Evaluation of a specific activity questionnaire to predict mortality in men referred for exercise testing

Paul McAuley, PhD,[a] Jonathan Myers, PhD,[b] Joshua Abella, MD,[b] and Victor Froelicher, MD[b] ***Los Angeles and Palo Alto, CA***

Background A self-administered symptom questionnaire developed at our institution (Veterans Specific Activity Questionnaire [VSAQ]) is routinely used to estimate a patient's exercise capacity to individualize the exercise test in accordance with current guidelines. This study was performed to evaluate the association of the VSAQ with all-cause mortality.

Methods The VSAQ was administered to 1185 consecutive male patients (mean age 58 ± 12 years) referred for exercise testing for clinical reasons. The VSAQ is designed to determine which specific daily activities are associated with cardiovascular symptoms (fatigue, chest pain, or shortness of breath) to provide an estimate of exercise tolerance (in metabolic equivalents [METs]) before exercise testing. Patients were classified into 1 of 3 groups according to VSAQ score: <5 METs, 5 to 8 METs, and >8 METs. The association between exercise capacity estimated by the VSAQ, other clinical and exercise test variables, and all-cause mortality was assessed by Cox proportional hazards. The mean follow-up period was 4.5 ± 2.9 years.

Results There were a total of 132 deaths during the follow-up period, resulting in an average annual mortality of 2.7%. In a multivariate analysis including clinical risk factors and exercise test variables, age-adjusted predictors of mortality, in rank order, were the VSAQ score in METs, history of chronic heart failure, history of smoking, and diabetes (for VSAQ: hazard ratio [HR] 0.90, 95% CI 0.83-0.98; for chronic heart failure: HR 2.67; 95% CI 1.51-4.72; for smoking: HR 1.74, 95% CI 1.18-2.57; and for diabetes: HR 1.84, 95% CI 1.15-2.95). Expressed in tertiles, age-adjusted relative risks for the VSAQ were 1.0, 0.54, and 0.22 (*P* for trend <.001). Each 1-MET increase in the VSAQ conferred a 10% survival benefit.

Conclusions A simple self-administered symptom questionnaire strongly and independently predicted all-cause mortality. The VSAQ is a useful adjunct to clinical and exercise test data for stratifying risk in patients undergoing exercise testing for clinical reasons. (Am Heart J 2006;151:890.e1-890.e7)

The exercise test is a valuable clinical tool which provides a wealth of diagnostic and prognostic information.[1,2] In recent years, exercise capacity has become increasingly recognized as a strong independent predictor of all-cause mortality.[3-5] Because maximal exercise testing is not always available, a number of surrogate measures have been used to estimate exercise tolerance. These include submaximal walk tests,[6-9] symptom questionnaires,[10-14] and a variety of nonexercise functional tools.[15,16] These have been particularly useful in multicenter pharmaceutical trials, in which exercise testing on a large scale is often not performed because of pragmatic or financial reasons. Although these measures generally correlate only modestly with measured exercise capacity, some have been shown to have prognostic value. For example, in the SOLVD trial, the inability to achieve >300 m in the 6-minute walk test strongly predicted mortality,[6] and this finding has been confirmed by subsequent trials in the United States and Europe.[7,8] In a recent study from WISE, the diagnostic and prognostic value of the Duke Activity Status Index (DASI),[12] a functional assessment tool derived from a patients' ability to perform daily activities, more strongly predicted cardiac events than other risk markers; each 1–metabolic equivalent (MET) increase in DASI score was associated with an 8% decrease in cardiovascular events.[17]

Consensus guidelines published by major organizations have suggested that the exercise test should be individualized, and the test duration should fall within a range of 8 to 12 minutes.[1,2] We originally developed the Veterans Specific Activity Questionnaire (VSAQ) in an effort to individualize the exercise test protocol to meet

