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Clinical Correlates and Prognostic Significance of the Ventilatory Response to Exercise in Chronic Heart Failure

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Objectives. **This study sought to investigate the clinical characteristics of patients with chronic heart failure and an increased ventilatory response to exercise and to examine the prognostic usefulness of this response.**

Background. **The ventilatory response to exercise is increased in many patients with chronic heart failure and may be characterized by the regression slope relating minute ventilation to carbon dioxide output ($\dot{V}E$–$\dot{V}CO_2$ slope) during exercise.**

Methods. **One hundred seventy-three consecutive patients (155 men; mean [±SD] age 59.8 ± 11.5 years; radionuclide left ventricular ejection fraction [LVEF] 28.4 ± 14.6%) underwent cardiopulmonary exercise testing (peak oxygen consumption 18.5 ± 7.3 ml/kg per min; $\dot{V}E$–$\dot{V}CO_2$ slope 34.8 ± 10.6) over a 2-year period. Using 1.96 standard deviations above the mean $\dot{V}E$–$\dot{V}CO_2$ slope of 68 healthy age-matched subjects (mean slope 26.3 ± 4.1), we defined a high ventilatory response to exercise as a slope >34.**

Results. **Eighty-three patients (48%) had an increased $\dot{V}E$–$\dot{V}CO_2$ slope (mean 43.1 ± 8.9). There was a difference in age (62.2 vs. 57.3 years, p = 0.005), New York Heart Association functional class (2.9 vs. 2.1, p < 0.001), LVEF (24.7 vs. 31.9%, p = 0.0016), peak oxygen consumption (14.9 vs. 21.7 ml/kg per min, p < 0.0001) and radiographic cardiothoracic ratio (0.58 vs. 0.55, p = 0.002) between these patients and those with a normal slope. In the univariate Cox proportional hazards model, the $\dot{V}E$–$\dot{V}CO_2$ slope was an important prognostic factor (p < 0.0001). In the multivariate Cox analyses using several variables (age, peak oxygen consumption, $\dot{V}E$–$\dot{V}CO_2$ slope and LVEF), the $\dot{V}E$–$\dot{V}CO_2$ slope gave additional prognostic information (p = 0.018) beyond peak oxygen consumption (p = 0.022). Kaplan-Meier survival curves at 18 months demonstrated a survival rate of 95% in patients with a normal $\dot{V}E$–$\dot{V}CO_2$ slope compared with 69% in those with a high slope (p < 0.0001).**

Conclusions. **A high $\dot{V}E$–$\dot{V}CO_2$ slope selects patients with more severe heart failure and is an independent prognostic marker. The $\dot{V}E$–$\dot{V}CO_2$ slope may be used as a supplementary index in the assessment of patients with chronic heart failure.**

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Chronic heart failure is a common condition with high morbidity and mortality. It has a prevalence of 4.5% in the population between 65 and 74 years old and an overall 5-year survival rate of <40% (1). Symptoms of chronic heart failure, such as dyspnea and fatigue, are debilitating and manifest especially during exertion. Although indexes such as left ventricular ejection fraction (LVEF), ventricular dimensions and hemodynamic measurements reflect the degree of cardiac dysfunction, there is little correlation between these variables and exercise capacity (2–5). Exercise testing therefore remains an important and objective means of assessing the functional capacity of these patients, especially when coupled to respiratory gas exchange analysis (6–10). During such cardiopulmonary exercise testing, peak oxygen consumption during exercise is traditionally used as the major index of functional impairment (11–14). Peak oxygen consumption has also been used in the assessment of response to therapy and in the triage of patients with chronic heart failure awaiting heart transplantation (15). However, it has important limitations and may not be accurately obtained because a plateau is not always reached at peak exercise (16). It is also influenced by the motivation of patients (17).

