

Hemodynamic Rounds

Cheyne-Stokes Respiration and Cardiac Hemodynamics in Heart Failure

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INTRODUCTION

John Cheyne in 1818 and William Stokes in 1854 described a regularly waxing and waning breathing pattern with central apnea (i.e., absence of respiratory effort), now known as Cheyne-Stokes respiration (CSR) [1].

This pattern of breathing has often been described in patients with congestive heart failure (CHF) where it has been used as a marker of severity of the disease state.

There have been previous reports describing a decrease in heart rate and blood pressure during the apneic phase, and an increase in both of them during hyperpneic phase of Cheyne-Stokes breathing. However, the effects of these changes on intracardiac hemodynamics have not been reported in literature. A recognition and understanding of these hemodynamic changes is important as they can significantly alter the evaluation and management of CHF. Moreover, these changes have also been shown to have prognostic implications by increasing the incidence of cardiac arrhythmias and mortality [2].

We report two cases of CHF with CSR and hemodynamic changes during cardiac catheterization.

Case 1

Fifty-six-year-old Asian male with known history of mitral valve prolapse was admitted to the hospital with h/o worsening exercise tolerance, orthopnea, and paroxysmal nocturnal dyspnea. Physical examination revealed jugular venous pressure of 10 cm at 45°, bibasilar crackles and 2+ pitting edema in the lower extremities. The apical impulse was displaced to the sixth intercostal space in the anterior axillary line. A four of six pansystolic murmur was heard best at the apex with radiation to the axilla, associated with a palpable thrill and a S3 gallop.

Transthoracic followed by a transesophageal echocardiogram revealed myxomatous mitral valve with ruptured chordae tendinae and prolapse of the anterior mitral leaflet, with severe mitral regurgitation. There was moderate enlargement of the left atrium and left ventricle with normal systolic function. Doppler assessment revealed moderately elevated pulmonary artery pressures. Coronary arteriogram was negative for any obstructive coronary artery disease.

Right heart catheterization showed mean right atrial pressure of 7 mm Hg, right ventricular pressure of 80/10 mm Hg, pulmonary artery pressure of 80/46 mm Hg with a mean of 58 mm Hg, pulmonary artery wedge pressure *a* wave of 35 mm Hg, and *v* wave of 45 mm Hg with mean of 32 mm Hg. Left heart hemodynamics showed aortic pressure of 138/90 mm Hg with mean of 106 mm Hg. Left ventricular pressure was 138/12 mm Hg (Table I).

While recording the right and left heart pressures, the patient was noted to have significant episodes of apnea alternating with periods of hyperpnea with marked variations in the hemodynamics.

During period of hyperpnea, aortic pressure peaked at 150/112 mm Hg with a mean of 124 mm Hg. Left ventricular pressure was 150/22 mm Hg. Simultaneously recorded pulmonary artery wedge pressure

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TABLE I. Hemodynamic Findings, Case 1

Right atrium	$a = 8; v = 9; \text{mean} = 7$
Right ventricle	80/10
Pulmonary artery	80/46; mean = 58
Pulmonary artery wedge	$a = 35; v = 45; \text{mean} = 32$
Left ventricle	138/12
Aorta	138/90; mean = 106

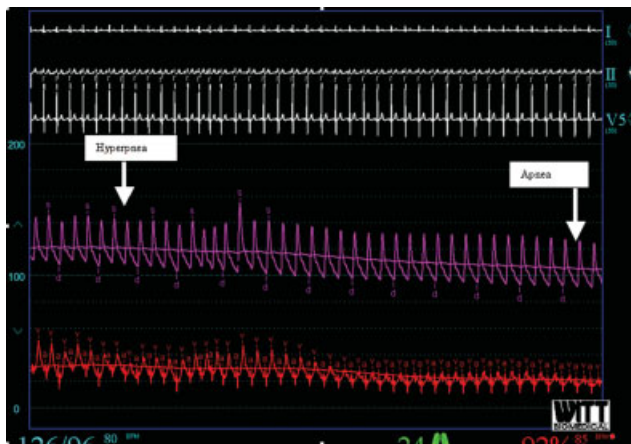


Fig. 1. Changes in aortic pressure and pulmonary artery wedge pressure from hyperpneic to early apneic phase. Mean aortic pressure decreased from 124 mm Hg to 102 mm Hg, v wave decreased from 50 mm Hg to 22 mm Hg. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