From the [a]Department of Natural Science, Loyola Marymount University, Los Angeles, CA, and [b]Cardiology Division, VA Palo Alto Health Care System/Stanford University, Palo Alto, CA[b]New England Research Institutes, Watertown, MA.
Submitted May 27, 2005; accepted September 15, 2005.
Reprint requests: Jonathan Myers, PhD, Cardiology Division, 111C, VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304.
E-mail: drj993@aol.com
0002-8703/$ - see front matter

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Table I. Demographic and clinical characteristics of all subjects and by questionnaire

Variable	All subjects (N = 1185)	VSAQ <5 METs (n = 92)	VSAQ 5-8 METs (n = 403)	VSAQ >8 METs (n = 690)	P*
Demographic characteristics					
Age (y)	58 ± 12	70 ± 10	62 ± 11	54 ± 11†	<.001
Duration of follow-up (y)	4.5 ± 2.9	–	–	–	–
Height (in)	69 ± 3	69 ± 3	69 ± 3	69 ± 3	NS
Weight (lb)	197 ± 40	182 ± 40	197 ± 45	200 ± 45	NS
Body mass index (kg/m^2)	29 ± 5	27 ± 6	29 ± 6	29 ± 6	.003
Smoking (pack-years)	23 ± 27	29 ± 31	27 ± 28	20 ± 25	NS
Medications (%)					
Digoxin	3.3	8.7	4.7	1.7	NS
Calcium antagonist	20.6	39.1	23.8	16.2†	<.01
β-Blocker	22.7	23.9	27.3	19.6	<.001
Nitrate	9.5	25.0	12.7	5.5	NS
Antihypertensive agent	18.0	19.6	20.6	16.2	<.001
Medical history (%)					
Atrial fibrillation	3.6	3.3	5.5	2.6	NS
Pulmonary disease	9.5	13.0	11.9	7.5†	<.001
Stroke	2.6	6.5	4.2‡	1.2‡	<.001
Claudication	4.6	7.6	6.2	3.3	NS
Typical Angina	10.8	23.9	13.4	7.4†	<.05
HF	5.6	12.0	6.9	3.9†	NS
Hypercholesterolemia (>220 mg/dL)	33.4	29.3	32.3	34.6	<.001
History of smoking	25.4	15.2	26.6	26.1	<.001
Hypertension	52.4	55.4	59.1	48.1	<.001
Diabetes	12.0	6.5	12.2	12.6	<.05
History of myocardial infarction	12.7	22.8	15.6	9.7†	<.001
Interventions (%)					
Coronary bypass surgery	8.1	17.4	10.7	5.4	NS
Percutaneous transluminal coronary angioplasty	7.3	13.0	9.4	5.2	<.01

*P value represents main effect across VSAQ groups.
†$P < .05$ versus <5 METs and 5-8 METs groups.
‡$P < .05$ versus <5 METs group.

these guidelines.[13,18] The VSAQ is a 13-item self-administered symptom questionnaire that estimates exercise capacity expressed in METs. We previously reported that the VSAQ obtained just before an exercise test is a strong predictor of subsequent exercise capacity.[12] Others have used the VSAQ to set the ramp rate to optimize the test duration,[18-20] to predict exercise capacity 1 year after coronary bypass surgery,[21] and to predict postoperative risk among patients undergoing coronary bypass surgery.[22] In the present study, we assessed the value of the VSAQ as an independent predictor of survival among consecutive patients referred for exercise testing for clinical reasons.

Methods

Patients

One thousand one hundred eighty-five consecutive male patients (mean age 58 ± 12 years) referred for exercise testing for clinical reasons were included in the study. Patients were classified into 1 of 3 groups according to VSAQ score: <5 METs, 5 to 8 METs, and >8 METs. Demographic and clinical characteristics of the study group, by VSAQ category, are listed in Table I. Twenty-three percent of patients were receiving β-blockers; 21%, calcium-channel antagonists; and 3%, digoxin. One hundred fifty-one patients (12.7%) had a history of myocardial infarction, and 182 (15.4%) had a history of either coronary angioplasty or coronary bypass surgery, and 5.6% had a history of heart failure (HF; Table 1).

