

## ORIGINAL ARTICLE

# Epicardial adipose tissue expression of adiponectin is lower in patients with hypertension

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Low plasma adiponectin levels are related to a higher risk of development of metabolic and cardiovascular disorders, including hypertension (HT). To date, there have been no studies supporting the relationship between epicardial adipose tissue (EAT) expression of adiponectin and HT. We collected samples of EAT from 116 patients undergoing elective cardiac surgery, mostly for coronary artery bypass grafting ( $n=54$ ), valve surgery ( $n=49$ ) or both ( $n=12$ ). Samples of subcutaneous adipose tissue (SAT) were harvested from 85 patients. After RNA isolation, the expression of adiponectin was analysed by real-time reverse transcriptase (RT)-PCR. Baseline clinical data were obtained from medical records. The diagnosis of HT was established mostly by the patients' general physicians following current guidelines. We included 84 hypertensive and 32 non-hypertensive patients. Mean ( $\pm$  s.d.) age was  $70.3 \pm 7.9$  years. EAT expression levels of adiponectin

were lower in hypertensives ( $14.0 \pm 3.6$  vs  $15.3 \pm 3.6$  arbitrary units (a.u.),  $P=0.06$ ). This difference was statistically significant (odds ratio (OR) 0.828 per a.u.,  $P=0.020$ ) after adjustment for age, gender, body mass index, diabetes mellitus, heart failure, coronary artery disease (CAD), total cholesterol and triglyceride levels. However, SAT adiponectin mRNA levels were similar in hypertensive and non-hypertensive patients ( $15.3 \pm 4.2$  vs  $15.3 \pm 5.0$  a.u.,  $P>0.99$ ). Adjustment for potential confounding factors hardly altered this result. Our findings indicate that EAT expression of adiponectin may be associated with HT status independently of CAD or other comorbidities, whereas SAT expression does not. These results support the hypothesis that EAT is actively implicated in global cardiovascular risk, describing its association with HT.

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## Introduction

Epicardial adipose tissue (EAT) acts as an endocrine organ that produces many biologically active molecules referred to as adipocytokines.<sup>1,2</sup> Most of these molecules, such as leptin, plasminogen-activator inhibitor type 1, tumour necrosis factor- $\alpha$  and interleukin-6, have been recognized as key factors in the pathogenesis of cardiovascular disease.<sup>3–5</sup> They have autocrine, paracrine and endocrine effects.<sup>6</sup> Interestingly, their paracrine effects might have a special relevance because of the close proximity of EAT to the myocardium and coronary arteries and the absence of an anatomic barrier

between EAT and these structures.<sup>7</sup> Accordingly, a recent study demonstrated that EAT thickness evaluated by cardiac computed tomography scan was strongly related to vascular risk factors and coronary calcification.<sup>8</sup>

Besides, EAT is closely related to total visceral adipose tissue, classically more linked to a higher risk of metabolic and cardiovascular disorders than 'peripheral' adipose tissue. In this line, the assessment of the amount of EAT by echocardiography is a more reliable method to calculate visceral adiposity than waist circumference measurements.<sup>9,10</sup>

Adiponectin is an adipocyte-derived collagen-like protein,<sup>11–14</sup> which was shown to have important effects on the cardiovascular system, particularly concerning the development of the metabolic syndrome.<sup>15</sup> It is related to glucose metabolism, insulin resistance and lipid metabolism.<sup>11–16</sup> Low circulating adiponectin levels have been associated with diabetes mellitus (DM),<sup>17</sup> obesity<sup>12</sup> and coronary artery disease (CAD).<sup>11,18–20</sup> However, in

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patients with congestive heart failure (CHF), reverse relationship was observed, as high plasma adiponectin levels have been associated with poorer prognosis.<sup>21,22</sup> Also, age may influence the circulating levels of this hormone; higher levels found in the elderly<sup>18</sup> might be due to a phenomenon of 'adiponectin resistance'.