showed a wave of 40 mm Hg, v wave of 50 mm Hg, and mean of 35 mm Hg. During the late phase of apnea, the aortic pressure gradually declined to 120/94 mm Hg with a mean of 102 mm Hg. Pulmonary artery wedge pressure similarly decreased to an a wave of 23 mm Hg and v wave of 22 mm Hg with a mean of 18 mm Hg. Left ventricular pressure also declined to 120/12 mm Hg (Figures 1–4).

In summary, during the apneic phase of CSR, there was a decrease in mean aortic pressure from 124 mm Hg to 102 mm Hg, associated with marked reduction in v wave of pulmonary artery wedge pressure from 50 mm Hg to 22 mm Hg.

Case 2

Sixty-two-year-old African American male was admitted to the hospital with a 6-month history of exertional chest pain, worsening bilateral lower extremity edema. Physical exam revealed a cachectic male with no evidence of jugular venous distension, fine bibasilar crackles, and 2+ bilateral lower extremity pitting edema. Cardiac exam revealed a nondisplaced apical impulse, normal S1, absent aortic component of S2, with a three of six late peaking systolic crescendo–decrescendo murmur at the right upper ster-

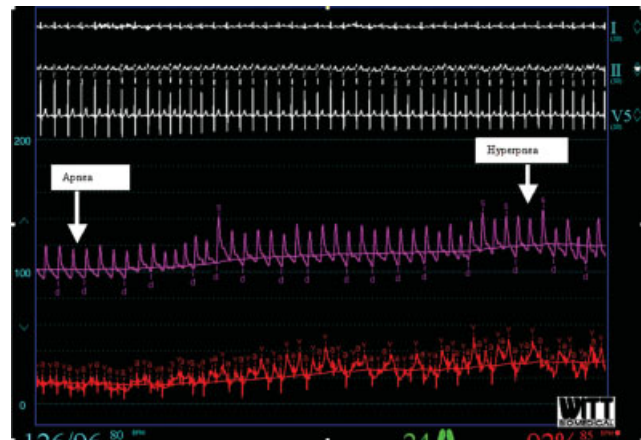


Fig. 2. Changes in aortic pressure and pulmonary artery wedge pressure from late apneic to hyperpneic phase. Mean aortic pressure increased from 102 mm Hg to 124 mm Hg. Mean pulmonary artery wedge pressure increased from 18 mm Hg to 35 mm Hg. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

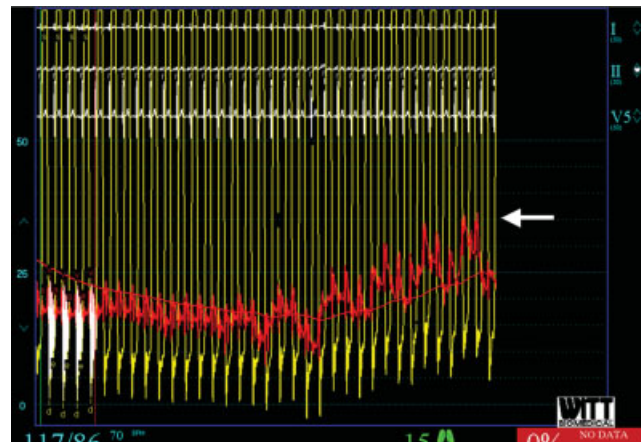


Fig. 3. Changes in left ventricular pressure and pulmonary artery wedge pressure from late apneic to hyperpneic phase showing reappearance of v waves (arrow) with increase in transmitral gradient during hyperpnea. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

nal border and a two of six holosystolic murmur at the apex with radiation to the axilla.