Questionnaire

Before exercise testing, the VSAQ was given to each patient. The VSAQ is a brief self-administered questionnaire designed to determine which specific daily activities are associated with symptoms of cardiovascular disease (fatigue, chest, pain, claudication, or shortness of breath).[13] The VSAQ consists of a list of activities presented in progressive order according to METs. Patients were instructed to determine which activities might typically cause these symptoms during daily activities (Table II). The MET values associated with each activity are in general agreement with the ACSM Compendium of Physical Activities.[23] In our laboratory, the VSAQ is routinely used to estimate exercise capacity to individualize the ramp rate used for the exercise protocol.[13,18]

Exercise testing

All patients underwent maximal exercise testing with the use of an individualized ramp treadmill protocol.[24] This test individualizes both warm-up and peak walking speeds (on the basis of a given patient's height, fitness, and familiarity with

Table II. The veterans specific activity questionnaire

Before beginning your exercise test today, we need to estimate what your usual limits are during daily activities. The following is a list of activities which increase in difficulty as you read down the page. Think carefully, then underline the first activity that, if you performed it for a period, would typically cause fatigue, shortness of breath, chest discomfort, or otherwise cause you to want to stop. If you do not normally perform a particular activity, try to imagine what it would be like if you did.

METs

1—Eating, getting dressed, working at a desk.
2—Taking a shower.
—Walking down 8 steps.
3—Walking slowly on a flat surface for 1 or 2 blocks.
—A moderate amount of work around the house, such as vacuuming, sweeping the floors, or carrying groceries.
4—Light yard work, that us, raking leaves, weeding, or pushing a power mower.
—Painting or light carpentry.
5—Walking briskly, that is, 4 mph.
—Social dancing, washing the car.
6—Play 9-hole golf carrying your own clubs; heavy carpentry, mow lawn with push mower.
7—Perform heavy outdoor work, that is, digging, spading soil, etc.
—Play tennis (singles), carry 60 lb.
8—Move heavy furniture.
—Jog slowly, climb stairs quickly, carry 20 lb upstairs.
9—Bicycling at a moderate pace, sawing wood, jumping rope (slowly).
10—Brisk swimming, bicycle up a hill, walking briskly uphill, jog 6 mph.
11—Cross-country ski.
—Play basketball (full court).
12—Running briskly, continuously (level ground, 8 min/mile).
13—Any competitive activity, including those which involve intermittent sprinting.
—Running competitively, rowing, backpacking.

Table III. Exercise test responses (mean ± SD) by questionnaire

Variable	VSAQ <5 METs (n = 92)	VSAQ 5-8 METs (n = 403)	VSAQ >8 METs (n = 689)	*P**
Rest				
Heart rate (beat/min)	71 ± 14	73 ± 13	73 ± 14†	<.001
Systolic blood pressure (mm Hg)	137 ± 24	134 ± 21	130 ± 19	.015
Diastolic blood pressure (mm Hg)	78 ± 13	81 ± 12	81 ± 11†	NS
Peak exercise				
Exercise capacity predicted by VSAQ (METs)	4.3 ± 0.6	6.6 ± 0.8	10.6 ± 2.0‡	<.001
Exercise capacity achieved (METs)§	4.9 ± 2.3	6.6 ± 2.6	10.1 ± 2.9‡	<.001
Heart rate (beat/min)	121 ± 22	132 ± 22	149 ± 21‡	<.001
Systolic blood pressure (mm Hg)	169 ± 26	174 ± 29	177 ± 26‡	<.001
Diastolic blood pressure (mm Hg)	85 ± 23	83 ± 17	83 ± 15	<.001
Double product (beats/mm Hg per min × 10^3)	20 ± 5	23 ± 6	27 ± 6	NS
Perceived exertion (Borg scale)	17 ± 2	17 ± 2	17 ± 3	NS

**P* value represents main effect from analysis of variance.
†*P*< .05 versus <5 METs groups.
‡*P*< .05 versus <5 METs and 5 to 8 METs groups.
§Calculated from treadmill speed and grade.

