Cheyne-Stokes Respiration

A Consequence of a Broken Heart?

Cheyne-Stokes respiration (CSR) with central sleep apnea (CSA) [CSR-CSA] is a breathing disorder seen in patients with advanced congestive heart failure (CHF) that is characterized by the presence of central apneas and hypopneas, alternating with periods of crescendo-decrescendo tidal volume.1 CSR-CSA has been associated, in a severity-dependent manner, with elevations of sympathetic nervous activity in CHF patients,2 which is an important predictor of CHF progression, arrhythmias, and mortality.3,4 Indeed, CSR-CSA, independent of other risk factors, elevates the risk of mortality in CHF by twofold to threefold.5 Successful treatment of CSR by continuous positive airway pressure (CPAP) leads to a significant reduction in sympathetic nervous activity2 and may reduce mortality rates by up to 40% in patients with CHF and CSR-CSA.6 Since CPAP has salutary effects on cardiac function (independent of its effect on CSR), it remains uncertain whether CSR-CSA is a mere epiphenomenon of a failing heart or a major contributor of poor outcomes of patients with CHF.

The article by Mansfield and colleagues in this issue of CHEST (see page 1675) provides some important insights on the potential (pathogenetic) role of CSR-CSA in patients with CHF. They prospectively studied 37 patients with very advanced CHF before and > 6 months after cardiac transplantation. Prior to transplantation, 16 patients had CSR-CSA, 6 patients had obstructive sleep apnea, and 15 patients had no sleep-disordered breathing. Cardiac transplantation abolished CSR-CSA in most but not all patients with pretransplant CSR-CSA. Approximately 20% (3 of 15 patients) still had CSA following transplantation, despite normalization of their cardiac performance parameters including their left ventricular ejection fraction.

Importantly, however, the phenotypic appearance of the respiratory events was substantially different than that observed prior to transplantation. The most striking change was a shortening of the ventilatory phase, leading to an overall reduction in the CSA cycle (from 65 to 31 s) and loss of the classic crescendo-decrescendo pattern of tidal volume. In addition, even after cardiac transplantation, those with pretransplant CSR-CSA continued to have lower Pco2 than those without CSR-CSA (39 mm Hg vs 43 mm Hg), consistent with the notion that these patients have heightened basal ventilatory drive.7 Notably, although sleep-disordered breathing persisted in some patients after transplantation, as a group, there was a marked reduction in the urinary norepinephrine excretion rates following transplantation, suggesting normalization or near-normalization of sympathetic nervous activity in such patients.

If these initial observations by Mansfield and colleagues can be corroborated in larger clinical studies, several conclusions are possible. First, their data indicate that cardiac transplantation is an effective treatment for CSR-CSA. Admittedly, approximately 20% of patients may still have “residual” CSA after transplantation. However, posttransplant events have much shorter cycle lengths and fail to demonstrate the classic waxing and waning appearance of CSR-CSA, resembling the pattern commonly related to idiopathic or postarousal CSA. This suggests that poor cardiac function is a necessary precondition for the classic crescendo-decrescendo appearance of CSR-CSA. Second, cardiac transplantation significantly attenuates the excess sympathetic nervous activity observed in CHF patients with or without CSR-CSA, probably by improving cardiac function. This suggests that even in patients with CSR-CSA, the most important therapeutic target is the heart (and not the breathing disorder per se).

The work by Mansfield and colleagues also raises some important questions. First, in their article, the authors do not distinguish CSA from CSR. In both pretransplant and posttransplant settings, central apneas were labeled as CSA with CSR, although, clearly, the appearances of these events in the two settings differed markedly (Fig 2). Admittedly, there is no universally accepted definition of CSR or CSA, and the distinction is not always clear. However, they provide different clinical and prognostic information.
Classic CSR usually occurs in patients with CHF or stroke and is, as mentioned previously, associated with a bad prognosis. However, idiopathic CSA is observed in those without any comorbidities and is not necessarily periodic in nature. Moreover, there are no data indicating that the presence of idiopathic or postaural CSA by itself is a poor prognostic marker for patients, and no consensus on when and how it should be treated. In view of these differences, there is a definite need to develop a more precise definition of CSR-CSA to better define the relevance of CSR-CSA in CHF, and to foster comparisons of data across studies. We believe that studies examining CSR-CSA should, as a minimum, report on the cycle length, magnitude of oxyhemoglobin desaturation, the timing of arousals relative to the respiratory events, and frequency and duration of apneas and hypopneas of their study patients to distinguish classic CSR-CSA from idiopathic CSA.

Second, the data by Mansfield and colleagues indicate that sympathetic nervous activity, which is overexpressed in those with CSR-CSA, can be markedly attenuated by cardiac transplantation. Indeed, in the posttransplant setting, those with classic CSR-CSA before transplantation had urinary norepinephrine levels remarkably similar to those without CSR-CSA following surgery. Some may argue that these data support the contention that CSR-CSA is responsible for the excess sympathetic nervous activity in the posttransplant setting. This statement, however, largely ignores the fact that 20% of patients with CSR-CSA in the study by Mansfield and colleagues had “residual” CSA on postransplant polysomnography. If CSR-CSA, indeed, contributes to the downward spiral of patients with CHF by perturbing the autonomic nervous system, one might have expected to see a higher urinary norepinephrine level in the CSR-CSA group than in the control group following transplantation (since none in the control group acquired CSR-CSA postransplant). An alternative explanation of the data of Mansfield and colleagues is that CSR-CSA by itself is not the primary cause of the sympathetic overactivity and that their expression is an epiphenomenon. Treatment of the “broken” heart is, therefore, the only relevant clinical issue. The study of Mansfield and colleagues was not designed to address this critically important question. Well-designed, larger prospective studies are needed to determine whether postransplant CSA is associated with elevations in the sympathetic nervous activity and, more importantly, whether their presence leads to worse clinical outcomes in cardiac patients.

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REFERENCES
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Getting the Most Out of Nocturnal Pulse Oximetry

Due to its noninvasive nature and the convenient patient interface consisting of a small sensor clipped or taped onto the skin, pulse oximetry is widely used in pulmonary medicine, critical care, and anesthesia. In sleep medicine, pulse oximetry is an essential tool for tracking the rapid fluctuations in arterial oxygen saturation that are characteristic for the unstable ventilation in patients with sleep apnea. Pulse oximetry has provided early insights into sleep-related breathing disturbances, and has opened the way for subsequent systematic investigations of sleep apnea. Today, the technique is an integral component of polysomnography and, by itself, is commonly used as a simple tool in the evaluation of sleep apnea.