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Obstructive sleep apnoea and atrial fibrillation: are we on time?!

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Editorial on 'Cardiac remodelling in patients with AF and OSA' by T-E Hunt and coauthors

The study by Hunt and coauthors focuses attention on possible positive cardiac remodelling following continuous positive airway pressure (CPAP) treatment. They analyse patients with paroxysmal atrial fibrillation (AF), mainly treated with pulmonary vein isolation (PVI), randomised to CPAP treatment or standard care, finding no significant differences in left ventricular (LV) ejection fraction, LV global longitudinal strain, left atrial volume index, left atrial reservoir strain and right atrium area.

These results seem to raise a doubt on the efficacy of CPAP treatment for obstructive sleep apnoea (OSA). This point needs to be clarified.

CPAP is the first-line treatment for OSA. Benefits on sleep disorders are well demonstrated, reducing the count of apnoea and hypopnoea per hour of sleep and the hypoxic and the hypercapnic burden. Nevertheless, despite encouraging results in observational studies, CPAP treatment has proven a neutral effect on secondary cardiovascular prevention in randomised controlled trials (RCTs).[1–3]

OSA has been involved in cardiovascular diseases with many pathophysiological mechanisms and, in particular, it acts both as a trigger and as a negative factor for structural modification in the setting of cardiac arrhythmias.

Specifically, recurring apnoea–hypopnoea episodes, cortical arousals from sleep, and sleep fragmentation result in sympathetic overactivity and increased serum catecholamine levels, stimulating both heart rate and blood pressure. Additionally, 1) intermittent hypoxia promotes local and systemic inflammation, 2) oxidative stress and endothelial dysfunction induce atherosclerosis and 3) intrathoracic pressure fluctuation induces mechanical damage in vascular and cardiac structure and 4) negative intrathoracic pressure impairs LV filling and reduce stroke volume by means of increased venous return.[4]

All these conditions contribute to structural cardiac remodelling, including LV hypertrophy and left atrial enlargement and, over time, can lead to diastolic heart failure.[5]

Moreover, a final pathway leading to AF could be found in the modification of electrical proprieties of the atria. Acute atrial stretch shortens the effective refractory period and slows the conduction velocity across the pulmonary vein–left atrium (LA) junction.[6] Similarly, strongly negative intrathoracic pressure activates intrathoracic baroreceptors, inducing autonomic reflex responses, which reduce the refractory period.[6]

In this contest, the study by Hunt has two specific strength points: the use of implantable loop recorders to assess AF episodes and burden, and the good compliance of patients to CPAP treatment.

The findings of the study are in contrast with several non-RCTs and observational studies showing a favourable relationship between reduction in sleep-disordered breathing and avoiding AF recurrence. Of note, a positive effect of CPAP has been also described in reversing atrial remodelling evaluated by increased atrial voltage, improved conduction velocity and reduction of complex ECGs at 6 months.[7]

In our opinion, the study by Hunt stimulates our thinking about some questions.

- Are we treating the right patients?

OSA severity can be assessed by means of different meausures, nevertheless the count of apnoea-hypopnea index (AHI) remains the official one. This study enrolled patients with with an AHI≥15/h, while atrial reverse remodelling has been shown in patients with a more severe disease (AHI≥45/h).[7] The AHI does not consider the hypoxic and hypercapnic burden related to increased cardiovascular events. An interesting research goal into the sleep medicine field could be to establish if OSA detrimental effects are more serious in specific cardiovascular risk profiles, OSA is particularly detrimental.[8]

- Few months of CPAP treatment might not be enough to reverse the negative cardiac remodelling of AF, moreover if this positive remodelling would occur in patients that show poor improvement in AF burden and blood pressure. Are we treating our patient with the correct CPAP parameters?

CPAP treatment might be tricky even when an adequate adherence to CPAP treatment is achieved, as in the study of Hunt and co. differently from other recent RCT, CPAP treatment might be tricky. Indeed, CPAP has emodynamic effects per se and might impact cardiac output in a deleterous way in some subject.[9] Moreover, despite reducing nocturnal hypoxia burden and sleep fragmentation, CPAP, in particular greater CPAP pressure levels, may perpetuate rather than ameliorate inflammatory processes in OSA.[10]

Have we waited long enough?

The deterioration in cardiac structure and electrophysiology that leads to AF takes years to develop. Few months of CPAP treatment might not be enough to reverse the negative cardiac remodelling of AF, especially if this positive remodelling would occur in patients with small variation in AF burden, episodes and blood pressure. However, we might expect that CPAP, reducing recurrent nocturnal cardiovascular stress, will be able to impact on further arrhythmias. In a study with longer follow up (48 months), OSA treatment after PVI was associated to lower blood pressure, LV mass, LA size and to paroxysmal rather than persistent AF compared with untreated OSA patients.[11]

Overall, it seems that the time needed to analyse AF recurrence is much shorter than that for cardiac remodelling. From this perspective, patient selection could be the most important limitation. Indeed, it is well known that benefits could be poor, both, in healthy patients without left atrial enlargement or LV impairment and in patients with more severe conditions, whose negative remodelling is too advanced for recovery.

All these speculations suggest the need for more dedicated understanding of comorbid AF in patients with OSA and patients with OSA in AF. Moreover, the recent evolution in OSA therapy also opens the field for a personalised treatment approach.[12]

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