Lower plasma levels of adiponectin have also been reported in patients with arterial hypertension (HT), regardless of age, body mass index (BMI) and cholesterol levels.<sup>23</sup> Moreover, hypo adiponectinaemia is an independent risk factor for HT both in men and women,<sup>24</sup> although some studies failed to show such an association.<sup>25</sup> A prospective study found that low adiponectin levels at baseline are related to a higher risk of development of HT.<sup>26</sup> The effect of some antihypertensive drugs (ramipril and valsartan) on plasma adiponectin levels seems to be parallel to their effects on blood pressure and insulin sensitivity in patients with metabolic syndrome.<sup>27</sup>

Hypertension being a prevalent disorder, its impact on cardiovascular diseases is very deep. A better knowledge of its physiopathology and its relationship with other pathological conditions can lead to proper management of hypertensive patients.

Although the association between EAT adiponectin expression levels and gender or CAD has already been described,<sup>2,28</sup> to date, its relationship with the presence of HT has not yet been elucidated. The aim of the present study was to determine whether EAT and subcutaneous adipose tissue (SAT) expression levels of adiponectin are different in hypertensive and non-hypertensive patients.

## Materials and methods

### Subjects

Samples of EAT were obtained from 116 consecutive patients (78 men, 38 women) who underwent elective heart surgery at our hospital, for coronary artery bypass grafting ( $n=54$ ), valve surgery ( $n=49$ ), both ( $n=12$ ) or atrial myxoma exeresis ( $n=1$ ). In 85 patients, we also collected samples of SAT.

Only those patients who had undergone a previous heart surgery were excluded.

The study was approved by the local IRB and followed the guidelines proposed by the Declaration of Helsinki. Written informed consent was obtained from each patient before study participation. The participation rate was 100%.

### Clinical data

Clinical data, including the antecedent of HT, were obtained retrospectively by checking medical records. At our clinics, the diagnosis of HT was done by calculating the average of three measurements of blood pressure after a resting period of 10 min, if systolic blood pressure exceeded 140 mm Hg and/or diastolic blood pressure was

higher than 90 mm Hg. The diagnosis of HT was performed by the patients' general physicians during regular outpatient follow-up before surgery. Non-hypertensive status was also properly assessed prior to surgery. Hypertensive patients were included in the HT group, no matter whether their blood pressure was adequately treated and targets reached at the time of inclusion in the study.

Body mass index was obtained from anthropometrical measurements upon admission to hospital. Blood samples were collected up to 1 week before surgery, except for cholesterol levels, which were analysed within 6 months prior to surgery. The presence or absence of CAD was assessed by checking coronary angiography studies carried out up to 6 months before surgery. Only angiographically significant stenoses (more than 50% of the luminal diameter) were considered.

### Collection and treatment of EAT and SAT samples

The SAT and EAT samples were obtained before extracorporeal circulation. EAT biopsies were harvested near the proximal tract of the right coronary artery. SAT samples were obtained from the thorax. All tissues were immediately frozen at  $-80^{\circ}\text{C}$  before RNA extraction.

RNA was extracted by Trizol method. Concentration and purity of the samples were estimated by the ratio between absorbances at 260 and 280 nm. Samples contaminated with genomic DNA were treated with DNase I. Each  $5\ \mu\text{g}$  of RNA was treated with  $10\ \text{U}\ \mu\text{l}^{-1}$  of DNase I and  $20\ \text{U}\ \mu\text{l}^{-1}$  of RNase inhibitor (both products from Invitrogen Ltd, Paisley, UK) for 2 h at  $37^{\circ}\text{C}$ . Proteins and DNA were removed from the samples with phenol, chloroform and isoamylalcohol. Eventually, RNA was precipitated with 96% ethanol and sodium acetate 0.3 M.