Transthoracic echocardiogram revealed moderately dilated left ventricle with mild hypertrophy and severe systolic dysfunction with an ejection fraction of 20–25%. The aortic valve appeared to be thickened and bicuspid with a mean gradient of 25 mm Hg, valve area of 1 cm² consistent with low-gradient severe aortic stenosis. There was moderate mitral annular calcification with moderate mitral regurgitation. Doppler assessment revealed mildly elevated pulmonary artery

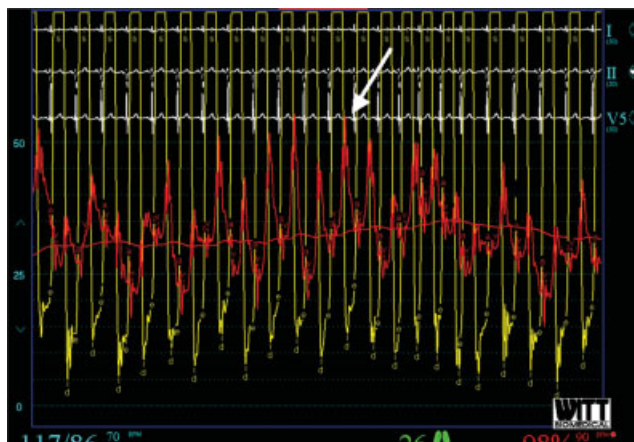


Fig. 4. Simultaneous left ventricular and pulmonary artery wedge pressure during hyperpneic phase showing large v wave of 50 mm Hg (arrow). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

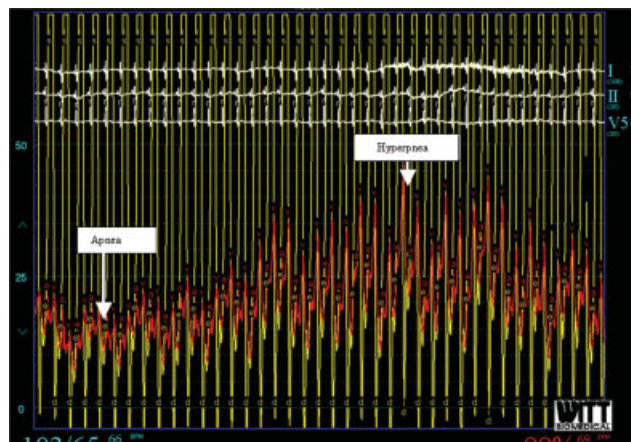


Fig. 5. Changes in left ventricular end diastolic and pulmonary artery wedge pressure from late apneic to hyperpneic phase, v wave increased from 18 mm Hg to 45 mm Hg. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

TABLE II. Hemodynamic Findings, Case 2

Right atrium	$a = 8; v = 5; \text{mean} = 4$
Right ventricle	40/8
Pulmonary artery	40/15; mean = 24
Pulmonary artery wedge	$a = 15; v = 18; \text{mean} = 15$
Left ventricle	130/35
Aorta	107/58; mean = 76

pressures. Coronary Arteriogram revealed total occlusion of distal left circumflex artery and proximal right coronary artery with both vessels filling in via collaterals from left anterior descending artery. Left ventricular angiography revealed severe impairment of systolic function with ejection fraction of 25% and 2+ mitral regurgitation. Right and Left heart hemodynamics are shown in Table II.

While recording the right and left heart pressures, patient was noted to have significant episodes of apnea alternating with periods of hyperpnea with noticeable variations in the hemodynamics.

