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Impact of sleep disordered breathing on carotid body size

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ABSTRACT

We tested the hypotheses that: (1) carotid body size can be measured by computed tomographic angiography (CTA) with high inter-observer agreement, and (2) patients with sleep apnea exhibit larger carotid bodies than those without sleep apnea. A chart review was conducted from patients who underwent neck CTA and polysomnography at the Mayo Clinic between January 2000 and February 2015. Widest axial measurements of the carotid bodies, performed independently by two radiologists, were possible in 81% of patients. Intra-class correlation coefficients ranged from 0.93 to 0.95 (Right carotid body: 0.93; Left: 0.94; Average: 0.95). Widest axial measurements of the carotid bodies were greater in patients with sleep apnea (n = 32) compared to controls (n = 46, *P*-value range 0.02–0.04). After adjusting for age, no differences in carotid body size were observed between the patient groups (*P*-value range 0.45–0.59). We conclude carotid body size can be detected by CTA with high inter-observer agreement; however, carotid body size is not increased in patients with sleep apnea.

1. Introduction

The carotid body chemoreceptors are located bilaterally at the bifurcation of the common carotid artery and are thought to be the body's primary oxygen sensors (Kumar and Prabhakar, 2012). The carotid body chemoreceptors respond to changes in the partial pressure of oxygen, such that a fall in arterial oxygen levels results in an increase in carotid body afferent activity and subsequently ventilation and sympathetic nervous system activity (Kumar and Prabhakar, 2012). Patients with sleep disordered breathing [clinically defined as an Apnea Hypopnea Index (AHI) of ≥30 events per hour] experience repeated intermittent hypoxic exposures at night and are at increased risk for heart disease, hypertension, diabetes, and related cardiovascular diseases (Herrscher et al., 2014). Tonic activity of the carotid body chemoreceptors is known to be increased in hypoxic conditions such as sleep apnea and recent evidence suggests that increased carotid body chemoreflex activity is a major driver of sympathetic activation in such conditions (Prabhakar, 2016). Furthermore, individuals with increased carotid chemoreceptor activity exhibit increased morbidity and mortality when compared to individuals with relatively low chemoreceptor activity (Ponikowski et al., 2001).

Long-standing evidence from patient populations has shown that those individuals who exhibit chronic hypoxemia also exhibit increased carotid body volume and/or carotid body hyperplasia (Arias-Stella and Valcarcel, 1976; Cramer et al., 2014; Habeck, 1986; Heath and Smith, 1994; Vinhaes et al., 2002). Such conditions include, but are not limited to: acute respiratory disease syndrome (Vinhaes et al., 2002), pulmonary emphysema (Heath and Smith, 1994), chronic obstructive pulmonary disease (Vinhaes et al., 2002), patients with severe lung diseases (Habeck, 1986), and high altitude natives (Arias-Stella and Valcarcel, 1976). The majority of our understandings of carotid body hypertrophy in patients with long-standing hypoxemia are from post-mortem analyses. The post-mortem nature of these assessments has understandable limitations to our ability to adequately interpret the clinical relevance of such results. However, recent work suggests the carotid body may be visible in up to 80% of normal adults undergoing computed tomography angiography (CTA) (Cramer et al., 2014; Nair et al., 2013). Thus, CTA has emerged as a potential new way to assess carotid body size in living individuals.

Carotid body resection was pursued in the 1960s for the treatment of dyspnea in patients with chronic obstructive pulmonary