### Reverse transcription and real-time retrotranscriptase PCR

Real-time retrotranscriptase (RT)-PCR was performed using  $1.2\ \mu\text{g}$  samples of purified RNA and 200 U of MMLV reverse transcriptase (Invitrogen Ltd) in  $30\ \mu\text{l}$  of a solution (pH 8.4) containing 20 mM Tris-HCl, 50 mM KCl, 2.5 mM  $\text{MgCl}_2$ , nucleotides (1 mM each), 20 U of RNase inhibitor and random primers under the following conditions: 50 min at  $37^{\circ}\text{C}$ , 10 min at  $42^{\circ}\text{C}$  and 5 min at  $95^{\circ}\text{C}$ .

The comparative analysis of adiponectin and glyceraldehyde 3-phosphate dehydrogenase expression in EAT was done with real-time RT-PCR using SybrGreen (Roche Diagnostics Corp., Indianapolis, IN, USA) as fluorochrome and the primers previously described.<sup>28</sup> Adiponectin mRNA amplification was performed: 5 min at  $95^{\circ}\text{C}$ , followed by 40 cycles of 30 s at  $95^{\circ}\text{C}$ , 45 s at  $60^{\circ}\text{C}$  and 60 s at  $72^{\circ}\text{C}$ .<sup>29</sup> Genomic contamination was ruled out by using negative controls at retrotranscription conditions without MMLV. Fluorescence curves were

analysed using Chromo 4 software (MJ Research Inc., Reno, NV, USA). Adiponectin mRNA was normalized to glyceraldehyde 3-phosphate dehydrogenase mRNA and expressed in arbitrary units (a.u.).

#### Immunohistochemistry

Sections of EAT and SAT from hypertensive and non-hypertensive patients were paraffin-embedded and afterward deparaffined and rehydrated. Slides were incubated overnight with antibodies to adiponectin (Santa Cruz Biotechnology, Delaware, CA, USA), dilution 1:250. The LSAB protocol (Dako Diagnostics, Glostrup, Denmark) was followed. Immunodetection was developed with 3,30-diaminobenzidine tetrahydrochloride kit (Dako Diagnostics). Negative controls were carried out by omitting the primary antibody.

#### Statistical analysis

Normality assumptions of continuous variables were checked with Kolmogorov–Smirnov tests. Non-skewed variables were summarized as mean  $\pm$  s.d. Differences between continuous variables were tested for statistical significance by means of *t*-test. Categorical variables were expressed as percentages and compared using  $\chi^2$ -test.

In case of missing data, we checked that there was no unequal distribution between groups.

We used logistic regression models to assess the association of EAT and SAT mRNA expression of adiponectin with HT, including possible confounding factors. Results are presented as ORs together with their 95% confidence intervals.

Statistical significance was defined as  $P < 0.05$ . All analyses were performed using SPSS 15.0 software for Windows (SPSS Inc., Tokyo, Japan).

## Results

#### Patient characteristics

The study sample included 84 hypertensive and 32 non-hypertensive patients. The main sample characteristics are given in Table 1. The mean ( $\pm$  s.d.) age was  $70.3 \pm 7.9$  years. Hypertensive patients were, on average, less than 2 years older than the non-hypertensive patients. The proportion of male was higher than that of female in both groups, notably in that of non-hypertensives, although not statistically different. HT and non-HT groups were quite similar, except for use of calcium channel blockers and triglyceride levels, both significantly higher in the former group. One-third of the patients of the whole