treadmill walking) and ramp rate (rate of change in speed and grade) to yield a test duration of between 8 and 12 minutes.[1,2,25] A microcomputer automatically increased workload after an individualized walking speed, and predicted values for maximal exercise capacity were entered. Standardized equations were used to determine the calculated peak METs on the basis of treadmill speed and grade.[2]

Because the VSAQ was designed to target symptoms associated with exercise limitations, patients were excluded if their exercise test was submaximal (ie, terminated by the supervising physician for reasons other than symptom or sign limits). Blood pressure was recorded in alternate minutes throughout the test, and a 12-lead electrocardiogram was recorded each minute. The patient's subjective level of exertion was assessed by the Borg 6-to-20 scale.[26] Standard clinical criteria for terminating the tests (eg, fall in systolic blood pressure, ST-segment depression >2 mm, or dangerous arrhythmias) were followed,[1,2] but no heart rate or time limit was imposed, and a maximal effort was encouraged. Patients were discouraged from holding onto the handrails for support as much as possible.

Statistical analysis

Number Crunching Statistical Software (Kaysville, UT) was used for all statistical analyses. Total (all-cause) mortality was used as the end point for survival analysis. Survival analysis was performed using Kaplan-Meier curves to compare variables and cut points, and a Cox proportional hazards model was used to determine which variables were significantly associated with time to death and to develop relative risks for tertiles of VSAQ score. Age-adjusted hazard ratios were calculated along with their 95% CIs. The Armitage test for trends in proportions was used to test the significance of relative risks for VSAQ scores. Vital status was determined as of January 2004, and the Social Security Death Index was used to match all patients using name and social security number.

In the Cox proportional hazards analysis, age-adjusted univariate and multivariate analyses were performed. The VSAQ was entered as a continuous variable in METs. Other clinical and historical variables, including history of diabetes, smoking, hypertension, obesity (body mass index $\geq$30 kg/m^2), family history of coronary artery disease (CAD; occurrence of CAD in an immediate family member before the age of 60 years), hypercholesterolemia (total cholesterol >220 mg/dL), and history of cardiovascular disease (CAD, stroke, peripheral vascular disease, or positive exercise test), were considered dichotomous variables. The proportionality assumption for VSAQ score was tested by evaluating the Schoenfeld residuals as functions of time[27] and also by analyzing the model with time as an independent variable.

To compare our results with those of previous studies and in accordance with disability evaluation under Social Security,[28] subjects with an exercise capacity of <5 METs were considered to have a high risk of mortality, whereas those with an exercise

Table IV. Age-adjusted predictors of mortality risk among clinical and exercise variables

Variable	HR	Lower CI	Upper CI	P
Univariate analysis				
VSAQ (METs)	0.84	0.78	0.91	<.001
Obesity (≥30 kg/m^2)	1.11	0.98	1.26	.09
History of smoking	1.69	1.14	2.49	.009
Diabetes	1.81	1.13	2.89	.01
Congestive HF	2.83	1.61	4.98	<.001
Hypertension				.74
Family history of CAD				.50
Hypercholesterolemia (>220 mg/dL)				.89
Cardiovascular disease history				.66
Multivariate analysis				
VSAQ (METs)	0.90	0.83	0.98	.02
History of smoking	1.74	1.18	2.57	.006
Diabetes	1.84	1.15	2.95	.02
Chronic HF	2.67	1.51	4.72	<.001

capacity >8 METs were considered to have the lowest risk. Thus, relative risks were calculated for each tertile (<5, 5-8, and >8 METs). The subgroup with the lowest VSAQ score was used as the reference category.

Results

The mean (±SD) follow-up period was 4.5 ± 2.9 years, and the average annual mortality was 2.7%. A total of 132 deaths occurred over the follow-up period. Compared with subjects scoring either 5 to 8 or >8 METs on VSAQ, subjects in the lowest VSAQ category (<5 METs) were older, had a lower body mass index, and had more extensive use of medications in addition to more cardiovascular interventions (Table I).