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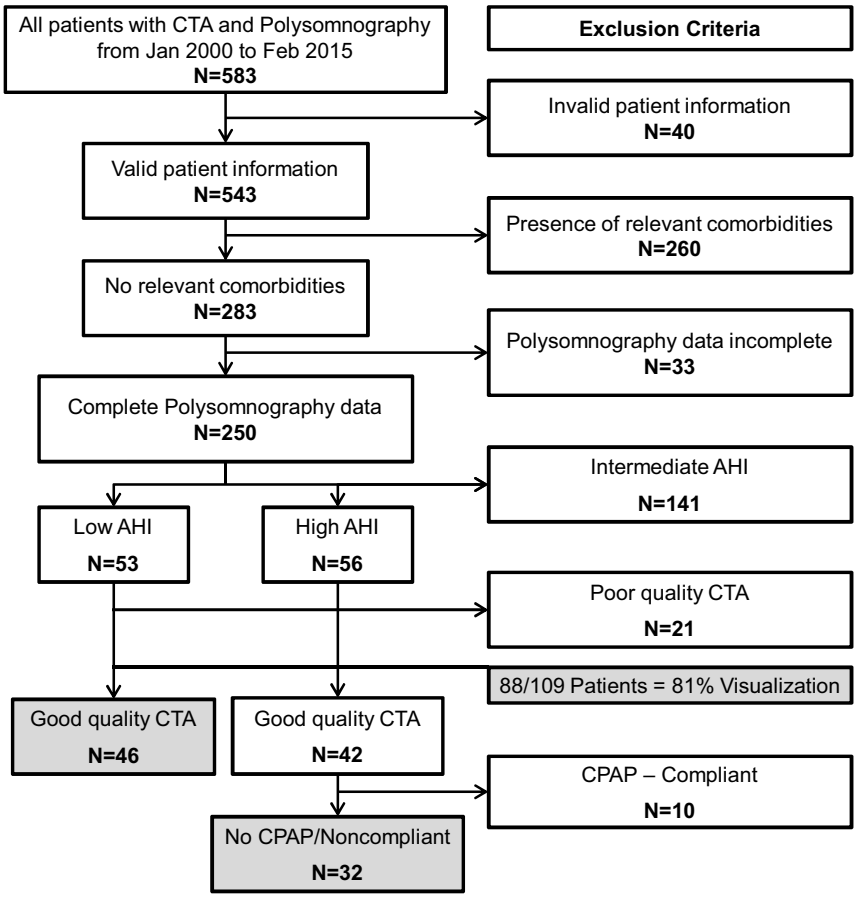

Fig. 1. Subject selection.

disease; however, its success was limited – likely due to poor patient selection (Joyner and Limberg, 2016). Recently, there has been renewed interest in the carotid chemoreceptors as a potential therapeutic target for conditions related to tonic activity of the carotid body (Paton et al., 2013). With this, CTA may provide an important screening tool to help identify individuals who exhibit increased carotid body size and may benefit from procedures such as carotid body denervation or resection. Using neck CTA, recent data suggest patients with diabetes mellitus, hypertension, and congestive heart failure exhibit a 20–25% larger mean carotid body size when compared with controls (Cramer et al., 2014). With this in mind, we sought to examine whether carotid body size detected by CTA would be increased in individuals with diagnosed sleep disordered breathing. Thus, the purpose of the present investigation was to test the hypotheses that: (1) Carotid body size can be identified by CTA with high inter-observer agreement, and (2) Carotid body size as measured by CTA is greater in individuals with diagnosed sleep apnea when compared to controls.

2. Methods

2.1. Approval

All procedures were approved by the Mayo Clinic Minimal Risk Institutional Review Board.

2.2. Patients

A retrospective chart review was conducted from patients at the Mayo Clinic who were seen between January 2000 and February 2015 that completed the following exams: (1) head/neck CTA, (2) Polysomnography. The clinical indication for CTA imaging was variable and not performed for isolated carotid body analysis, while the clinical indication for polysomnography was for the diagnosis and assessment of sleep apnea. The protocols for both clinical measurements (CTA and polysomnography) followed institutional standardization (see below "2.3. CTA and carotid body measurement").

The initial review resulted in 583 patients (See Fig. 1). Demographic data (age, sex, height, weight, resting heart rate and blood pressure) were extracted from medical visits surrounding (±10 weeks) the CTA visit. Subjects were excluded if: (1) the CTA was not performed at Mayo Clinic (n = 27), (2) CTA images were not on record (n = 2), (3) the subject was <18 years of age at the time of either exam (n = 3), (4) the subject could not be identified by their Mayo Clinic identification number (n = 8). Clinical data from the electronic medical record were also collected for all patients to exclude potential confounding comorbidities that could impact carotid body size independent of sleep disordered breathing [Type 2 Diabetes, n = 114; Heart Failure, n = 95; Type 2 Diabetes and Heart Failure, n = 42; Type 1 Diabetes, n = 7; Type 1 Diabetes and Heart Failure, n = 2, (Cramer et al., 2014; Nair et al., 2013)]. Comorbid conditions were extracted based upon physician completion or billing code.

Data from 283 patients were then collected from the Polysomnography exam, including: total sleep duration, AHI, lowest saturation during REM/NREM sleep, average duration of apneic events, and percentage of time during sleep (%TST) spent between 80 and 89% oxygen saturation (S_pO_2). Hypopneas were scored using the American Academy of Sleep Medicine recommended guidelines (Berry et al., 2015). Subjects were excluded if data from the polysomnography exam were incomplete (n = 8), if CPAP was