During cardiopulmonary exercise testing, a close linear relation exists between carbon dioxide output ($\dot{V}CO_2$) and minute ventilation ($\dot{V}E$); this relation is more linear and less variable than that between oxygen consumption and minute ventilation (18,19). The slope of the regression line relating carbon dioxide output and minute ventilation ($\dot{V}E$–$\dot{V}CO_2$ slope) can therefore be used to describe the ventilatory response to exercise (20–22). Much interest has been directed toward the excessive exercise ventilatory response demonstrated in patients with chronic heart failure, characterized by a steeper $\dot{V}E$–$\dot{V}CO_2$ slope (5,21–26). This steeper slope is associated with reduced cardiac output during exercise (5,23), increased pulmonary artery and capillary wedge pressures (5,23), increased

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Abbreviations and Acronyms

CI	=	confidence interval
HR	=	hazard ratio
FEV_1	=	forced expiratory volume in 1 s
FVC	=	forced vital capacity
LVEF	=	left ventricular ejection fraction
$\dot{V}_{CO_2}$	=	carbon dioxide output
$\dot{V}_E$	=	minute ventilation
$\dot{V}_E$–$\dot{V}_{CO_2}$ slope	=	slope of regression relating minute ventilation to carbon dioxide output

dead space/tidal volume ratio (5,23,26) and, more recently, an augmented chemoreceptor sensitivity (27). In summary, it is still not precisely known whether the increased ventilatory response to exercise in patients with chronic heart failure is predominantly due to reduced pulmonary perfusion and hemodynamic abnormalities causing ventilation–perfusion mismatching or to the altered control of ventilation, as suggested by the augmentation in chemosensitivity. The latter, in turn, may be related to sympathetic overactivity (27), abnormal potassium metabolism (28,29), ergoreflex activation (30), early lactic acidosis (31) or altered central command (32). The mechanisms causing an increased ventilatory response to exercise may well be multifactorial.

Other than being steeper, the $\dot{V}_E$–$\dot{V}_{CO_2}$ slope has also been observed to be inversely correlated with peak oxygen consumption in patients with chronic heart failure (22,23). Therefore, we reasoned that it may be used as a supplementary index in the assessment of patients with chronic heart failure. However, there are to date no comprehensive data on the clinical characteristics of patients with chronic heart failure exhibiting an excessive ventilatory response to exercise. The prognostic significance of an increased $\dot{V}_E$–$\dot{V}_{CO_2}$ slope in patients with chronic heart failure is also not known.

The aims of our study were to 1) determine the normal values of the ventilatory response to exercise in healthy subjects; 2) characterize patients with chronic heart failure exhibiting an abnormally high ventilatory response to exercise in terms of clinical indexes of severity, including peak oxygen consumption, LVEF, radiographic cardiothoracic ratio and New York Heart Association functional class; and 3) investigate the usefulness of the ventilatory response to exercise as a prognostic index of survival in patients with chronic heart failure.

Methods

Patients. One hundred seventy-three consecutive patients with chronic heart failure who performed a cardiopulmonary exercise test over a 2-year period between January 1993 and December 1994 inclusive were studied retrospectively. Treadmill cardiopulmonary exercise testing was performed using a modified Bruce protocol (33) with the addition of a "stage 0" at 1.0 mph and a 5% gradient. All patients were encouraged to exercise to exhaustion, with a peak respiratory exchange ratio >1.1. Respiratory gas exchange analysis was carried out by respiratory mass spectrometry (Amis 2000, Innovision, Odense, Denmark) every 10 s using the inert gas dilution technique (34). The $\dot{V}_E$–$\dot{V}_{CO_2}$ slope was calculated by linear regression analysis using the above values of minute ventilation and carbon dioxide output obtained every 10 s of the exercise. In all patients, the regression coefficient was >0.93 (mean [±SD] 0.98 ± 0.01). Both minute ventilation and carbon dioxide output were measured in liters/min, and thus the slope has no dimensions.

To define an excessive ventilatory response to exercise, the cardiopulmonary exercise data of 68 age-matched healthy subjects were analyzed. Using 1.96 standard deviations above the mean level of the $\dot{V}_E$–$\dot{V}_{CO_2}$ slope in the healthy subjects, we defined an abnormally high ventilatory response to exercise as >34. Before cardiopulmonary exercise testing, spirometric lung function tests were also performed. The characteristics of the healthy subjects and patients are shown in Table 1.