**Table 1** Baseline characteristics of the hypertensive and the non-hypertensive groups

	All subjects	With HT (n = 84)	Without HT (n = 32)	P*
<i>Demographics</i>				
Male (%)	67	63	78	0.12
Age (years)	$70.3 \pm 7.9$	$70.7 \pm 6.9$	$69.0 \pm 10.1$	0.30
<i>Comorbidities and risk factors</i>				
Current smoker (%)	8	10	4	0.23
Body mass index (kg/m <sup>2</sup> )	$28.8 \pm 4.1$	$27.6 \pm 4.2$	$29.2 \pm 3.9$	0.06
Diabetes mellitus (%)	36	41	24	0.13
Coronary artery disease (%)	61	66	48	0.10
Heart failure (%)	30	32	25	0.45
LVEF (%)	$60 \pm 15$	$60 \pm 14$	$60 \pm 15$	0.91
<i>Treatment prior to surgery</i>				
ACEIs/ARBs (%)	41	43	35	0.63
Statins (%)	40	43	32	0.48
Beta blockers (%)	36	38	32	0.71
Calcium channel blockers (%)	27	37	3	0.001
<i>Laboratory findings</i>				
Urea (mg per 100 ml)	$57 \pm 27$	$57 \pm 23$	$58 \pm 37$	0.82
Creatinine (mg per 100 ml)	$1.1 \pm 0.3$	$1.1 \pm 0.4$	$1.1 \pm 0.3$	0.37
Triglycerides (mg per 100 ml)	$119 \pm 50$	$126 \pm 51$	$102 \pm 42$	0.023
Cholesterol (mg per 100 ml)	$181 \pm 43$	$178 \pm 39$	$183 \pm 44$	0.41
HDL cholesterol (mg per 100 ml)	$37 \pm 13$	$36 \pm 13$	$38 \pm 13$	0.58
LDL cholesterol (mg per 100 ml)	$108 \pm 35$	$106 \pm 36$	$112 \pm 32$	0.53
EAT adiponectin mRNA (a.u.)	$14.4 \pm 3.6$	$14.0 \pm 3.6$	$15.3 \pm 3.6$	0.06
SAT adiponectin mRNA (a.u.) (n = 85)	$15.3 \pm 4.4$	$15.3 \pm 4.2$	$15.3 \pm 5.0$	> 0.99

Abbreviations: a.u., arbitrary units; ACEIs, angiotensin converter enzyme inhibitors; ARBs, angiotensin receptor blockers; EAT, epicardial adipose tissue; HDL, high-density lipoprotein; HT, arterial hypertension; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; SAT, subcutaneous adipose tissue.

Values expressed as mean  $\pm$  s.d.

\*P-value referred to the comparison between HT and non-HT groups.

group presented DM and one-third CHF. CAD was diagnosed in more than half of the study sample. However, none of these comorbidities differed significantly between both groups. The prevalence of overweight and obesity in our sample was remarkably large, with 51% subjects meeting the criteria for overweight (BMI > 25 and < 30 kg/m<sup>2</sup>) and 34% meeting the criteria for obesity (BMI > 30 kg/m<sup>2</sup>). In our sample, BMI was higher in the group of non-hypertensive patients ( $P = 0.06$ ).

#### EAT adiponectin mRNA levels in hypertensive vs non-hypertensive patients

Hypertensive patients had lower EAT mRNA expression levels of adiponectin than non-hypertensive patients ( $14.0 \pm 3.6$  vs  $15.3 \pm 3.6$ ), although in this unadjusted analysis, the difference failed to reach statistical significance ( $P = 0.06$ ) (Figure 1).

However, when the association between EAT expression of adiponectin and HT was explored by means of multivariate logistic regression analysis, we found that the relationship between lower EAT adiponectin mRNA levels and HT achieved statistical significance (OR for adiponectin mRNA = 0.828 per a.u.,  $P = 0.020$ ) (Table 2). Variables considered in the model included possible confounding factors, such as age, gender, BMI, DM, CHF, CAD and triglyceride levels. In this analysis, only older age and lower EAT adiponectin mRNA

levels were found to be significantly associated with the presence of HT.

Further adjustment introducing consumption of calcium channel blockers—distributed differently in both groups—led to a similar result (OR = 0.825 per a.u.,  $P = 0.031$ ).

#### SAT adiponectin mRNA levels in hypertensive vs non-hypertensive patients

We found that SAT adiponectin mRNA levels were similar in hypertensive and non-hypertensive patients ( $15.3 \pm 4.2$  vs  $15.3 \pm 5.0$ ,  $P > 0.99$ ) (Figure 2).

