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Clinical Research

Effect of Nocturnal Intermittent Hypoxia on Left Atrial Appendage Flow Velocity in Atrial Fibrillation

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ABSTRACT

Background: The mechanism underlying the associations of sleep-disordered breathing (SDB) with stroke and atrial fibrillation (AF) is not well established. We explored the relationship between nocturnal intermittent hypoxia, a marker of SDB, and left atrial (LA)/LA appendage (LAA) function among AF patients.

Methods: We evaluated 134 consecutive AF candidates for catheter ablation (age, 59.6 ± 9.4 years; body mass index [BMI], 24.8 ± 3.2; **C**ongestive Heart Failure, **H**ypertension, **A**ge (≥75 years), **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge (65-74 years), **S**ex (Female) (CHA_2DS_2-VASc) score, 1.2 ± 1.1, paroxysmal AF, n = 83) using nocturnal pulse oximetry, a noninvasive screening method for nocturnal intermittent hypoxia. Based on 3% oxygen desaturation index (3% ODI), patients were divided into nocturnal intermittent hypoxia (3% ODI > 15; n = 32) and control groups (3% ODI ≤ 15; n = 102).

Results: The nocturnal intermittent hypoxia group demonstrated significantly higher weight, BMI, **C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack ($CHADS_2$) and CHA_2DS_2-VASc scores, serum hemoglobin A1c and plasma brain natriuretic peptide levels, LA size, and prevalence of hypertension, vascular disease, and sick sinus syndrome. Echocardiographically, nocturnal intermittent hypoxia was associated with a higher grade of

RÉSUMÉ

Introduction : Le mécanisme qui sous-tend l'association entre les troubles respiratoires du sommeil (TRS), et l'accident vasculaire cérébral et la fibrillation auriculaire (FA) n'est pas bien établi. Nous avons examiné le lien entre l'hypoxie intermittente nocturne, un marqueur des TRS, et le fonctionnement de l'oreillette gauche (OG) et de l'appendice auriculaire gauche (AAG) chez les patients souffrant de FA.

Méthodes : Nous avons évalué l'ablation par cathéter chez 134 candidats consécutifs souffrant de FA (âge, 59,6 ± 9,4 ans; indice de masse corporelle [IMC], 24,8 ± 3,2; score CHA_2DS_2-VASc [**C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge (65-74 years), **S**ex (Female), soit l'insuffisance cardiaque congestive, l'hypertension, l'âge, le diabète, l'accident vasculaire cérébral/l'ischémie cérébrale transitoire, la maladie vasculaire, l'âge (65 à 74 ans), le sexe (féminin)], 1,2 ± 1,1, FA paroxystique, n = 83) à l'aide de l'oxymétrie de pouls nocturne, une méthode de dépistage non invasive de l'hypoxie intermittente nocturne. À partir de l'indice de désaturation en oxygène de 3 % (IDO de 3 %), les patients ont été divisés comme suit : hypoxie intermittente nocturne (IDO de 3 % > 15; n = 32) et groupes témoins (IDO de 3 % ≤ 15; n = 102).

Résultats : Le groupe souffrant d'hypoxie intermittente a démontré un poids, une IMC, un score $CHADS_2$ (Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke/Transient Ischemic Attack, soit l'insuffisance

Sleep-disordered breathing (SDB) is a common but largely undiagnosed disease that is associated with increased cardiovascular morbidity and mortality.[1] SDB patients tend to be older, with a higher body mass index (BMI), and increased prevalence of hypertension and diabetes.[2] These risk factors for SDB are also common in stroke and atrial fibrillation (AF).[3,4] Approximately 50% of AF patients were reported to have SDB,[5] and SDB is associated with increased incidence of AF.[6] Severe SDB was also observed in 29% of Japanese stroke patients[7] and was also associated with stroke.[8] AF is also an established major risk factor for stroke and quintuples stroke incidence.[9] Thus, SDB, AF, and stroke are closely related, but studies on the association among these pathologies have been limited thus far. Left atrial (LA) appendage (LAA) has been recognized as the embolic source in 90% of cardiogenic stroke cases.[10] Because SDB is associated with adverse cardiac remodelling,[11-13] we hypothesized that SDB could be associated with reduced LA/LAA function in patients with AF.

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spontaneous echo contrast and low LAA flow velocity. Multiple regression analysis adjusted for type of AF, CHA_2DS_2-VASc score, BMI, plasma brain natriuretic peptide level, LA size, and rhythm on echocardiography revealed that 3% ODI was a factor independently associated with LAA flow velocity ($\beta = -0.184$; 95% confidence interval, -0.818 to -0.006).