Most patients were followed up at the outpatient clinic of our hospital. Other variables analyzed in this study included

Table 1. Characteristics of Healthy Subjects and Patients With Chronic Heart Failure

	Healthy Subjects (n = 68)	Patients With CHF (n = 173)
Age (yr)	56.4 ± 9.5	59.8 ± 11.5
Men/women	56/12	155/18
Height (cm)	174.4 ± 9.5	173.1 ± 8.5
Weight (kg)	78.2 ± 13.1	78.4 ± 13.8
FEV_1 (% predicted)	113.9 ± 26.2	85.8 ± 22.6
FVC (% predicted)	119.0 ± 24.1	89.5 ± 20.5
Peak O_2 consumption (ml/kg per min)	32.5 ± 8.3	18.5 ± 7.3
$\dot{V}_E$–$\dot{V}_{CO_2}$ slope		
Overall	26.3 ± 4.1	34.8 ± 10.6
Men	26.2 ± 4.1	34.4 ± 10.6
Women	26.6 ± 4.1	35.6 ± 7.6
Etiology of CHF		
IHD		96
DCM		69
Others*		8
NYHA functional class		
I		30
II		57
III		61
IV		25
LVEF (%)		28.4 ± 14.6
Radiographic CTR		0.56 ± 0.06
Furosemide		n = 173
ACE inhibitor		n = 124

*Valvular heart disease in six patients, hypertension related in two. Data presented are mean value ± SD or number of patients. ACE = angiotensin-converting enzyme; CHF = chronic heart failure; CTR = cardiothoracic ratio; DCM = dilated cardiomyopathy; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity; IHD = ischemic heart disease; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; $\dot{V}_E$–$\dot{V}_{CO_2}$ slope = regression slope relating minute ventilation and carbon dioxide output during exercise.

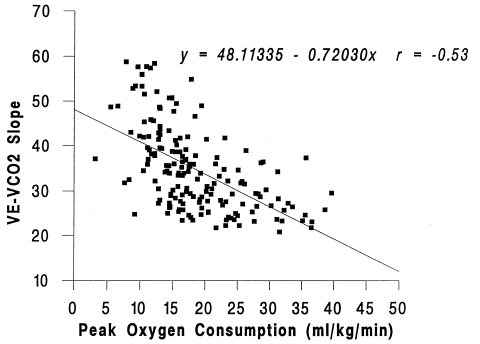

Figure 1. Inverse relation between peak oxygen consumption and ventilatory response to exercise ($\dot{V}E$–$\dot{V}CO_2$ slope) in patients with chronic heart failure.

age, etiology of chronic heart failure, New York Heart Association functional class, peak oxygen consumption, radionuclide multigated acquisition (MUGA) LVEF, radiographic cardiothoracic ratio and medication. Mortality data were obtained through outpatient clinic attendance records and telephone interviews with the patients or with the patients' primary care physician, where appropriate. Seven patients were lost to follow-up. Our study focused on all-cause mortality.

Studies of reproducibility. The reproducibility of the ventilatory response to exercise as characterized by the $\dot{V}E$–$\dot{V}CO_2$ slope was previously assessed in our laboratory. There was good agreement between repeated measures ($r = 0.93$, $p < 0.001$) in 20 patients with chronic heart failure, with a mean coefficient of variation of 6.2%.

Statistical analysis. The significance of results was assessed using a two-tailed Student *t* test and the relation between variables using linear regression analysis, where appropriate. Chi-square testing was used for analysis of categoric data. The prognostic value of the $\dot{V}E$–$\dot{V}CO_2$ slope and other clinical variables (age, chronic heart failure etiology, LVEF, exercise time, peak oxygen consumption, functional class and radiographic cardiothoracic ratio) were assessed using a Cox proportional hazards regression model. Kaplan-Meier estimates of the survival function were accordingly plotted for patients with normal and high $\dot{V}E$–$\dot{V}CO_2$ slopes; $p < 0.05$ was considered significant.

