

Ventricular Remodeling after Myocardial Infarct: A Minireview on the Impact of Obstructive Sleep Apnea Syndrome

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and coagulation abnormalities. Continuous positive airway pressure CPAP might represent a non pharmacological treatment in addition to the global management of patients with AMI.

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ABSTRACT

Obstructive sleep apnoea (OSA) is recognized as an important cardiovascular risk factor and is intricate with coronary disease. OSA could be involved in worsening the cardiac remodeling following the acute myocardial infarction (AMI). Cardiac remodeling is an important determinant of the clinical outcome of heart failure and is linked to disease progression and poor prognosis. The aims of this minireview are to address the frequency reported in the literature of OSA in patients with AMI and to summarize the main mechanisms of cardiac remodeling by OSA and its consequences on cardiovascular system. In addition, we aim to identify new strategies in the management of AMI. OSA is frequent in patients with AMI. OSA may have a role in cardiac remodeling after AMI and especially in relationship with the increased sensitivity of the reperfused tissue to all underlying mechanisms: a complex interplay of mechanical or haemodynamic factors, reactive oxygen species balance, sympathetic nerve activity, endothelial dysfunction, proinflammatory factors

INTRODUCTION AND BACKGROUND

Heart failure (HF) is a progressive disorder characterized by (1) a poor quality of life; (2) a poor prognosis (5-year survival < 50%, worse than most common types of cancer); and (3) an enormous burden on health care costs. In Europe and in the United States ~1-2 % of the entire health care budget is spent on HF^[1]. The prevalence of HF is expected to rise due to the aging population and better treatment of cardiovascular disease that precedes HF^[2]. Therefore, it is mandatory to explore innovative approaches to improve treatment of HF. The leading cause of HF remains coronary artery disease (CAD). Successful rapid reperfusion reducing infarct size^[3] and primary percutaneous coronary intervention (PCI) remain the cornerstone of treatment^[4] and represent the most important treatment of acute myocardial infarction (AMI). Despite contemporary revascularization strategy and pharmacological treatment, clinical outcomes following an acute coronary syndrome (ACS) remain unsatisfactory.

Sleep apnoea syndrome (SAS)

Sleep apnoea syndrome (SAS) is a frequent pathology, but still underestimated and underrecognized by cardiologists. Sleep-disordered breathing disorders (SDB) are particularly frequent in patients with cardiovascular diseases. Obstructive sleep apnoea (OSA) is the most common form of SDB and is recognized as an important cardiovascular risk factor. Obstructive sleep apnoea syndrome (OSAS) is characterized by repetitive episodes of breathing cessation due to complete or partial collapse of the upper airway resulting in intermittent oxygen desaturation, increased respiratory effort, arousal, and sleep fragmentation. Other sleep breathing disorders such as hypoventilation, central sleep apnoea, complex sleep apnoea, and Cheyne-Stokes respiration are less common and are sometimes associated with cardiovascular disorders. Patients typically present with witnessed apnoeas, loud intermittent snoring, and excessive daytime somnolence. The OSA is defined by scoring its severity. The severity is defined by 1/ the apnoea-hypopnea index (AHI) defined as follows: mild=5-15 HA per hour; moderate=15-30 HA per hour; severe as >30 HA per hour) and 2/ Excessive daytime sleepiness after discarding every other causes. The syndrome is associated with impairment in quality of life, cognitive functioning, and work performance, and with an increased risk of road-traffic accidents.

