CHEST

Sleep-Disordered Breathing in Hypertrophic Cardiomyopathy

Challenges and Opportunities

Tomas Konecny, MD, PhD; and Virend K. Somers, MD, DPhil, FCCP

Sleep-disordered breathing (SDB) may be a treatable risk factor in patients with hypertrophic cardiomyopathy (HCM), the most common inherited cardiomyopathy. Evidence suggests a high prevalence of SDB in HCM. We summarize the pathophysiology of SDB as it relates to hypertension, coronary artery disease, atrial fibrillation, and sudden cardiac death in patients with HCM. The implications regarding the care of patients with HCM and SDB are discussed as well as the knowledge deficits needing further exploration. CHEST 2014; 146(1):228-234

ABBREVIATIONS: AF = atrial fibrillation; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter-defibrillator; LV = left ventricular; SCD = sudden cardiac death; SDB = sleep-disordered breathing

Documented morbidity and mortality related to hypertrophic cardiomyopathy (HCM) possibly reach as far back as the ancient Greek messenger Pheidippides, who shouted "Niki!" ("Victory!"), collapsed, and died in 490 BC after running from the battlefield in Marathon to Athens.[1] However, to our knowledge, the first modern pathologic and clinical reports of HCM were published only in the latter half of the 20th century.[2] HCM is the most common inherited cardiomyopathy, which phenotypically affects one in 500 adults in the general population.[3] At least 11 causative genes expressed primarily or exclusively in the heart have been identified, and these are believed to encode thick and thin myofilament proteins or contiguous Z-discs in the cardiac myocytes. Even though the exact disease mechanisms remain targets of ongoing investigation, the key processes at the cellular level involve increased myocyte size, accumulation of fibroblasts in the myocardium (collagen secretion leading to fibrosis), and malalignment of myocytes and sarcomeres. At the macroscopic level, the hearts of patients with HCM commonly manifest asymmetric ventricular septal hypertrophy leading to dynamic left ventricular outflow tract obstruction, systolic anterior motion of the mitral valve leading to mitral regurgitation, and increased stiffness of the ventricular myocardium leading to impaired diastolic filling. Occurrences of sudden cardiac death (SCD), exemplified by

Manuscript received January 10, 2014; revision accepted March 27, 2014.

AFFILIATIONS: From the Mayo Clinic (Drs Konecny and Somers), Rochester, MN; and International Clinical Research Center (Dr Konecny), St Anne's Hospital, Brno, Czech Republic.

FUNDING/SUPPORT: This study was supported by the Mayo Clinic Foundation; the National Institutes of Health [Grant HL65176]; the European Regional Development Fund [Grant CZ.1.05/1.1.00/02.0123]; and the Internal Grant Agency, Ministry of Health, Czech Republic [Grants NT11401-5/2011 and CZ.1.07/2.3.00/20.0022].

CORRESPONDENCE TO: Tomas Konecny, MD, PhD, Mayo Clinic, Division of Cardiovascular Diseases, 200 First St SW, Rochester, MN 55905; e-mail: konecny.tomas@mayo.edu

DOI: 10.1378/chest.14-0084

the tragic on-court death of the Boston Celtics and National Basketball Association all-star Reggie Lewis in 1993, represent an important, but small minority of patients with HCM. More typical is a gradual progression of symptoms, with eventual development of chronic heart failure.[4-6] Importantly, many patients are relatively asymptomatic throughout their lives.[4-6]

Current Therapeutic Options

Even though the management of HCM should be tailored to the needs of each affected individual, both the 2003 and the 2011 guidelines list the three most prevalent symptomatic presentations to be[2]: (1) heart failure, which may be progressive and can lead to end-stage dysfunction; (2) atrial fibrillation (AF), which in patients with HCM carries a particularly unfavorable prognosis and often is itself associated with worsening heart failure; and (3) SCD, which strikes a small minority of patients with HCM for whom primary and secondary preventive placement of an implantable cardioverter-defibrillator (ICD) may play a crucial role.[2,7] The treatment algorithm outlined in the guidelines integrates the use of medical therapy (β-blocking agents, verapamil, and disopyramide) as well as invasive measures (surgical myectomy, alcohol ablation, and placement of an ICD) when appropriate indications arise. Unfortunately, many heart failure symptoms progress despite the best available treatments; hence, novel therapeutic approaches are needed.

Identifying the Need

Clinical investigation of the role of sleep-disordered breathing (SDB) in patients with HCM is in a relatively early stage, hence, screening and treatment of SDB have not been incorporated into the routine management of HCM.[2,8] Identifying potential links between SDB and HCM is important because SDB may contribute a uniquely reversible risk factor for HCM pathophysiology given that it has widely available and relatively benign treatment options that carry a favorable profile of side effects (weight loss, postural therapy, mandibular devices, and CPAP).[9] Here, we explore some of the key pathophysiologic consequences of SDB, which may have direct relevance to patients with HCM, and review the emerging evidence suggesting associations between SDB and adverse outcomes in HCM.

Definitions

The current guidelines define HCM as a disease state characterized by unexplained left ventricular (LV) hypertrophy associated with nondilated ventricular chambers in the absence of another cardiac or systemic disease that itself would be capable of producing the magnitude of hypertrophy evident in a given patient.[2] In clinical practice, HCM is usually recognized by asymmetric LV wall thickening (commonly ≥ 15 mm on echocardiography).[2]

SDB is defined according to the standard criteria set forth by the American Academy of Sleep Medicine.[10-13] The most common type of SDB is OSA, and much of the pathophysiologic understanding of SDB relies on studies of OSA in patients without HCM. A further limitation is that many of the studies of sleep pathology in patients with HCM used overnight oximetry in the diagnosis of SDB. This technique is more readily available and affordable than polysomnography; however, oximetry alone provides only a limited characterization of SDB and cannot differentiate among the various types of sleep apnea.

Relevance of SDB Pathophysiology to HCM

The current HCM guidelines support management algorithms beginning with the screening and treatment of comorbidities known to be particularly deleterious in patients with HCM (ie, hypertension, hyperlipidemia, diabetes mellitus, AF).[2,7,14] An increasing body of evidence emerging from non-HCM study cohorts supports the notion that SDB may increase cardiovascular risk and that treatment of SDB may lead to improved outcomes.[15] Given that patients with HCM are uniquely susceptible to the dangers of cardiovascular comorbidities, such as AF[7] and coronary artery disease,[14] it would be reasonable to consider whether their initial management should include routine screening for SDB and its effective treatment, if applicable (Fig 1). This section summarizes the key findings on the relationships between SDB and cardiac pathologies most relevant to patients with HCM; however, much of these data originated from non-HCM studies, and caution is advisable in their extrapolation to HCM. (For studies focusing on SDB in patients with HCM, see the Implications of Comorbid SDB in Patients With HCM section.)

Hypertension

Hypertension in patients with HCM is believed to result in additive adverse consequences.[16] Well-conducted prospective non-HCM studies link increasing BP and incident hypertension with the presence and severity of SDB, independent of confounding variables (especially age, sex, and obesity).[17] The physiologic nocturnal decrease in BP is attenuated in patients with SDB,