Results

Patients (Table 1). The mean age of patients was 59.8 ± 11.5 years; peak oxygen consumption was 18.5 ± 7.3 ml/kg per min; radionuclide LVEF was 28.4 ± 14.6%; and the mean $\dot{V}E$–$\dot{V}CO_2$ slope was 34.8 ± 10.6. There was an inverse relation between peak oxygen consumption and $\dot{V}E$–$\dot{V}CO_2$ slope ($r = -0.53$, $p < 0.0001$), in agreement with previous studies, as shown in Figure 1. The mean age of the healthy subjects in our study was 56.4 ± 9.5 years; peak oxygen consumption was 32.5 ± 8.3 ml/kg per min; and the mean $\dot{V}E$–$\dot{V}CO_2$ slope was 26.3 ± 4.1. There was no significant difference in mean $\dot{V}E$–$\dot{V}CO_2$ slope between healthy men and women in our study, as shown in Table 1.

Using the $\dot{V}E$–$\dot{V}CO_2$ slope of healthy subjects, we defined an abnormally high ventilatory response to exercise as >34 (>mean ± 1.96 SD). The $\dot{V}E$–$\dot{V}CO_2$ slope was below this value (mean 27.2 ± 4.4) in 90 patients (52%) and above this value (mean 43.1 ± 8.9) in 83 (48%). The clinical characteristics of these two groups of patients were analyzed on the basis of these findings, as follows.

Age, chronic heart failure etiology and functional class. Patients with an increased ventilatory response to exercise were older than those with a normal response (62.2 ± 9.4 vs. 57.3 ± 12.6 years, $p = 0.005$) and were also in a higher functional class (2.9 vs. 2.1, $p < 0.001$). However, the ventilatory response to exercise was not different in patients with idiopathic dilated cardiomyopathy ($n = 69$, $\dot{V}E$–$\dot{V}CO_2$ slope 34.3 ± 10.4) and those with ischemic heart disease ($n = 96$, $\dot{V}E$–$\dot{V}CO_2$ slope 35.7 ± 10.8).

Lung function test. The lung function tests were more impaired in patients with an increased ventilatory response to exercise than in those with a normal response. The forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC), expressed in terms of percentage predicted, were 79 ± 23% versus 93 ± 20% for FEV_1 and 85 ± 21% versus 94 ± 19% for FVC ($p = 0.002$ and 0.004, respectively).

Cardiopulmonary exercise variables. Patients with a high ventilatory response to exercise had a reduced peak oxygen consumption (14.9 ± 5.7 vs. 21.7 ± 7.1 ml/kg per min, $p < 0.0001$), and exercise duration was shorter (410 ± 173 vs. 583 ± 202 s, $p < 0.0001$). Rest heart rate was not different in the two groups (87 ± 18 vs. 84 ± 18 beats/min, $p = 0.4$), but heart rate at peak exercise was lower in patients with a high $\dot{V}E$–$\dot{V}CO_2$ slope (136 ± 26 vs. 146 ± 25 beats/min, $p = 0.01$). Both rest and peak exercise systolic blood pressure were lower in patients with a high ventilatory response to exercise (118 ± 26 vs. 128 ± 23 mm Hg, $p = 0.009$ and 142 ± 33 vs. 163 ± 35 mm Hg, $p < 0.0001$, respectively).

Radionuclide LVEF and radiographic cardiothoracic ratio. LVEF was lower (24.7 ± 13.1% vs. 31.9 ± 14.7%, $p = 0.0016$) and the radiographic cardiothoracic ratio greater in patients with an increased ventilatory response to exercise (0.58 ± 0.07 vs. 0.55 ± 0.05, $p = 0.002$).