OSA is a highly prevalent breathing disorder in sleep affecting at least 2-4% of the adult population, but the prevalence is highly dependent on the age, gender, BMI and associated comorbid conditions. A large number of studies have demonstrated that OSA is an independent risk factor of cardiovascular morbidity and mortality^[5]. It has been shown to be associated with hypertension, ischemic heart disease, stroke, pulmonary hypertension, cardiac arrhythmia and cardiovascular mortality. OSA is now recognized as a risk factor for the development of hypertension in European and US International Guidelines^[6]. OSA and hypertension are linked in a dose-response fashion. Growing experimental and clinical evidences corroborate the association of OSA with subclinical signs of cardiovascular morbidity such as endothelial dysfunction and vasculature remodeling, oxidative stress, activation of inflammatory pathways and increased leukocytes/endothelial cells adhesion. Altogether this suggests that OSA could be a major although underestimated player in the atherogenesis. The gold-standard treatment for OSA, nasal continuous positive airway pressure (CPAP), might improve cardiac symptoms and hemodynamic parameters in patients with the disease^[6].

OSA is intricate with coronary disease. From a pathophysiological point of view, recurrent ischemias lead to endothelial dysfunction and could play an important role in the atherosclerotic process. Obviously, OSA as a risk factor if confirmed is intricately involved with other ones such as hypertension and overweight. After AMI, OSA could be involved at least at two levels:

1. worsening the infarct size^[3,4,7]. OSA exerts deleterious effects additional to ischemia-reperfusion injury at the very onset of the reperfusion: endothelial dysfunction, enhanced fibrosis, intricate with other comorbidities such as hypertension, diabetes, overweight... Whether its modulation could be beneficial remains unknown until now. Many studies target this early point.

2. worsening the cardiac remodeling following the AMI. This is precisely the aim of this minireview.

Cardiac remodeling

Cardiac remodeling is an important determinant of the clinical outcome of HF and is linked to disease progression and poor prognosis. The remodeling process is characterized by activation of

“compensatory” systems, including the renin-angiotensin system (RAS) and the sympathetic nervous system (SNS). Although initially aimed at maintaining adequate circulation, over time the sustained activation of compensatory neurohormonal systems actually contributes to the adverse remodeling process of the heart, and accelerates the transition towards HF.

Despite current treatment regimens for HF that effectively target known neurohormonal system activation, overall the prognosis remains poor for many patients. Other targets, such as tissue fibrosis, may be left untreated^[8]. Whether the presence of OSAS could impact the post-MI remodeling is unclear.

The aim of this minireview is to address the frequency reported in the literature of OSA in patients with AMI. Secondly, we will summarize shortly the main mechanisms of cardiac remodeling by OSA and its consequences on cardiovascular system. Finally we aim to analyze the place of OSA in cardiac remodeling in patients with AMI: identifying the influence of OSA on ischemic cardiac diseases may provide new strategies in the management of AMI.

OSA IS FREQUENT IN PATIENTS WITH AMI

Several studies have reported a high prevalence (40 to 66%) of OSA in patients with CAD^[9-15]. Nevertheless the interpretation should be cautious considering the chosen cut-off of the AHI used to define OSA and verifying that central sleep apnoea (CSA) were accurately identified and excluded.

A recent French study reported a prevalence of OSA in patients admitted for ST-segment elevation myocardial infarction STEMI of 79%^[9]. Lee *et al*^[10] found a prevalence of 65.7% of patients presenting with STEMI and with undiagnosed OSA. The same team demonstrated two years later that 40% of patients admitted for STEMI had undiagnosed severe OSA defined as AHI ≥ 30 ^[11]. A similar high prevalence of at least moderate sleep apnoea in the early phase after the acute coronary event was found in at least two other studies. In the study of Schiza *et al*^[12], 54% of patients presented AHI ≥ 10 /h compared to 55% reported by Buchner *et al*^[13] considering AHI ≥ 15 /h. In the population of first-AMI patients who underwent PCI for AMI, Nakashima *et al*^[16] found that 43% fulfilled criteria for OSA (AHI ≥ 15). Yumino *et al*^[17] studied the impact of OSA on major adverse cardiac events (MACEs) after PCI and found a high prevalence (57%) of patients who were diagnosed as with OSA after revascularization. Meng *et al* (14) found that 61,8% of patients presented coexisting ACS and OSA (defined as AHI ≥ 5 /h). In the study of Mehra *et al*^[15] 66.4% of patients were reported to have AHI>10/h and 26.0% patients had an AHI >30 with the prevalent apnoea pattern being obstructive (72.1%). Importantly this diagnosis was not efficiently detected by self-reports of sleepiness. This observation seems to be independent of gender^[18,19].