Adjustment for possible confounding factors as described above for EAT mRNA expression of adiponectin did not alter the result at all, as shown on Table 3. None of the variables introduced in this model showed to be significantly related to HT. Eventually, further adjustment including consumption of calcium channel blockers in the model hardly changed the results (OR for EAT adiponectin mRNA = 0.999 per a.u.,  $P = 0.98$ ).

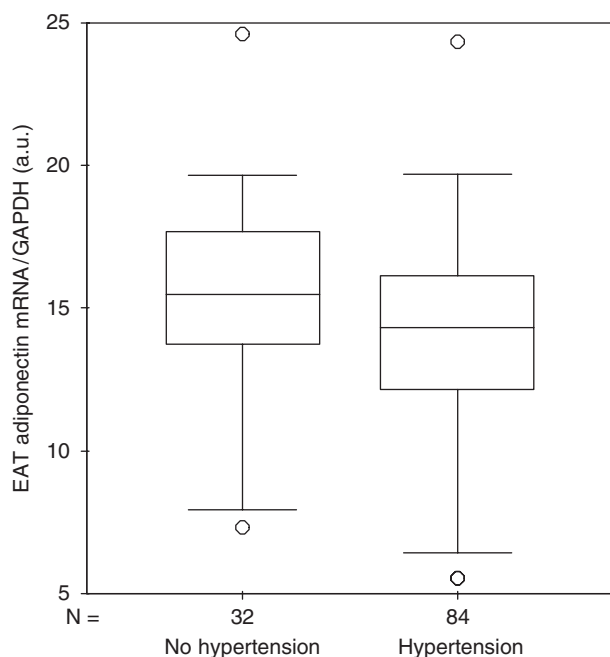
#### Immunohistochemistry

We performed immunohistochemistry to illustrate tissue expression of adiponectin. Figure 3 shows adiponectin expression in EAT and SAT samples from both a hypertensive and a non-hypertensive patient.

## Discussion

This is the first study to report that EAT mRNA expression of adiponectin is lower in patients with HT, independently of other factors that can influence this cytokine's levels, such as the presence of DM, CAD or CHF.

Our results are relevant as they can have two distinct implications. The first one is that the lack of



**Figure 1** Box plot comparing epicardial adipose tissue (EAT) adiponectin mRNA levels in patients with and without hypertension. Box-and-whiskers plot with mean values, interquartile range and lower and upper values. Outliers/extreme values are represented by the small circular symbols.  $P$ -value of the difference of EAT adiponectin mRNA levels between hypertensive and non-hypertensive patients is 0.06 (unadjusted). a.u., arbitrary units; GAPDH, glyceraldehyde 3-phosphate dehydrogenase.

**Table 2** Relationship between hypertension, epicardial adipose tissue adiponectin expression and other confounding factors

	Odds ratio (95% CI)	P-value
EAT adiponectin mRNA (per a.u.) <sup>a</sup>	0.828 (0.707–0.971)	0.020
Age (per year)	1.061 (1.000–1.126)	0.048
Gender (female)	2.932 (0.886–9.704)	0.08
Body mass index (per kg/m <sup>2</sup> )	1.111 (0.954–1.292)	0.18
Coronary artery disease	0.752 (0.247–2.286)	0.62
Heart failure	0.587 (0.188–1.828)	0.36
Diabetes mellitus	0.708 (0.239–2.102)	0.53
Triglycerides (per mg/100 ml)	1.010 (0.996–1.025)	0.17

