Canadian Journal of Cardiology 31 (2015) 909–917

Review

Sleep-Disordered Breathing and Coronary Artery Disease

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ABSTRACT

Coronary artery disease (CAD) is one of the most frequent diseases in industrial nations. Despite significant advances in diagnosis and therapy, CAD and its long-term consequences are important contributors to morbidity and mortality. Therefore, in addition to management of traditional CAD risk factors, there are continued efforts to evaluate other factors and comorbidities that might contribute to the development and progression of CAD. One such factor is sleep-disordered breathing (SDB), which is characterized by repetitive apneas, arousals from sleep, and intermittent hypoxia. There is increasing evidence that SDB is a risk factor for CAD. In the early phase after myocardial infarction (MI) the heart might be in a vulnerable state sensitive to the negative consequences of SDB, including increased cardiac workload and endothelial dysfunction, which might ultimately lead to a mismatch between oxygen demand and supply. Despite successful percutaneous coronary intervention, patients with acute MI and SDB have prolonged myocardial ischemia, less salvaged myocardium, and impaired left and right ventricular remodelling compared with those without SDB, all of which predispose to heart failure. Suppression of SDB with positive airway pressure therapy in the early phase after MI is feasible. However, whether treatment of SDB with positive airway pressure will be an effective non-pharmacological treatment approach that will prevent the development of heart failure after MI remains to be determined and is the subject of current investigations.

RÉSUMÉ

La maladie coronarienne (MC) est l'une des maladies les plus fréquentes dans les pays industrialisés. En dépit d'avancées considérables dans le diagnostic et le traitement, la MC et ses conséquences à long terme sont des facteurs contributifs importants de la morbidité et de la mortalité. Par conséquent, outre la prise en charge des facteurs de risque traditionnels de la MC, les efforts pour évaluer d'autres facteurs et comorbidités qui contribueraient au développement et à la progression de la MC se poursuivent. Parmi ces facteurs, l'on retrouve les troubles respiratoires du sommeil (TRS), qui sont caractérisés par les apnées répétitives, les périodes d'éveil durant le sommeil et l'hypoxie intermittente. De plus en plus de données probantes montrent que les TRS représentent un facteur de risque de MC. À la phase précoce après l'infarctus du myocarde (IM), le cœur serait dans un état vulnérable et donc sensible aux conséquences négatives des TRS, dont l'augmentation du travail du cœur et la dysfonction endothéliale, qui conduiraient finalement à un déséquilibre entre besoins et apports en oxygène. En dépit du succès de l'intervention coronarienne percutanée, les patients souffrant d'IM aigu et de TRS comparativement à ceux n'ayant pas de TRS ont une ischémie myocardique prolongée, un potentiel de sauvetage moindre du myocarde et une détérioration du remodelage ventriculaire gauche et droit, qui prédisposent tous à l'insuffisance cardiaque. La suppression des TRS par pression positive expiratoire continue à la phase précoce après l'IM est réalisable. Cependant, il reste à déterminer si le traitement des TRS par pression positive expiratoire continue, qui fait l'objet des études actuelles, sera une approche de traitement non pharmacologique efficace pour prévenir le développement de l'insuffisance cardiaque après l'IM.

Coronary artery disease (CAD) is one of the most common causes of morbidity and mortality in industrialized nations.[1] The lifetime prevalence of CAD in adults aged ≥ 40 years is estimated to be 49% in men and 32% in women.[2] Projections show that prevalence of CAD will have increased by approximately 18% by 2030.[1]

CAD occurs secondary to arteriosclerotic alterations of the epicardial coronary arteries. The most important modifiable risk factors for arteriosclerosis are hypercholesterolemia, arterial hypertension, diabetes mellitus, visceral obesity, and smoking. However, nonmodifiable risk factors such as age and male sex also play an important role. The coexistence of multiple risk factors disproportionately increases the risk of developing CAD.

There is a bidirectional relationship between sleep-disordered breathing (SDB) and CAD.[3] Although SDB is a

Received for publication December 10, 2014. Accepted March 25, 2015.

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See page 915 for disclosure information.

http://dx.doi.org/10.1016/j.cjca.2015.03.032

risk factor for CAD and might contribute to further disease progression,[4-6] impairment of cardiac function by CAD contributes to the severity of SDB. The presence of SDB potentially plays a major role in the early phase after myocardial infarction (MI), when the heart might be in a vulnerable state and therefore sensitive to the consequences of SDB such as increased cardiac workload, endothelial dysfunction, excessive desaturations, and ultimately to a mismatch of myocardial oxygen demand and supply.