Conclusions: Nocturnal intermittent hypoxia was an independent determinant for low LAA flow velocity in patients with AF, suggesting that the connection between SDB and LAA function might underlie the association of AF with stroke.

cardiaque congestive, l'hypertension, l'âge, le diabète, l'accident vasculaire cérébral/l'ischémie cérébrale transitoire) et un score CHA_2DS_2-VASc, une concentration sérique d'hémoglobine A1c et une concentration plasmatique du peptide natriurétique de type B, une taille de l'OG, et une prévalence de l'hypertension, de la maladie vasculaire et de la maladie du nœud sinusal significativement plus élevés. Échocardiographiquement, l'hypoxie intermittente nocturne a été associée à un degré plus élevé de contraste échographique spontané et à une vélocité du flux de l'AAG. L'analyse de régression multiple ajustée du type de FA, du score CHA_2DS_2-VASc, de l'IMC, de la concentration plasmatique du peptide natriurétique de type B, de la taille et du rythme de l'OG à l'échocardiographie a révélé que l'IDO de 3 % était un facteur indépendamment associé à la vélocité du flux de l'AAG ($\beta = -0{,}184$; intervalle de confiance à 95 %, $-0{,}818$ à $-0{,}006$).

Conclusions : L'hypoxie intermittente nocturne était un déterminant indépendant de la faible vélocité du flux de l'AAG chez les patients souffrant de FA, ce qui suggère que le lien entre les TRS et le fonctionnement de l'AAG pourrait sous-tendre l'association entre la FA et l'accident vasculaire cérébral.

Despite the importance of SDB in managing AF,[14-19] the prevalence of undiagnosed SDB is surprisingly high, as shown in the Wisconsin Sleep Cohort Study.[20] Although polysomnography (PSG) has been used as a standard for the diagnosis of SDB, referral to sleep study is often difficult, inconvenient, and expensive. Performing fully equipped sleep studies in all AF patients is not feasible. Here, we chose to perform nocturnal pulse oximetry to detect nocturnal intermittent hypoxia, a surrogate marker for SDB,[21,22] as a simple screening utility to identify undiagnosed SDB in all patients hospitalized for AF catheter ablation in our facility.

In the present study we aimed to estimate the prevalence of nocturnal intermittent hypoxia among AF catheter ablation candidates using nocturnal pulse oximetry and to clarify its relationship with background characteristics, and laboratory, echocardiographic, and Holter monitoring data. Additionally, we assessed the association of LA/LAA function and nocturnal intermittent hypoxia.

Methods

The study protocol conformed to the ethical guidelines of the Declaration of Helsinki of 1975 as reflected in a priori approval by our institution's human research committee. All patients provided written informed consent to participate.

Study population

One hundred thirty-four consecutive AF patients who were candidates for catheter ablation in our facility were evaluated retrospectively. The indication for AF catheter ablation was determined according to symptoms due to AF attacks, anti-arrhythmic drug resistance, or patient request, regardless of the type of AF. We excluded patients who were previously diagnosed with SDB and treated with continuous positive airway pressure (CPAP). Patients with chronic obstructive pulmonary disease who required home oxygen therapy were not included in this study. Patients who were contraindicated for anticoagulation or with pre-existing thrombi in the LA were also excluded.

Nocturnal intermittent hypoxia

Nocturnal pulse oximetry was performed to identify the presence of nocturnal intermittent hypoxia in all patients 1 day before ablation. Arterial oxyhemoglobin saturation was recorded using a finger probe at a 1-Hz sampling frequency and 5-second average time (PULSOX-Me300; Teijin Pharma, Tokyo, Japan). These recordings were scored using specialized software (DS-Me; Teijin Pharma, Tokyo, Japan). Because the measurement time of pulse oximetry is often longer than the true total sleep time, we used a single-night sleep log to exclude waking time from the analysis and minimize the potential for overestimating total sleep time. We used oxygen desaturation index $\geq$ 3% (3% ODI), the frequency of episodes of 3% desaturation per hour, as an indicator of nocturnal intermittent hypoxia. Based on 3% ODI, patients were divided into nocturnal intermittent hypoxia (3% ODI $>$ 15) and control groups (3% ODI $\leq$ 15). The validity of pulse oximetry has been previously reported based on synchronous overnight recording of pulse oximetry and standard PSG, and its sensitivity and specificity were 85% and 100%, respectively, for detecting apnea hypopnea index of $\geq$ 20 determined using PSG and a cutoff threshold of 3% ODI = 15.[23-25]

Parameters for analysis

Patient background data including age, height, weight, BMI, **C**ongestive Heart Failure, **H**ypertension, **A**ge, **D**iabetes, **S**troke/Transient Ischemic Attack ($CHADS_2$) score,[26] **C**ongestive Heart Failure, **H**ypertension, **A**ge ($\geq$75 years), **D**iabetes, **S**troke/Transient Ischemic Attack, **V**ascular Disease, **A**ge (65-74 years), **S**ex (Female) (CHA_2DS_2-VASc) score,[27] paroxysmal AF duration from initial diagnosis to ablation, duration of persistent AF, number of anti-arrhythmic drugs before ablation, number of ablation sessions, type of AF, history of dyslipidemia, and sick sinus syndrome (SSS) were collected and compared between groups. Type of AF was classified as paroxysmal (persisting $<$ 1 week), persistent (persisting longer than 1 week and $<$ 1 year), or longstanding persistent (persisting longer than 1 year) according to American College of Cardiology/American Heart Association/Heart