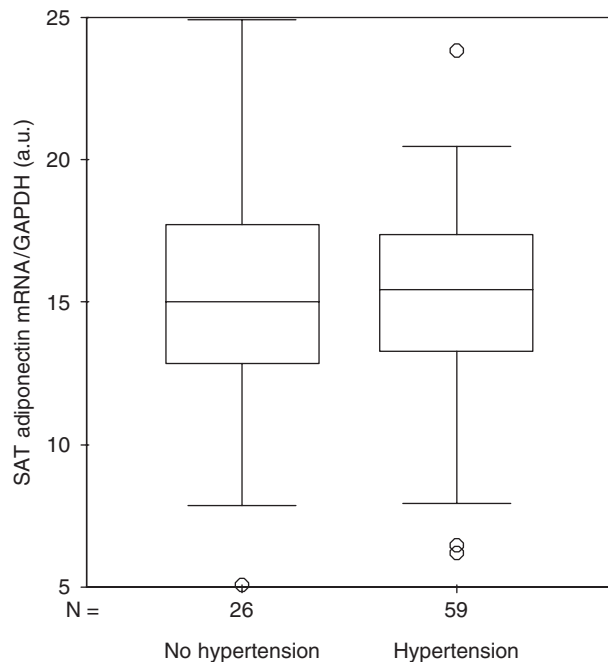
Abbreviations: a.u., arbitrary units; CI, confidence interval; EAT, epicardial adipose tissue; GAPDH, glyceraldehyde 3-phosphate dehydrogenase.

$R^2$  (Cox) = 0.183.

$N = 101$ .

<sup>a</sup>Per GAPDH unit.

Results of multivariable logistic regression analysis.



**Figure 2** Box plot comparing subcutaneous adipose tissue (SAT) adiponectin mRNA levels in patients with and without hypertension. Box-and-whiskers plot with mean values, interquartile range and lower and upper values. Outliers/extreme values are represented by the small circular symbols. *P*-value of the difference of SAT adiponectin mRNA between hypertensive and non-hypertensive patients  $>0.99$  (unadjusted). a.u., arbitrary units; GAPDH, glyceraldehyde 3-phosphate dehydrogenase.

**Table 3** Relationship between hypertension, subcutaneous adipose tissue adiponectin expression and other confounding factors

	Odds ratio (95% CI)	<i>P</i> -value
SAT adiponectin mRNA (per a.u. <sup>a</sup> )	0.999 (0.880–1.134)	0.98
Age (per year)	1.039 (0.975–1.106)	0.24
Gender (female)	1.440 (0.427–4.850)	0.56
Body mass index (per Kg/m <sup>2</sup> )	1.053 (0.904–1.227)	0.51
Coronary artery disease	0.637 (0.189–2.142)	0.47
Heart Failure	0.596 (0.183–1.940)	0.39
Diabetes mellitus	0.611 (0.193–1.934)	0.40
Triglycerides (per mg/dl)	1.012 (0.997–1.027)	0.13

Abbreviations: a.u., arbitrary units; CI, confidence interval; mRNA, messenger ribonucleic acid; SAT, subcutaneous adipose tissue; GAPDH, glyceraldehyde 3-phosphate dehydrogenase.

$R^2$  (Cox) = 0.123.

*N* = 76.

<sup>a</sup>Per GAPDH unit.

Results of multivariable logistic regression analysis.