During the period of hyperpnea, aortic pressure peaked at 120/64 mm Hg with a mean of 85 mm Hg. Simultaneously recorded pulmonary artery wedge pressure showed an a wave of 25 mm Hg, v wave of 45 mm Hg, and mean of 23 mm Hg. During the late phase of apnea, the aortic pressure gradually declined to 108/62 mm Hg with a mean of 77 mm Hg. Pulmonary artery wedge pressure similarly decreased to an a wave of 15 mm Hg, v wave of 18 mm Hg with a mean of 15 mm Hg (Figures 5–7).

In summary, during the apneic phase of CSR, there was a decrease in mean aortic pressure from 85 mm Hg to 77 mm Hg, associated with marked reduction



Fig. 6. Simultaneous left ventricular and pulmonary artery wedge pressure during hyperpneic phase showing large v wave of 45 mm Hg (arrow). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

in v wave of pulmonary artery wedge pressure from 45 mm Hg to 18 mm Hg.

DISCUSSION

The above two cases highlight the importance of reporting hemodynamic data in both phases of CSR. As illustrated in both the cases, a significant increase in arterial blood pressure during hyperpnea was associated with a marked increase in v wave amplitude on pulmonary artery wedge pressure tracings. The resultant increase in mean pulmonary artery wedge pressure could be erroneously interpreted by clinicians as indicative of pulmonary edema, which could lead to inappropriate therapy.

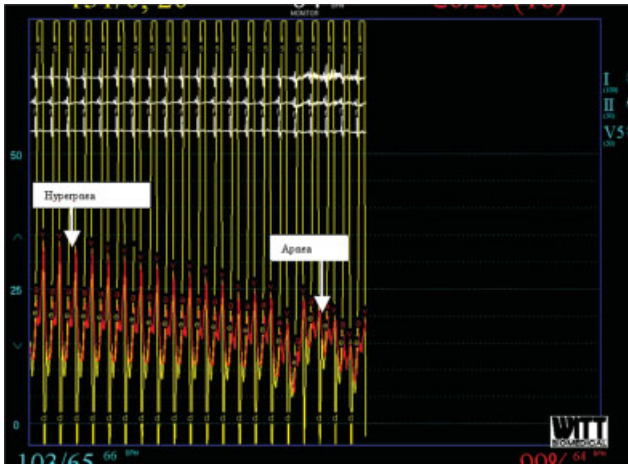


Fig. 7. Changes in LV end diastolic pressure and pulmonary artery wedge pressure from hyperpneic to early apneic phase. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Similarly, while studying the hemodynamic effects of drug interventions, the variations in intracardiac pressures with CSR may be misinterpreted as a significant effect of the drug.

Pathophysiology of CSR

Cheyne-Stokes respiration (CSR) is a rhythmic breathing pattern characterized by recurring periods of hyperpnea, hypopnea, and apnea. It is most often observed in abnormalities of the heart or the brain that can cause an unstable ventilatory control. However, it can also occur in normal people at high altitudes where the simultaneous presence of hypoxia and hypocapnia increases the influence of oxygen control on ventilation over carbon dioxide [1,3,4].

The pathophysiology of CSR is described as instability of the feedback loop controlling respiration. Some of the proposed mechanisms for Cheyne-Stokes breathing in CHF are

1. Change in circulation time: In CHF, pulmonary congestion, increased intracardiac dimensions, and low-cardiac output prolong the transit time between the lungs and the chemoreceptors in the brain [3,4].
2. Changes in arterial oxygen and carbon dioxide tensions and respiratory center sensitivity: Pulmonary congestion causes a decrease in the ability of the lungs to store both oxygen and carbon dioxide and also interferes with the oxygen transfer across the alveolar membrane. This leads to both hypoxemia and hypocapnia. Hypoxemia increases the sensitivity of the respiratory center to carbon dioxide and hypocapnia causes the arterial carbon dioxide partial pressure to move closer to apneic threshold favoring CSR [3].

