avoiding unnecessary exams.

The echocardiographic assessment of epicardial fat may also have the potential to be a simple and reliable marker of atherosclerosis and increased CV risk. Because echocardiography is likely to be routinely performed in hypertensive patients, this measure may be readily available at no extra cost.

Conflict of interest: none declared.

References

1. Beer-Borst S, Morabia A, Hercberg S, Vitez O, Bernstein MS, Galan P et al. Obesity and other health determinants across Europe: the EURLIM project. J Epidemiol Community Health 2000;54:424–30.
2. Hubert HB, Feinleib M, Mchamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968–77.
3. Lapidus L, Bengsson C, Larsson B, Pennert K, Rybo E, Sjostrom L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12-year follow-up of participants in the population study of women in Gothenberg, Sweden. Br Med J 1984;289:1257–61.
4. Ruxrude KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ et al. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280:1843–8.
5. Iacobellis G, Assael F, Ribaudo MC, Zappaterreno A, Alessi G, Di Mauro U et al. Epicardial fat from echocardiography: a new method for visceral adipose tissue assessment. J Endocrinol Invest 2008;31:330–40.
6. Jeong JW, Jeong MH, Yun KH, Oh SK, Park EM, Kim YK et al. Echocardiographic epicardial fat thickness and coronary artery disease. Circ J 2007;71:536–9.
7. Iacobellis G, Pellicelli AM, Sharma AM, Grisorio B, Barbarini G, Barbaro G. Relation of subepicardial adipose tissue to carotid intima-media thickness in patients with human immunodeficiency virus. Am J Cardiol 2007;99:1470-2.
8. Iacobellis G, Ribaudo MC, Zappaterreno A, Iannucci CV, Leonetti F. Relation between epicardial adipose tissue and left ventricular mass. Am J Cardiol 2004;94:1084–7.
9. Iacobellis G, Ribaudo MC, Assael F, Vecchi E, Tiberti C, Zappaterreno A et al. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. J Clin Endocrinol Metab 2003;88:5163–8.
10. Willens HJ, Byers P, Chirinos JA, Labrador E, Hare JM, de Marchena E. Is it possible to derive a reliable estimate of human visceral and subcutaneous abdominal adipose tissue from simple anthropometric measurements? Metabolism 1995;44:1617–25.
11. Iwao S, Iwao N, Muller DC, Elahi D, Shimokata H, Andres R. Does waist circumference add to the predictive power of the body mass index for coronary risk? Obes Res 2001;9:685–95.
12. Wildman RP, Mackey RH, Bostom A, Thompson T, Sutton-Tyrrell K, Neale LAC et al. Central fat mass versus peripheral fat and lean mass: opposite (adverse versus favorable) associations with arterial stiffness? The CARDIA study. J Hypertens 2002;20:16–23.
13. Czernichow S, Bertrais S, Oppert JM, Galan P, Blacher J, Ducimetiere P et al. Body composition and fat repartition in relation to structure and function of large arteries in mid-aged adults (the SU.VI.MAX. study). Int J Obes 2005;29:826–32.
14. Mackey RH, Sutton-Tyrrell K, Vatikievicz PV, Sakkinen PA, Lyles MF, Segal MR et al. Correlates of aortic stiffness in elderly individuals: a subgroup of the Cardiovascular Health Study. Am J Hypertens 2002;15:16–23.
15. Sutton-Tyrrell K, Newman A, Simonsick EM, Havlik R, Pahor M, Lakatta E et al. Aortic stiffness is associated with visceral adiposity in older adults enrolled in the study of health, aging, and body composition. Hypertension 2003;42:468–73.
16. Czernichow S, Bertrais S, Oppert JM, Galan P, Blacher J, Ducimetiere P et al. Body composition and fat repartition in relation to structure and function of large arteries in mid-aged adults (the SU.VI.MAX. study). Int J Obes 2005;29:826–32.
17. Vissers M, Boutier LM, McGillian GM, Wener MH, Harris TB. Elevated C-reactive protein levels in overweight and obese adults. JAMA 1999;282:2121–5.
18. Teljeira-Fernandez E, Eiras S, Grigorian-Shamagian L, Fernandez A, Adiro B, Gonzales-Juanyatey JR. Epicardial adipose tissue expression of adiponectin is lower in patients with hypertension. J Hum Hypertens 2008;22:856–63.

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40. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001; 37:1236–41.

41. London GM, Guerin A. Influence of arterial pulse and reflected waves on blood pressure and cardiac function. *Am Heart J* 1999; 138: 220–4.

42. Ohtsuka S, Kakihana M, Watanabe H, Enomoto T, Ajitsaka R, Sugishita Y. Alterations in left ventricular wall stress and coronary circulation in patients with isolated systolic hypertension. *J Hypertens* 1996; 14: 1349–55.

43. Cohn JN, Hoke L, Whitwam W, Sommers PA, Taylor AL, Duprez D et al. Screening for early detection of cardiovascular disease in asymptomatic individuals. *Am Heart J* 2003; 146: 679–85.

44. Sierra C, de la Sierra A. Early detection and management of the high-risk patient with elevated blood pressure. *Vasc Health Risk Manag* 2008; 4: 289–96.