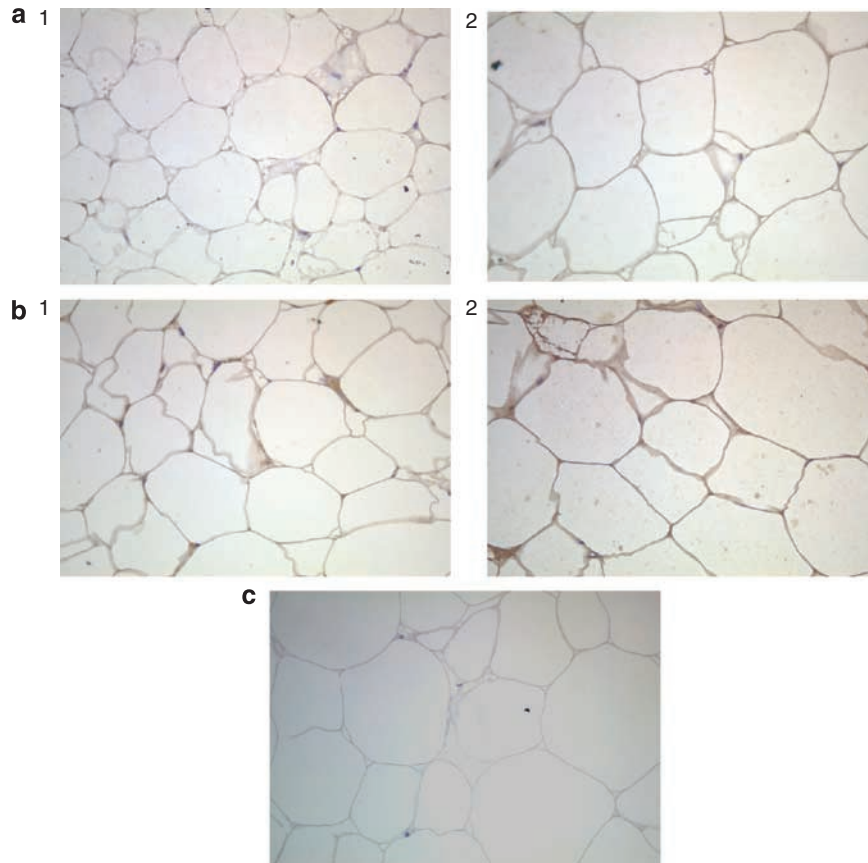
adiponectin produced by EAT may play an important role in the physiopathology of HT by the absence or reduction of its beneficial effect on the cardiovascular system, although other factors affecting adiponectin levels, specially the presence of inflammation, not evaluated here, are possibly implicated. On the other hand, a higher risk of CAD in HT patients might be related to the decrease of the protective endocrine and also local paracrine

effects of adiponectin, as low levels of adiponectin detected in hypertensive patients would increase the risk of the latter. Accordingly, in our study population, the prevalence of CAD, although not significantly, was higher among hypertensive patients. In this regard, hypo adiponectinaemia has been recognized as a risk factor for CAD and the cluster of components of the metabolic syndrome, including HT.<sup>15</sup>

Interestingly, SAT expression of adiponectin does not seem to differ between hypertensive and non-hypertensive patients in our study. This observation is in accordance with prior evidence that showed no changes in SAT expression of adiponectin in patients with or without cardiovascular diseases, or even after therapeutic interventions that increase plasma adiponectin levels.<sup>30</sup> It is possible that, unlike SAT, visceral adipose tissue plays a relevant role in the pathogenesis of HT. And it could also partly explain why the amount of visceral fat is more closely related to the metabolic syndrome and the risk of cardiovascular diseases than that of SAT. Echocardiographic and cardiac computed tomographic scan assessments of the EAT have been shown to correlate well with the risk of cardiovascular disease.<sup>9,10</sup> In this regard, a study designed by de Vos *et al.*<sup>8</sup> including more than 500 postmenopausal women recently demonstrated that EAT thickness measured by cardiac computed tomography has a graded relation to coronary calcification. In the same study, EAT was positively related to the use of antihypertensive drugs ( $P=0.007$ ) and systolic blood pressure ( $P=0.03$ ), which in some extent is in accordance with our findings. Although we did not analyse the correlation between EAT adiponectin expression levels and EAT thickness, it is likely that the increase of the latter is associated with lower expression of this hormone, as demonstrated in other visceral adipose tissues.<sup>31</sup>

Regarding SAT, some proposed that post-transcriptional regulation changes of adiponectin could occur and SAT might also be relevant in the development of cardiovascular diseases.<sup>30</sup> But should this hypothesis be true, two different mechanisms—different expression levels and post-transcriptional regulation—could explain the role of visceral fat in the differential plasma adiponectin levels in patients with and without metabolic syndrome or cardiovascular diseases.

