

consciousness because of a sustained ventricular tachycardia. This patient's son (III-1) was considered to have the identical underlying disease. The sudden death in the brother and sister of patient II-2 potentially resulted from a ventricular tachycardia based on the diagnosis LVNC in two family members. However, this is an assumption since post-mortem investigation has not been performed.

In LVNC there are three potential mechanisms for thrombo-embolic complications. First, when heart failure occurs with dilation of the left ventricle, an intra-cavitary thrombus can be formed. Secondly, atrial flutter or atrial fibrillation can lead to cardiac embolism. And thirdly, the changing haemostasis in the deep endomyocardial recesses makes patients with LVNC more vulnerable to thrombus formation [2–5]. Anticoagulation diminishes the risk of thrombo-embolic complications. The exact individual attribution of oral anticoagulation on each of these three mechanisms remains unclear. Moreover, Oechslin et al. described thrombo-embolic events in 8 out of 34 patients (24%) with LVNC [2]. In our opinion, this is a considerable number of patients. Therefore patient III-1 (family B) started anticoagulation therapy.

The distribution of LVNC did not differ between the two families; as shown in Table 1 in Ref. [1], the apico-lateral wall was most severely affected. However, the morphology was different between the two families; in family A, there was a fine network of non-compacted myocardium versus a coarser network of non-compacted myocardium in family B. This probably reflects the heterogeneous nature of this condition.

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21 August 2006

doi:10.1016/j.ejheart.2006.10.011

Obstructive sleep apnoea and adipocyte death

Keywords: Obstructive sleep apnoea; Adipocyte; Inflammation

Dear Editor,

The recent review on heart failure and sleep apnoea by Ferreira et al. [1] correctly and clearly underlines the evidence-based association between those two conditions. However, as the authors clearly state, confounding factors such as obesity make the full meaning of that relationship uncertain. As it might be linked to adverse outcomes, it would be of utmost interest to clarify the nature of this association.

Inflammation with origin in adipose tissue leads to a number of important health complications, macrophage accumulation playing a central role in that physiopathology [2]. Cinti et al. [3] have provided sound evidence for macrophage aggregation around dead adipocytes, a phenomenon more frequent in adipose tissue with large size adipocytes.

In a recent publication [4] we show that adipocyte rupture, the more facile the bigger the adipocyte, is most probably at the origin of the inflammatory state accompanying obesity. Adipocyte rupture as the basis of inflammation with origin in adipose tissue is in good agreement with the fact that adipose tissue localization markedly influences its consequences on health, the most pathogenic obesity being the visceral one [5]. As a matter of fact, adipocytes in abdominal cavity are subject to suddenly varying pressures, as occurs for example during cough, abdominal crunch or diverse physical exercises [6].

Obstructive apnoeas during sleep elicit a series of mechanical responses. Futile inspiratory efforts against the occluded pharynx cause abrupt reductions in intrathoracic pressure, what has been shown to result in an increase in left ventricular transmural pressure [7]. Pressures as low as 65 mm Hg have been recorded during obstructive apnoeas in patients with heart failure [8]. This huge pressure variation may lead to intrathoracic adipocyte rupture. On the other hand, intrathoracic pressure variations will have direct repercussion on intra-abdominal pressure [6,9].

Shamsuzzaman et al. [10] found that compared with control subjects matched for age, sex, and body mass index, patients with obstructive sleep apnoea had higher plasma C-reactive protein concentrations that were proportional to the frequency of apnoeas.

We suggest that intrathoracic and intra-abdominal pressure variations accompanying obstructive apnoeas will lead to adipocyte rupture, the subsequent inflammation impending on cardiovascular health. Measures to prevent adipocyte hypertrophy would most probably reduce the pathogenic burden of obstructive sleep apnoeas.

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28 June 2006

doi:10.1016/j.ejheart.2006.10.010

Obstructive sleep apnoea and adipocyte death:

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Keywords: Obstructive sleep apnoea; Adipocyte; Inflammation; Pathophysiology

We thank Azevedo et al. for their interest in our review on heart failure and sleep apnoea [1].

We agree that obesity might be a confounding factor in the relationship between heart failure (HF) and obstructive sleep apnoea (OSA). The suggested hypothesis is attractive and pertinent and should lead to further investigation.

Sleep apnoea (SA) has been treated as a respiratory mechanical abnormality but evidence suggests that it is a systemic metabolic illness [2]. Inflammation is a potential mechanism for development and progression of HF in patients with SA [1]. Increased levels of C-reactive protein [3], inter-

leukin-6 (Il-6) and tumor necrosis factor (TNF)- α [4] have been observed in OSA, both in plasma and in airways, and decrease with CPAP therapy [5].

Experimentally produced resistive breathing induces Il-6 and TNF- α production [6]. Intermittent hypoxia and intrathoracic pressure variations might be pathophysiological links [7]. However, increasing body mass index correlates positively with both cytokine levels and SA severity [3,4]. Adipose tissue localization influences its pathogenicity [8]. Patients with OSA have a significantly greater amount of visceral fat without difference in total or subcutaneous body fat [2]. Visceral adipocytes in the abdominal cavity are more susceptible to rupture because they are bigger and more exposed to suddenly varying pressures [8]. This suggests that visceral obesity might play a central role in cardiovascular consequences of SA, through monocyte and inflammatory activation following adipocyte death triggered by pressure variations related to OSA, as hypothesized by Azevedo et al.

On the other hand, SA may accelerate cardiovascular and metabolic abnormalities, possibly through progressive elevations of stress hormones and cytokines [2]. TNF- α correlates strongly with lipolysis and induces leptin secretion which has been associated with sympathetic systemic activation [9]. Elevated leptin levels were reported in OSA independently of obesity which might be related to higher levels of visceral fat [2]. Adiponectin levels are also increased, suggesting a stimulatory effect of OSA on the endocrine function of adipose tissue [10]. This leads to the hypothesis that SA may be responsible for cardiovascular consequences often attributed to obesity.

In summary, the pathophysiology of cardiovascular and metabolic complications of sleep apnoea is multifactorial and probably associated.

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