Bakker *et al*^[20] called OSA the “elephant in the room” because it was often ignored even in high-risk patients. The clinical impact of this high prevalent disease has to be investigated. On the one hand Mehra *et al*^[15] for instance found that despite a high prevalence detected, OSA had no significant impact on 6-month clinical outcomes. On the other hand Yumino *et al*^[17] reported that OSA was associated with lower 8-month event free survival rates following PCI for ACS.

PATHOPHYSIOLOGICAL IMPACT OF OSA LEADING TO CARDIAC REMODELING

At first glance, as regards cardiovascular pathophysiology, OSA

could at least induce systemic hypertension, pulmonary hypertension, right HF, cardiac arrhythmias, endothelial dysfunction and CAD^[5,21-23]. Indeed, repetitive apneic events disrupt the normal physiological interaction between sleep and the cardiovascular system. The underlying pathophysiological mechanisms involve a complex interplay of mechanical or haemodynamic factors, reactive oxygen species balance, sympathetic nerve activity, endothelial dysfunction, proinflammatory factors and coagulation abnormalities. Because of ischemia-reperfusion lesions, myocardium after AMI is highly sensitive to all these factors in addition to the tissue perfusion grade. Mechanical factors.

In clinical settings, left ventricular (LV) systolic function is highly dependent on loading conditions. Especially, acute increase in afterload can reduce LV systolic function^[24,25]. During apnoea profound changes on cardiac preload and afterload may occur because of the rise of both heart rate and blood pressure (BP). The elevation of afterload seems to be more linked to activation of sympathetic innervation than intrathoracic negative pressure^[21]. On the other hand, it has been reported that the increase in systolic transmural pressure as an index of afterload is correlated to the severity of negative intrathoracic pressure swings^[26]. Hetzenecker *et al*^[27] showed in a multivariate analysis that SDB was significantly associated with an increased 24 h cardiac workload, independently of age, gender, body mass index (BMI), left ventricular ejection fraction (LVEF) and anti-hypertensive medications. Preload seems also to be increased in patients with OSA because of a right ventricular enlargement and elevated pulmonary artery pressure^[23]. By this way, a repeated acute increase of afterload during apnoea upon the preload capacity could at least partly explain LV systolic dysfunction in patients with OSA.

High blood pressure (HBP) is considered as marker of increased afterload. The relation between OSA and BP is complex because of the vicious circle. Indeed, beside of the afterload role of BP which potentiate the effect of apnoea, OSA is an important risk factor for hypertension, according to the Joint Committee on the Detection and Management of Hypertension^[28], and represent the most common secondary cause of resistant hypertension^[29]. The nocturnal hypertension or “non dipper profile” is the most common clinical presentation of hypertension due to OSA. Moreover a dose response relationship seems to exist between HBP and OSA^[5,21]. For Laaban *et al* the main mechanism of HBP is systemic vasoconstriction due to sympathetic hyperactivity causing nocturnal hypoxia and microarousals.

Sympathetic nerve activity

Sympathetic nerve activity increases and reaches its peak level at the end of the apnoea^[30] and was reported in clinics to inhibit the recovery of LV systolic function in patients with OSA. One of the mechanisms is the imbalance between oxygen demand and supply created by systemic and coronary vasoconstriction. As sympathetic tonus is one of the main pathophysiological actors both in HF and CAD, this appears as the obvious culprit pathway linking OSA and cardiovascular diseases^[31].

