CLINICAL RESEARCH STUDY

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Cheyne-Stokes Breathing and Reduced Ejection Fraction

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ABSTRACT

BACKGROUND: The accuracy of Cheyne-Stokes breathing as a sign of left ventricular dysfunction and its overall prognostic significance are unknown.

METHODS: Between 2001 and 2006, the author examined 386 inpatients at a Department of Veterans Affairs Medical Center and compared the finding of Cheyne-Stokes breathing and its cycle length with the patients' echocardiographic ejection fraction (EF) and 5-year survival.

RESULTS: A total of 45 of 386 patients (11.7%) had Cheyne-Stokes breathing. Two variables were independently associated with Cheyne-Stokes breathing: reduced EF ($P < .001$) and age > 80 years ($P = .006$). The presence of Cheyne-Stokes breathing increased the probability of a markedly reduced EF (ie, EF < 40%; likelihood ratio, 5.3; 95% confidence interval, 3.1-9), especially in patients aged ≤ 80 years (likelihood ratio, 7.8; 95% confidence interval, 3.9-15.5). The finding was present in 1 of 3 affected patients (sensitivity = 34%). The correlation between cycle length and EF was poor ($r = 0.23$, $P = .14$). The 5-year survival of patients with Cheyne-Stokes breathing (37.2%) was similar to that of patients without the finding (42.9%, $P = .18$, log-rank test).

CONCLUSIONS: In hospitalized patients, Cheyne-Stokes breathing increases the probability of left ventricular dysfunction. It is present in 1 of 3 patients with markedly reduced EF. When detected during physical examination, Cheyne-Stokes breathing does not indicate worse prognosis.

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KEYWORDS: Cheyne-Stokes breathing; Ejection fraction; Heart failure; Physical examination

Cheyne-Stokes breathing is an abnormal respiratory pattern consisting of periods of apnea alternating with periods of rapid breathing, first described by John Cheyne in 1818 and William Stokes in 1854. During the breathing phase, the respiratory rate is stable, but tidal volume varies from shallow to deep and then shallow again in a smooth crescendo-decrescendo pattern (**Figure 1**). Cheyne-Stokes breathing is usually associated with congestive heart failure or neurologic disorders (especially stroke),[1] although the finding's overall accuracy as a sign of ventricular dysfunction has never been investigated. Previous research on Cheyne-Stokes breathing, using prolonged sleep studies to detect the finding, has demonstrated a strong linear relationship between the period of Cheyne-Stokes breathing ("cycle length") (**Figure 1**) and circulation time[2-6] and has concluded the presence of Cheyne-Stokes breathing carries a gloomy prognosis.[7-11]

The purpose of this study is to examine a group of hospitalized patients, identify those with Cheyne-Stokes breathing detected by physical examination, and address 3 questions:

- Does Cheyne-Stokes breathing indicate ventricular dysfunction?
- Does cycle length correlate with the severity of left ventricular dysfunction?
- Does Cheyne-Stokes breathing portend poor prognosis?

MATERIALS AND METHODS

Between 2001 and 2006, the author examined a sample of 409 inpatients (previously characterized in a study of systolic murmurs[12]) at the Seattle-Puget Sound VA Healthcare System. All patients underwent transthoracic echocardiography as part of their usual care (indications for echocardiography were assessments for structural heart disease [59%], progression of preexisting valvular disease [16%],

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source of arterial emboli [8%], suspected endocarditis [7%], unexplained murmur [7%], or suspected pericardial disease [2%]). The author was blinded to the echocardiographic results at the time of examination.

At the beginning of the physical examination, respirations were observed for 60 seconds while ostensibly examining the radial pulse. Cheyne-Stokes breathing was defined as periodic central apneas (ie, no movements of abdomen or chest) alternating with breathing that had a gradual crescendo-decrescendo shape. All patients were supine and awake during examination (although some with Cheyne-Stokes breathing became less responsive during the apnea phase). Cycle length was measured from the beginning of 1 apnea to the beginning of the subsequent apnea, using the second hand of a watch. Ejection fraction (EF) was determined independently by a cardiologist unaware of the bedside observations. Patients were followed until death or for the duration of the study (through May 2012, mean follow-up 7.2 years). The study protocol was approved by the institutional review board at the Seattle-Puget Sound Veterans Affairs Medical Center.