Pathophysiology of Obstructive and Central Sleep Apnea

There are 2 main types of SDB in patients with CAD: obstructive sleep apnea (OSA) and central sleep apnea (CSA).[7] Most patients with SDB and impaired cardiac function have OSA and CSA.[8] OSA is characterized by repetitive collapses of the upper airway during sleep and continued respiratory effort during apnea (Fig. 1A). Apnea is usually terminated by an arousal from sleep, resulting in sleep fragmentation. Arousals allow the upper airway to open again and normal ventilation to resume. Inspiratory efforts against the occluded pharynx during obstructive apneas generate exaggerated negative intrathoracic pressure[9] that increases left ventricular transmural pressure and, as a result, afterload (Fig. 1A and B).[9] Additional acute consequences of OSA include repetitive oxygen desaturations, sympathetic activation, and increased heart rate and blood pressure (Fig. 1A and B).[9,10]

The likelihood is that a cardiac patient would have CSA increases as the extent of cardiac dysfunction increases.[7] CSA in patients with impaired cardiac function is usually related to pulmonary congestion, stimulation of pulmonary irritant receptors, increased sensitivity to carbon dioxide, and chronic hyperventilation.[11] In contrast to OSA, there is no upper airway obstruction and no respiratory effort during central apneas. CSA in patients with impaired cardiac function typically shows a characteristic periodic breathing pattern with a waxing and waning of tidal volume (Cheyne Stokes Respiration).[11] Similar to OSA, CSA causes intermittent nocturnal hypoxia, arousals from sleep, repetitive sympathetic activation, and swings in heart rate and blood pressure, but does not generate negative intrathoracic pressures.[12]

Prevalence of SDB in CAD With and Without Impaired Cardiac Function

Approximately 2%-7% of adult women and 3%-14% of adult men without overt heart disease have coexisting SDB.[13] In the presence of cardiovascular disease the prevalence of SDB is significantly greater. Approximately 50% of patients with CAD have SDB of an at least a moderate degree (Apnea-Hypopnea Index [AHI] $\geq$ 15 per hour).[14-16] In patients with stable CAD and preserved cardiac function most apneas are of obstructive origin.[14-16] In patients with acute MI and impaired cardiac function the prevalence of moderate or severe SDB (AHI $\geq$ 15 per hour) is slightly greater (55%) than that in patients with CAD and preserved cardiac function.[7] In this group of patients with impaired cardiac function secondary to acute MI (mean N-terminal pro-brain natriuretic peptide level, 1572 pg/mL), approximately half of the patients with

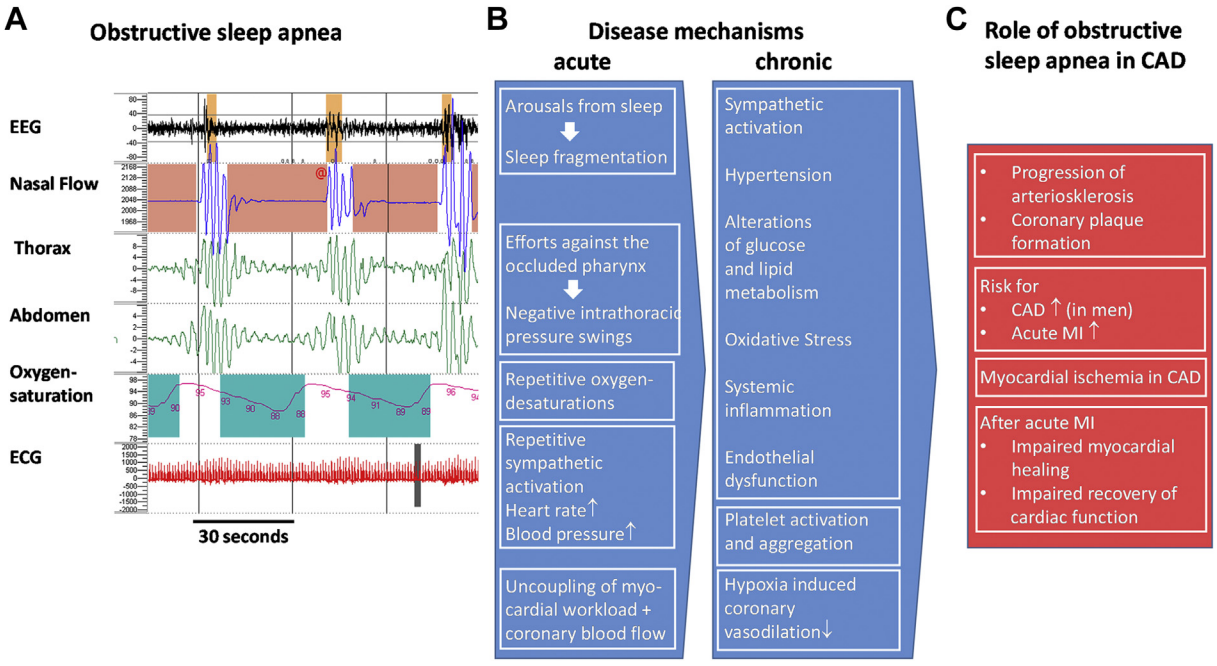

Figure 1. (**A**) Polysomnographic recording of a patient with severe obstructive sleep apnea: the example shows obstructive apneas with cessation of nasal air flow for > 10 seconds and continued respiratory effort in the thoracic and abdominal leads. Apneas end with an arousal from sleep (electroencephalogram [EEG]) and are associated with oxygen desaturations and with repetitive increases in heart rate (electrocardiogram [ECG]). (**B**) Summary of acute and chronic disease mechanisms for sleep-disordered breathing and cardiovascular disease. (**C**) Summary of the potential role of obstructive sleep apnea in coronary artery disease (CAD), including acute myocardial infarction (MI).