Hypertension is recognized as a major cardiovascular risk factor. However, epidemiological studies have demonstrated that the control of blood pressure levels, although improving, is still very poor, especially in high-risk patients such as those with metabolic syndrome and/or diabetes.<sup>32–34</sup> In these populations, blood pressure targets are reached in less than 20% cases and usually more than three antihypertensive drugs are needed.<sup>35</sup> Therefore, both the promotion of the adherence to the guidelines of clinical practice and investigation on new



**Figure 3** Immunohistochemical staining of epicardial (EAT) and subcutaneous adipose tissue (SAT) samples with antibodies to adiponectin. (a1) EAT sample from a hypertensive patient. (a2) SAT sample from the same patient. (b1) EAT sample from a non-hypertensive patient. (b2) SAT sample from the same patient. (c) Negative control with omission of primary antibody (SAT). Original magnification  $\times 40$ .

pharmacological strategies to improve HT control, and thus reduce the cardiovascular risk of these patients, are relevant goals for medicine at present.<sup>36</sup> Accordingly, plasma adiponectin levels could be used not only as an extra tool to determine the individual metabolic and cardiovascular risk, but adiponectin could also serve as a new therapeutic target. The better understanding of the regulation and effects of adiponectin can result in the use of new interventions to prevent or treat the metabolic syndrome and cardiovascular disorders. In animal models, adiponectin infusion has beneficial effects concerning the metabolic syndrome, insulin sensitivity and cardiovascular function. In humans, different factors can cause hyperadiponectinaemia and hence its beneficial effects: weight loss,<sup>37</sup> diet factors (soy protein, oils)<sup>38</sup> and drugs, such as thiazolidinediones,<sup>30</sup> angiotensin converter enzyme inhibitors<sup>39</sup> or angiotensin receptor blockers.<sup>40</sup> In our sample, prescription of the latter two groups of drugs was in total almost 10% higher in hypertensive patients. This could contribute to attenuate our results, and therefore the difference in EAT adiponectin expression levels could be even slightly higher than what we described here.

Several investigations focused on the use of thiazolidinediones to treat the metabolic syndrome. These PPAR- $\gamma$  agonists downregulate tumour necrosis factor- $\alpha$  and upregulate plasma adiponectin levels and reverse some features of the metabolic syndrome also in non-diabetic patients.<sup>41</sup> Thiazolidinediones do not upregulate SAT expression of adiponectin<sup>30</sup> or adiponectin receptors (AdipoR1 and AdipoR2).<sup>42</sup> Our results are in line with these findings as we found differences in adiponectin expression in hypertensive patients in EAT but not in SAT.

The removal of EAT at the time of heart surgery could be beneficial for the prevention of cardiovascular disorders. Obviously, this is just a hypothesis that should be tested, as the harmlessness of these interventions has not been proved so far.

Future therapeutic strategies for the treatment of HT, especially if associated with the metabolic syndrome, should focus on adiponectin and visceral adipose tissue. However, further investigations are needed to improve our knowledge on the effects of adiponectin and its interactions with other adipocytokines.

### Study limitations

The main limitation of this cross-sectional study is that it cannot demonstrate causality but only association between variables. Besides, clinical data were collected retrospectively. The synthesis/secretion of adiponectin was not analysed; therefore, we just focused on the differences in adiponectin expression levels. HT was treated categorically. Blood pressure levels at the time of inclusion in the study were not considered provided that adequately treated patients with HT were also included in the HT group.

Even though all subjects were heart surgery patients, there are possibly no reasons to believe that this could lead to a lack of validity of the results.

### Conclusions

Our findings indicate that EAT expression of adiponectin may be associated with HT status independently of CAD or other comorbidities, whereas SAT expression does not. These results support the hypothesis that EAT is actively implicated in global cardiovascular risk, describing, for the first time, its association with HT. They can also partly contribute to explain why central obesity is more related to HT than peripheral obesity.

#### What is known about this topic

- Epicardial fat produces adiponectin.
- Adiponectin is related to a lower cardiovascular risk.

#### What this study adds

- Epicardial fat expression of adiponectin is lower in hypertensive patients.
- Subcutaneous fat expression is similar in hypertensive and non-hypertensive patients.

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## Conflicts of interest

The authors state no conflict of interest.

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