CLINICAL SIGNIFICANCE

- Cheyne-Stokes breathing—a physical sign requiring less than 1 minute to detect—predicts the presence of left ventricular dysfunction, especially in patients aged ≤ 80 years.
- Cheyne-Stokes breathing is present in 1 of 3 patients with an ejection fraction < 40%.
- In hospitalized patients, Cheyne-Stokes breathing does not indicate worse survival.

Statistical Methods

All descriptive statistics are mean ± standard deviation or number of patients (and %). The 2-sided *t* test was used for group comparisons of continuous data, chi-square test was used for categoric comparisons, and logistic regression was used to identify independent associations with the dichotomous variable (ie, Cheyne-Stokes breathing present or absent). Pearson's correlation coefficient was applied to cycle length and EF, and Kaplan-Meier statistics were used to test for differences in survival (log-rank test, SPSS 16 software [SPSS Inc, Chicago, Ill]). Diagnostic accuracy was expressed using likelihood ratios (LRs). A P value < .05 was considered significant.

RESULTS

Patients

Of 409 patients examined, 23 were excluded because they had irregular breathing patterns (N = 7), had obstructive apneas (N = 2), were mechanically ventilated (N = 10), or lacked measurements of EF (N = 4). In the remaining 386 patients, Cheyne-Stokes breathing was present in 45 (11.7%). Cycle length was 55.3 ± 19.8 seconds (range, 25-115 seconds), apnea duration was 24.2 ± 8.6 seconds (10-45 seconds), and ventilation duration was 31.1 ± 17.6 seconds (15-90 seconds). As of May 2012, 105 patients (27%) were still alive, 261 patients (68%) had died, and 20 patients (5%) were lost to follow-up.

Presence of Cheyne-Stokes Breathing

Patients with Cheyne-Stokes breathing had reduced EFs compared with those without Cheyne-Stokes breathing (EF 40% vs. 53.1%; $P = .03$) (**Table 1**) and were significantly older (72.8 vs 68.6 years; $P = .03$). Both reduced EF and age > 80 years were independently associated with the presence of Cheyne-Stokes breathing ($P < .001$ for EF and $P = .006$ for age > 80 years by logistic regression). There were no significant differences in mean blood pressure, pulse rate, body mass index, or frequency of systolic murmurs or valvular heart disease in the 2 groups. The difference in respiratory rate (24.7 vs 19.7 min^{-1}) reflects the rapid breathing of the ventilatory phase of Cheyne-Stokes breathing.

Cheyne-Stokes breathing increased the probability of EF < 40% in patients of all ages (LR, 5.3; 95% confidence interval, 3.1-9) (**Table 2**) and especially in patients aged ≤ 80 years (LR, 7.8; 95% confidence interval, 3.9-15.5). The finding was present in 1 of 3 patients with EF < 40% (sensitivity 34%).

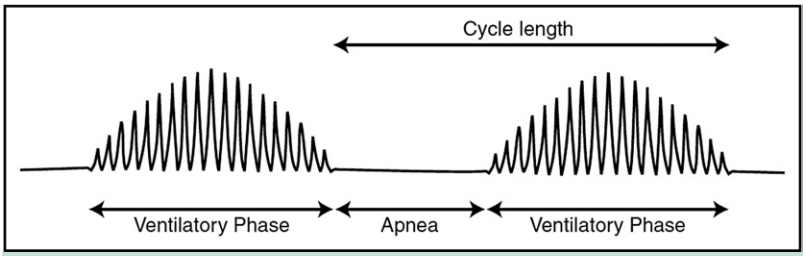

Figure 1 Cheyne-Stokes breathing.