Medication. Patients with an increased ventilatory response to exercise received an increased dose of furosemide daily, although this dose did not reach statistical significance (84.8 vs. 75.9 mg, $p = 0.43$). An equal number of patients ($n = 62$) in each group received angiotensin-converting enzyme inhibitors.

Survival analysis. The mean duration of follow-up ($n = 166$) was 759 ± 340 days (range 4 to 1,484). Thirty-six patients died during follow-up, and heart transplantation was performed in two. Although the latter were alive at the time of study data analysis, each heart transplantation was classified as equivalent to a death for analysis purposes. For survivors, the duration of follow-up was 889 ± 229 days (range 595 to 1,484). Of those who died, the duration of follow-up was 322 ± 285

Table 2. Clinical Characteristics of Patients With Chronic Heart Failure: Survivors Versus Nonsurvivors*

	Survivors (n = 128)	Nonsurvivors (n = 38)	p Value
Age (yr)	59.3 ± 11.8	62.0 ± 11.0	0.2
Men/women	113/15	35/3	0.5
Etiology (DCM/IHD)	51/69	14/24	> 0.5
NYHA functional class	2.2	3.2	< 0.0001
LVEF (%)	31.1 ± 14.6	22.8 ± 14.7	0.002
Radiographic CTR	0.55 ± 0.06	0.57 ± 0.06	0.19
Peak O_2 consumption (ml/kg per min)	20.0 ± 6.9	14.0 ± 6.8	< 0.0001
$\dot{V}E$–$\dot{V}CO_2$ slope	32.3 ± 7.8	41.9 ± 14.1	< 0.0001
Exercise time (s)	540.1 ± 197.5	394.3 ± 194.4	< 0.0001

*Seven patients were lost to follow-up for survival analysis (thus, n = 166). Data presented are mean value ± SD or number of patients. Abbreviations as in Table 1.

days (range 4 to 1,166). The overall 1-year cumulative survival rate was 86% (23 deaths).

There was no difference in age and etiology of heart failure between survivors and nonsurvivors (Table 2). However, those who died were in a higher functional class ($p < 0.0001$) and had reduced peak oxygen consumption ($p < 0.0001$) and exercise duration ($p < 0.0001$) and a lower LVEF ($p < 0.002$). The $\dot{V}E$–$\dot{V}CO_2$ slope was also significantly higher (41.9 ± 14.1 vs. 32.3 ± 7.8, $p < 0.0001$). In contrast, the radiographic cardiothoracic ratio was not significantly different ($p = 0.19$).

In the univariate Cox proportional hazards model, exercise duration, peak oxygen consumption, functional class, LVEF and $\dot{V}E$–$\dot{V}CO_2$ slope were significant prognostic indicators (Table 3). With multivariate analyses using two variables, the $\dot{V}E$–$\dot{V}CO_2$ slope remained an important prognostic indicator independent of age, peak oxygen consumption, functional class, exercise duration and LVEF. With multivariate analyses using peak oxygen consumption, exercise duration and $\dot{V}E$–$\dot{V}CO_2$ slope as covariates, only the $\dot{V}E$–$\dot{V}CO_2$ slope (hazard ratio [HR] 1.046, 95% confidence interval [CI] 1.013 to 1.080, $p = 0.006$) and peak oxygen consumption (HR 0.874, 95% CI 0.780 to 0.979, $p = 0.02$), but not exercise duration (HR 1.001, 95% CI 0.998 to 1.004, $p = 0.59$), provided prognostic information. With multivariate analyses using age, peak oxygen consumption, LVEF and the $\dot{V}E$–$\dot{V}CO_2$ slope as covariates, the $\dot{V}E$–$\dot{V}CO_2$ slope again provided additional prognostic information beyond peak oxygen consumption (Table 4). When Kaplan-Meier survival curves censored at 1 year were constructed, patients with a normal $\dot{V}E$–$\dot{V}CO_2$ regression slope had a survival rate of 98% (2 deaths) compared with 73% (21 deaths) in those with a high $\dot{V}E$–$\dot{V}CO_2$ slope ($p < 0.0001$). Kaplan-Meier survival curves for 18 months of follow-up (547 days) showed a survival rate of 95% (4 deaths) for patients with a normal $\dot{V}E$–$\dot{V}CO_2$ slope and 69% (24 deaths) for patients with a high $\dot{V}E$–$\dot{V}CO_2$ slope ($p < 0.0001$), as shown in Figure 2.