Endothelial dysfunction

Impaired endothelium dependent vascular relaxation is a marker of atherosclerosis and cardiovascular disease. OSA has been found to be a factor involved in endothelial dysfunction. Subjects with OSA had lower endothelium dependent flow mediated dilatation (FMD) on the brachial artery studied with Doppler ultrasound^[22] and an impairment of resistance vessel endothelium dependent vasodilatation^[32]. They

have also increased intracellular reactive oxygen species production due to repetitive oxygen desaturation/reoxygenation^[33,34] and reduced antioxidant capacity^[35]. In clinical settings the abnormally positive balance in reactive oxygen species metabolites increases the infarct size.

The role of inflammation in vascular dysfunction is additional with oxidative stress^[36,37]. Levels of CRP and IL-6 and spontaneous production of IL-6 by monocytes are elevated in patients with OSA^[38]. All these factors could explain the involvement of OSA in the metabolic syndrome.

The effect of OSA on microvascularisation and myocardial ischemia remains controversial. Some studies found no differences between OSA-positive and OSA-negative groups with regard to the percentage of patients with <70% ST-segment resolution, myocardial blush grade or corrected TIMI frame count. On the other hand Nakashima *et al*^[39] reported a higher incidence of impaired ST segment resolution in OSA patients.

OSA may induce also coagulation abnormalities with blood hypercoagulability and increased platelet aggregation^[40].

OSA COULD WORSEN THE CORONARY ARTERY DISEASE

OSA inhibits the recovery of left ventricular function in patients with AMI^[41]. In an important paper, patients admitted for the first STEMI (left ventricular main artery or right coronary artery), were subdivided into two groups, with or without OSA. 86 consecutive patients were evaluated initially during the emergency PCI and with a further PCI three weeks later. Improvement of LVEF and other performance indexes was significantly lower in patients with OSA (53+/-12% became 59+/-13% in controls versus 54+/-12% became 52+/-12% in patients with OSA, and multiple regression analysis showed that the presence of OSA was independently associated with a less improvement of LVEF ($P=0.008$, level of significance similar to the anterior localization).

Ejection fraction was evaluated by ventriculography during the first PCI and repeated 21 days later. The patients with OSA presented a worse recovery. Similarly in a small population of 120 patients, the patients with a severe OSA presented significantly more clinical outcomes (death, reinfarction, stroke revascularisation, hospitalizations for HF)^[11].

HOW CARDIAC REMODELING HAS BEEN EXPLORED AFTER AMI?

The changes in ventricular size, shape and thickness that occur after AMI are referred to ventricular remodeling. OSA is also associated with alteration of structural and functional cardiac parameters^[23]. First, the main consequence of OSA is LV dysfunction that is the main predictor of mortality following AMI^[42]. In Laaban *et al*^[21] LV systolic dysfunction as defined as LVEF <50% is noted in 7.7% of OSA patients. This was also well illustrated in animal models with decreased fractional shortening^[43]. Results concerning the effects of OSA on diastolic function remained unclear because of the interaction with HBP. Indeed, Niroumand *et al*^[44] showed that OSA was not associated with increased left ventricular mass (LVM) or impaired left ventricular diastolic function (LVDF) independently of obesity, hypertension or age.

As systolic and diastolic dysfunction frequently coexist, the left ventricular myocardial performance index (MPI) has been shown as a reproducible, widely applicable and a simple non invasive method

for the estimation of LV global function in patients with OSA. A positive correlation between MPI and the severity of OSA has been demonstrated^[45]. The severity of OSA was significantly correlated to structural and functional remodeling of left atrium (LA). The OSA group was characterized by larger LA volume and by an impaired LA wall compliance and passive contraction^[46].

LVM and left ventricular hypertrophy (LVH)^[47] were linked to the severity of OSA and are established as an important risk factor for cardiovascular morbidity and mortality^[48]. SDB defined by AHI index was associated by Chami *et al*^[49] with echocardiographic evidence of increased LV mass and reduced LV systolic function. Hedner *et al*^[50] were the first to consider this direct link showing that LVM was around 15% higher in normotensive OSA patients than in normotensive control subjects. Nevertheless, we can wonder whether there is really an independent link between OSA and LVM, because OSA patients are more often hypertensive, obese or diabetic, all well characterized risk factors for LVH. For example, Niroumand *et al*^[44] demonstrated higher LVM in OSA patients but with confounding factors as listed before.