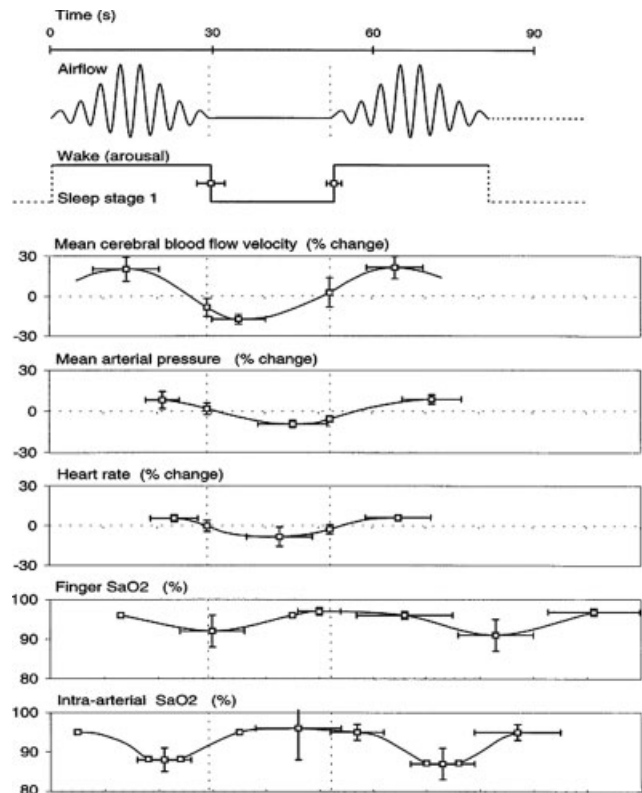


Fig. 8. Mean percent changes from baseline for CBFV, MAP, heart rate, SaO₂ and their temporal onsets to apnea (Reproduced from *J Appl Physiol* 1997;83:1184-1191.)

3. Decrease in wakefulness drive: Metabolic disturbances produced by decreased cardiac output along with morphine and various sedatives used in the treatment of pulmonary edema remove the wakefulness drive and increase the possibility of apnea [3].

Franklin et al. [1] studied the hemodynamic effects of CSR in 10 patients (nine patients with CHF) and observed an average of 16 mm Hg decrease in the mean arterial pressure from 98 mm Hg during hyperpnea down to 82 mm Hg during apnea. The heart rate also decreased by an average of 9 bpm from 70 bpm during hyperpnea to 61 bpm during apnea. The mean percentage changes in both blood pressure and heart rate during apnea in these groups of patients is shown in Figure 8.

The changes in the blood pressure and heart rate during the hyperpneic phase have been attributed to an increase in the underlying sympathetic nerve activity along with the increased concentrations of norepinephrine in plasma and urine [2]. This may have a negative effect on the already failing left ventricle due to increased afterload [2].

Massumi et al. [5] also described a decrease in heart rate and varying degrees of bradyarrhythmias in the

late apneic or early hyperpneic phases of CSR, due to high vagal tone in 9 of 14 patients with CHF.

Maze et al. [6] studied the Doppler flow velocity profiles of left ventricle inflow and outflow during CSR and found a 25% decrease in stroke volume during the apneic phase. They attributed this to an increase in the pulmonary vascular resistance causing a decrease in preload due to hypercarbia and an abnormal relaxation pattern of the left ventricle causing abnormal diastolic filling [6].

In our case, we believe that the changes in the afterload reflected in changes in blood pressure were responsible for marked variation in intracardiac hemodynamics.

CSR as a prognostic indicator

Changes in preload and afterload, sympathetic activation, and arterial desaturations related to fragmented sleep pattern in CSR may induce episodes of nocturnal ischemia especially in patients with hibernating myocardium [7]. This may lead to worsening of left ventricular function and increased cardiovascular mortality [7–9]. Therefore, CSR is no longer solely considered a sign of CHF, but an independent risk factor for reduced survival in patients with CHF [8]. Lanfranchi et al. [9] suggested that apnea/hypopnea index (AHI) ≥ 30 /hr (i.e., the number of apneas and hypopneas per hour of sleep recording) is a very powerful independent predictor of cardiac mortality.