Table 4. Multivariate Cox Regression Analysis of Study Variables*

Variable	r Coeff	SE	p Value	HR (95% CI)
Age	0.001	0.018	0.95	1.001 (0.967–1.037)
Peak O_2 consumption	− 0.095	0.042	0.022	0.909 (0.838–0.987)
$\dot{V}E$–$\dot{V}CO_2$ slope	0.039	0.017	0.018	1.040 (1.007–1.074)
LVEF	− 0.022	0.014	0.122	0.978 (0.952–1.006)

*$\dot{V}E$–$\dot{V}CO_2$ provided additional prognostic information beyond peak oxygen consumption. Abbreviations as in Tables 1 and 3.

Discussion

General findings. Our study confirms previous observations that the exercise ventilatory response is increased in some patients with chronic heart failure, as demonstrated by a higher $\dot{V}E$–$\dot{V}CO_2$ slope. It also confirms the inverse relation between peak oxygen consumption and the $\dot{V}E$–$\dot{V}CO_2$ slope. However, the modest correlation suggests that although these two variables are related, they are determined by different factors. As shown by our study, the slope is abnormal in ~50% of patients with heart failure. These patients were in a higher functional class. Patients with an increased ventilatory response to exercise also demonstrated poorer exercise tolerance, as indicated by a reduced peak oxygen consumption. Heart rate and blood pressure response at peak exercise were also reduced; LVEF

Table 3. Univariate Cox Regression Analysis of Association Between Variables Studied and Survival Time

Variable	r Coeff	SE	p Value	HR (95% CI)
Age	0.021	0.015	0.15	1.023 (0.993–1.053)
Gender	− 0.049	0.53	0.9	0.952 (0.337–2.688)
Etiology	− 0.069	0.279	0.8	0.933 (0.540–1.613)
NYHA functional class	1.055	0.201	< 0.0001	2.872 (1.936–4.262)
LVEF	− 0.041	0.14	0.003	0.959 (0.934–0.986)
Radiographic CTR	3.612	2.66	0.17	37.04 (0.202–6,807.5)
Peak O_2 consumption	− 0.169	0.036	< 0.0001	0.845 (0.787–0.907)
Ventilatory response to exercise ($\dot{V}E$–$\dot{V}CO_2$ slope)	0.077	0.13	< 0.0001	1.080 (1.053–1.107)
Exercise time	− 0.003	0.001	0.0002	0.997 (0.995–0.998)

CI = confidence interval; Coeff = coefficient; HR = hazard ratio; other abbreviations as in Table 1.

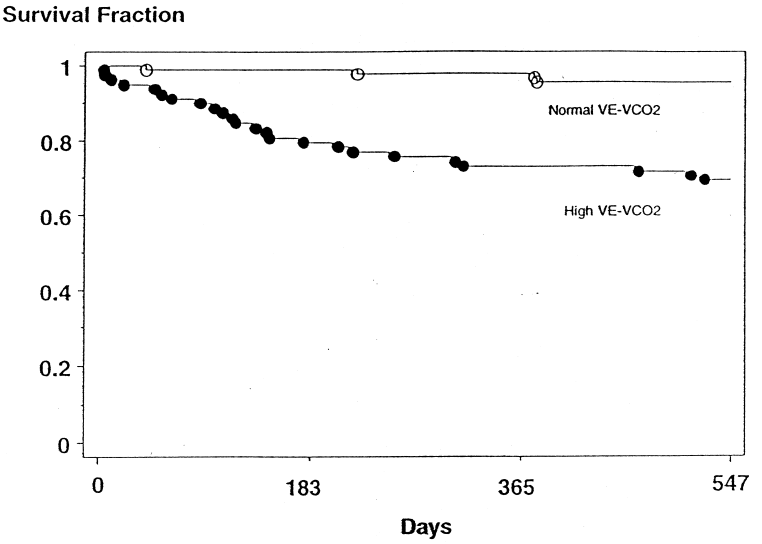

Figure 2. Kaplan-Meier survival curves for 18-month follow-up (547 days) showing a significant difference ($p < 0.0001$) in survival in patients with a normal ventilatory response to exercise versus those with a high response.