The prevalence of right ventricular hypertrophy by echocardiography in sleep apnoea is 71% according to Berman *et al*^[51] with nevertheless a large variability in the literature due to the use of different criteria. Sanner *et al*^[52] demonstrated using radionuclide ventriculography that OSA was independently associated with depressed right ventricular ejection fraction. Pulmonary hypertension and right ventricular (RV) dysfunction have been well described in OSA^[53]. Concomitant chronic pulmonary disorders were often associated to OSA to cause right heart failure. Untreated chronic obstructive pulmonary disease (COPD) co-existing with OSA, also known as overlap syndrome, has higher cardiovascular mortality than COPD alone but its underlying mechanism remains unclear. Untreated overlap syndrome may cause more extensive RV remodeling than COPD alone^[54].

In the study of Buchner *et al*^[55] cardiovascular magnetic resonance imaging (CMRI) as the accepted gold standard for the assessment of left ventricular systolic function was performed to first determine LVEF with the lowest possible variability of measurement and then to relate changes in the severity of AHI to changes in LVEF. The assessment of these parameters can be also done by transthoracic echocardiography (TTE) but to intend to demonstrate an effect on LVEF, studies using echocardiography require a seven fold larger sample size compared to studies using CMRI^[56]. Other largely used methods were angiographic or isotopic ventriculography.

COULD OSA EXERT AN EFFECT ON CARDIAC REMODELING AFTER AMI?

Taken these pathophysiological considerations together, it could be hypothesized that OSA may have a role in cardiac remodeling after AMI and especially in relationship with the increased sensitivity of the reperfused tissue to all underlying mechanisms involved in OSA (mechanical or haemodynamic factors, reactive oxygen species balance, sympathetic nerve activity, endothelial dysfunction...). It is important for interpretation of results to catch attention on two characteristics of studies. First, regarding the ischemic CAD several studies were performed without differentiating stable or unstable angina and AMI. They focused on AMI and the involvement of OSA in this acute phase, by studying its consequences on cardiac remodeling which can be the first step leading to the development of HF. Secondly, although the generally accepted AHI, the cut-off value that can show worse clinical and functional outcomes is not yet

determined, the chosen different definitions of AHI in each study are crucial for the interpretation.

Nakashima *et al*^[16] showed that OSA inhibits the recovery of LV function in patients with AMI. Similarly, Buchner *et al* showed first in 2012 that an improvement of LVEF is associated with an alleviation of OSA. The 40 studied patients with AMI and who underwent PCI, had first within 5 days and then within 12 weeks after the event a polysomnography (PSG), and an assessment of cardiac function by CMRI. AHI was significantly more reduced in the group of patients who improved their LVEF compared with the group without improvement of LVEF (-10 ± 3 vs 1 ± 3 events/h). This was correlated to a significant alleviation of obstructive events which were well distinguished in the study from the central obstructive apnoea. In 2013, Buchner *et al*^[55] demonstrated that sleep disorder breathing was associated with less myocardial salvage and a smaller reduction in infarct size. They enrolled patient with AMI and PCI stratified classically with the AHI (cut-off 15 events/h), who underwent CMRI to define salvaged myocardium and infarct size within first three to five days and then at 3 months after AMI. They showed in patients with OSA a larger final infarct size (23% vs. 12%, $p < 0.001$), smaller reduction in infarct size (0.3% vs 6.5%, $p < 0.001$), lower final LVEF (48% vs 54%, $p = 0.023$). Some criticisms have been raised on the study of Buchner *et al*^[57]: the threshold chosen to assess an improvement or not in LVEF was 5% which is questionable as well as the lack of precision regarding the body weight and its variation during the follow up, the sleep position, the gender, smoking habit, the presence of overlap syndrome and sleep efficiency. Obesity is known as an important attribute in patients with OSA and can really influence the treatment.