Therapy of CSR

Therapy of CSR is the treatment of central sleep apnea with continuous positive airway pressure (CPAP). Nocturnal administration of CPAP has been shown to reduce AHI, improve short term left ventricular function significantly, and alleviate symptoms of CHF [9]. Because duration of therapy with CPAP is expected to be lifelong, compliance is an important issue in the management of these patients. Philippe et al. [10] compared compliance and efficacy of adaptive servo-ventilation (ASV, a servo-controlled bilevel positive pressure support) with CPAP in 25 patients with CHF and CSR. They reported significantly greater compliance and improved quality of life at 6 months with SAV. Pepperell et al. [11] showed a decrease in daytime sleepiness and neurohumoral activation manifested as significant reduction in plasma brain natriuretic peptide and urinary met-adrenaline excretion with SAV in patients with CSR. However, the long-term effects of CPAP and SAV on left ventricular

function, cardiac mortality, and transplant-free survival are unknown at present.

CONCLUSION

CSR is a state of phase-linked cyclic changes in cerebral, respiratory, and cardiovascular functions [1]. There is a high prevalence of CSR in patients with CHF, but its presence is under recognized.

The variations in cardiac hemodynamics during apneic and hyperpneic phases of Cheyne-Stokes breathing can have significant clinical implications when interpreting valvular hemodynamics and therapeutic effects of drugs used for treatment of heart failure. Neurohormonal activation and hemodynamic alterations associated with CSR lead to worsening heart failure and increased mortality. It is important to recognize this entity in patients with CHF and treat it appropriately, as therapy with CPAP or SAV has been shown to significantly improve short-term outcomes.

REFERENCES

1. Karl AF, Sandstrom E, Eva MB. Hemodynamics, cerebral circulation, and oxygen saturation in Cheyne-Stokes respiration. *J Appl Physiol* 1997;83:1184–1191.
2. Nocturnal insights in chronic heart failure. *Eur Heart J* 1999; 20:1140–1141.
3. Cherniack NS, Longobardo GS. Cheyne-Stokes breathing: An instability in physiologic control. *N Engl J Med* 1973;288:952–957.
4. Pryor WW. Cheyne-Stokes respiration in patients with cardiac enlargement and prolonged circulation time. *Circulation* 1951;4: 233–238.
5. Massumi RA, Nutter DO. Cardiac arrhythmias associated with Cheyne-Stokes respiration. *Dis Chest* 1968;54:21–32.
6. Maze SS, Kotler MN, Parry WR. Doppler evaluation of changing cardiac dynamics during Cheyne-Stokes Respiration. *Chest* 1989;95:525–529.
7. Mehta RM, Groth ML. Continuous positive airway pressure in patients with congestive heart failure and Cheyne-Stokes respiration with central sleep apnea. *Circulation* 2001;103:e121.
8. Brack T. Cheyne-Stokes respiration in patients with congestive heart failure. *Swiss Med Weekly* 2003;133:605–610.
9. Lanfranchi PA, Giannuzzi P. Prognostic value of nocturnal Cheyne-Stokes respiration in chronic heart failure. *Circulation* 1999;99:1435–1440.
10. Philippe C, D'ortho MP. Compliance with and efficacy of adaptive servo-ventilation (ASV) vs. continuous positive airway pressure (CPAP) in the treatment of Cheyne-Stokes respiration in heart failure over a six-month period. *Heart* 2006;92:337–342.
11. Pepperell JC, Davies RJ. A randomized controlled trial of adaptive ventilation for Cheyne-Stokes breathing in heart failure. *Am J Respir Crit Care Med* 2003;168:1109–1114.