was lower and radiographic cardiothoracic ratio larger. In short, the ventilatory response to exercise reflects the severity of heart failure patients from several aspects, namely, clinical symptoms (functional class), cardiac function (LVEF, radiographic cardiothoracic ratio, heart rate and blood pressure response) and functional capacity (peak oxygen consumption). The findings were unlikely to be affected by medication, such as angiotensin-converting enzyme inhibitors, because the number of patients receiving this medication was similar in both patient groups. The $\dot{V}E$–$\dot{V}CO_2$ slope may therefore be a useful supplementary measurement in the assessment of patients with chronic heart failure and one that could easily be obtained during cardiopulmonary exercise testing.

In our study, patients who had an increased ventilatory response to exercise were slightly older. Age has been previously shown to affect the ventilatory response to exercise both in healthy subjects (35) and in patients with chronic heart failure (5). The reasons for this are not known but may reflect declining ventilatory efficiency with age. Pulmonary function tests in terms of FEV_1 and FVC were also more impaired in patients with an increased $\dot{V}E$–$\dot{V}CO_2$ slope. It may be that severe heart failure is associated with worse parenchymal lung disease, as observed by other workers (36,37).

Possible reasons for prognostic significance. This study was not designed to investigate the mechanisms of the increased ventilatory response to exercise in patients with chronic heart failure. Nevertheless, that it is related to several indexes of severity suggests that it serves as a compensatory response to maintain arterial blood gas tension and oxygen saturation within normal limits during exercise in these patients. Given that several factors may contribute to the increased ventilatory response to exercise, its prognostic value in chronic heart failure is more difficult to explain. We showed that the $\dot{V}E$–$\dot{V}CO_2$ slope is an important predictor of mortality, independent of other factors affecting survival in chronic heart failure, such as peak oxygen consumption and LVEF. Indeed, if the increased ventilatory response to exercise in patients with chronic heart failure is due both to ventilation–perfusion mismatch arising from hemodynamic dysfunction and to the altered control of ventilation, as indicated by the augmentation of chemoreflex, then the ventilatory response to exercise may well assess these aspects of the pathophysiology of heart failure that also correlate with an advanced stage of the disease. Abnormal hemodynamic variables are known to be associated with a poor prognosis in this condition (38,39), and the mechanisms of augmentation of the chemoreflex may lie in sympathetic overactivity and neurohormonal imbalance, both of which also affect survival in chronic heart failure (40,41). Catecholamines have been shown to increase chemosensitivity (42), which in turn may further perpetuate the sympathetic drive and contribute to neurohormonal imbalance (43). The chemoreflex may also be augmented directly by reduced blood flow to the chemoreceptors, again reflecting hemodynamic dysfunction. Thus, patients with an increased $\dot{V}E$–$\dot{V}CO_2$ slope have a worse prognosis.

Limitations of the study. This was a retrospective study that requires prospective confirmation. Similarly, further studies are required to assess the usefulness of the ventilatory response to exercise in the monitoring of patients during treatment. A larger cohort of patients with more severe heart failure would also be needed to investigate the use of the $\dot{V}E$–$\dot{V}CO_2$ slope in the selection and triage of patients for heart transplantation.

Conclusions. The ventilatory response to exercise may be used as a supplementary index in the assessment of patients with chronic heart failure. It is highly reproducible in repeated cardiopulmonary exercise tests and was abnormal in ~50% of patients with chronic heart failure in our study. It is also an important prognostic indicator in chronic heart failure.

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