In the study of Grandi *et al*^[58], studying the effect of continuous positive airway pressure (CPAP) on OSA, 20 patients with OSA with decreased body weight showed diastolic BP decrease, LV hypertrophy regression and diastolic function improvement, whereas, despite similar respiratory improvement, BP and LV parameters were unchanged in the 21 patients with body weight unchanged or increased. In addition, smoking reduction after an acute cardiac event is usually accompanied by improvement in other behaviours like exercise, alcohol consumption and alterations in diet that may improve underlying sleep disordered breathing. Subjective long sleepers with cardiac heart failure (CHF) have poor sleep efficiency. They showed that sleep efficiency assessed by PSG was demonstrated to be an independent predictor for death in the multivariable model after accounting for the significant confounders age, LVEF, cause of CHF and NYHA class^[59]. Hence in addition to OSAS, other sleep-related abnormalities such as sleep duration/deprivation, insomnia with objective short sleep duration, and restless legs syndrome may impact on blood pressure control that may modify prognosis of CVD *per se*.

COULD THE LINK BE CLEARER IN PATIENTS WITH SEVERE OSA?

Interestingly, current data suggest that the impact of OSA on CAD could be more pronounced in severe form, with AHI ≥ 30 (60,61). It has been well demonstrated that group with severe OSA (AHI ≥ 30) was linked with a negative prognostic impact for this group of patients. Indeed, in the study of Lee (10) finding a high incidence (42%) of severe undiagnosed severe OSA in patient with STEMI, the incidence of major adverse events was significantly higher in the severe OSA group (15.9% vs 3.3%). In addition the severe OSA group was associated with lower event-free survival

rate at 18 months. In a recently published prospective longitudinal epidemiological study including more than 4,000 patients^[61], patients with AHI ≥ 30 events/h were more likely to develop CAD than those with AHI <5 events/h. Regarding the recovery of LV function after AMI, in the study of Nakashima *et al* patients with AHI <5 events/h and $5 \leq \text{AHI} < 15$ events/h showed similar recovery of LV function. While patients with $15 \leq \text{AHI} < 30$ events/h and AHI ≥ 30 events/h showed a poor improvement of LV function compared with patients with AHI <5 events/h.

The precise mechanisms underlying this “threshold effect” remain to be investigated.

COULD CPAP EXERT AN IMPACT ON CARDIAC REMODELING?

Medical therapies as angiotensin-converting enzyme (ACE) inhibitors, β -blockers attenuate cardiac remodeling and improve the prognosis of patients after AMI. Early revascularization remains the cornerstone of the management of the patients. However, despite such improvements, the risk of LV remodeling and developing of HF after AMI remains high. There is certainly a place for non-pharmacological strategies in addition to current medical management.

Beyond CAD, it has been demonstrated that CPAP could be involved in cardiac reverse remodeling. Regular use of CPAP has been shown to be correlated with reduction in CV mortality, especially in patients with HF^[62]. This effect was mainly explained through the mild lowering of blood pressure. Preliminary studies suggested an improvement of LVEF^[23,63] and a decrease in LV hypertrophy^[64]. MRI could be particularly useful for the assessment of right cavities (especially in obese patients with OSAS) and has been reported to be able to show positive effects on right cardiac chambers^[65]. By the way CPAP has been reported to decrease the right ventricular systolic pressure^[53].

In a prospective study^[66] in 47 patients with OSAS, concomitant assessment of biomarkers including C- Reactive protein (CRP), NT-proBNP, troponins and cardiac imaging (echography and magnetic resonance imaging) was performed to evaluate the cardiac remodeling over 1 year, after the CPAP treatment. Interestingly, these patients were known to present a OSAS but no cardiac diseases. Although the biomarkers were not statistically significantly different over time, imaging showed significant differences. The echocardiographic study demonstrated an improvement in right ventricular end-diastolic diameter (30 ± 4 mm versus 41 ± 3 mm, $p < 0.05$), left atrial volumes. CMRI showed similar results but also a significant decrease in ventricular mass (137 ± 6 g/m² versus 159 ± 9 g/m²), corroborating a ventricular reverse remodeling not only on the volumes but also on the structural anatomy. This positive impact of CPAP was even observed as early as the 3rd month^[66]. Interestingly, this study also showed improvement in diastolic parameters. In other words, cardiac reverse remodeling has been clearly demonstrated mainly in right cardiac chambers in patients without cardiac disease and treated with CPAP. Similarly, CPAP could improve diastolic function and filling pressures, leading to reverse remodeling on left cardiac chambers in patients with structural changes in the left ventricle such as patients with acute myocardial infarction.

Supporting this suggestion, Colish *et al*^[66] showed by TTE and CMRI that CPAP treatment is associated with a reduction in right atrial and ventricular size as well as a reduction in LVM as early as three months with progressive improvement in cardiovascular remodeling over 1 year. The same period of

treatment was reported by Koga *et al*^[67] who demonstrated that three months of CPAP treatment in patients without CAD resulted in significant decreases in left ventricular mass index (LVMI) and the proportion of cases with concentric hypertrophy (both $p = 0.025$). This treatment which significantly reduced the LV afterload was effective in the improvement of LVEF in OSA patients with dilated cardiomyopathy^[62]. Therapy with continuous positive airway pressure has been demonstrated to improve cardiopulmonary hemodynamic in patients with OSA and may reverse the endothelial cell dysfunction. It has been proposed that CPAP could exert beneficial effects on long term cardiovascular outcomes^[60,68,69], by this way.

Taken all these considerations together, very early diagnosis of OSA after AMI could be clinically important because CPAP could attenuate the adverse cardiovascular effects of OSA. Importantly, it should be kept in mind that these patients are poorly symptomatic despite the high level of AHI^[15] and are not detected by self reports of sleepiness or composite risk of. However, the question of ideal timing of an investigation of OSA after an ACS remains unresolved. Indeed, the findings of early done PSG are discussed because OSA may be transient and linked to the acute phase of myocardial infarction. Especially in case of AMI, central disorders could be transient and disappear in the following months. The relationship remains under debate^[70,71]. In the study of Schiza *et al*^[12] the prevalence of OSA (AHI >10 events/h) in patients with ACS was 62% but did not persist 6 months later with a prevalence of 21%. It may appear important to target the population of patients with severe OSA, the group of very high cardiovascular risk. In the Buchner's study^[13] 31% of OSA patients shifted from a moderate-to-severe degree of sleep apnoea to mild or no sleep apnoea (AHI <15). By contrast, Bahammam *et al*^[72], showed a high prevalence of OSA persisting at 6 months after the index acute cardiac event. Furthermore, in patients with stable CAD, treatment of coexisting OSA by CPAP reduces systolic blood pressure, HR and improves LV systolic function with significant reduction in LV end systolic dimension^[62]. The treatment is associated with a decrease in the occurrence of new cardiovascular events^[68].

CONCLUSION

There is a complex relationship between OSA and CAD. Moreover this is a frequent clinical concern. OSA exerts detrimental effects on LV remodeling in patients with AMI, leading to heart failure and a worse cardiovascular prognosis. CPAP might represent an adjunction in the global management of patients with AMI.

Among the main concerns future investigations have to define clearly the targeted population (patients with NSTEMI or by contrast patients with large STEMI ?), study precisely the sleep disorders (is the AHI enough ?), propose the optimal window to diagnose OSA, the optimal way to treat OSA, the clinical outcomes having to be explored, the comorbidities and concomitant treatments and so on. The cost-effectiveness and the duration of treatment remain unsolved concerns. The first step appears to better know and understand the OSA disorders in the field of cardiovascular disease.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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