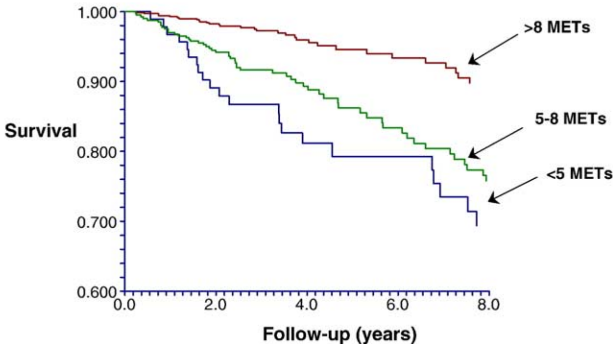
Exercise responses

Exercise test results are listed in Table III. The mean peak heart rate was 141 ± 24 beat/min, corresponding to 87% ± 12% of the age-predicted maximum heart rate. The mean peak rating of perceived exertion was 17 ± 2, suggesting that a maximal effort was achieved by most patients. Significant (>1.0 mm) exercise-induced ST-segment depression occurred in 47% of the subjects, whereas angina occurred in 13%, and ventricular tachycardia (≥3 premature ventricular contractions in succession) occurred in 17 subjects (1.4%).

Achieved versus predicted exercise capacity

Mean peak METs predicted from the VSAQ (8.8 ± 2.7) were similar to those calculated from the final speed and grade of the treadmill (8.5 ± 3.4). The correlation coefficient between the 2 values was 0.68 ($P < .001$). Directly measured METs (by gas exchange) were obtained in a subset of our patient population (n = 321). Correlation coefficients between directly measured METs and the VSAQ and estimated METs (from treadmill speed and grade) were 0.56 and 0.72, respectively ($P < .001$).

Figure 1



Kaplan-Meier survival curves (age-adjusted) for the VSAQ.

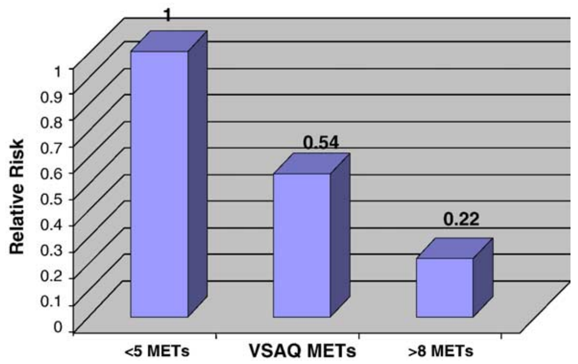
Survival

After adjustment for age, exercise capacity expressed as either peak METs achieved on the treadmill or as the VSAQ score was a stronger predictor of mortality than other clinical and exercise test variables. Both univariately and multivariately, the VSAQ score, history of diabetes, history of chronic HF, and history of smoking were the only significant predictors of mortality (Table IV). Each 1-MET increase in VSAQ score conferred a 10% increase in survival.

To compare the relative prognostic power of METs achieved on the treadmill to that estimated from the VSAQ, proportional hazards analyses were performed with the 2 variables entered together and also separately with other predictor variables. When entered separately, peak METs achieved and VSAQ score had similar prognostic power (per MET for VSAQ: hazard ratio [HR] 0.90, 95% CI 0.83-0.98, $P = .01$; for peak METs achieved on the treadmill: HR 0.89, 95% CI 0.85-0.97, $P = .001$). When in the model together, METs achieved on the treadmill had a similar HR (HR 0.91, 95% CI 0.84-0.99, $P = 0.02$), whereas the VSAQ was not a significant predictor of risk (HR 0.95, 95% CI 0.86-1.04, $P = .27$). Receiver operator characteristic analyses demonstrated that areas under the curve of both the VSAQ and METs achieved were 0.67.

Kaplan-Meier survival curves applying commonly recognized indices for exercise capacity (<5 vs 5-8 and >8 METs) demonstrated that higher VSAQ scores were associated with better survival ($P < .001$; Figure 1). Subjects with higher VSAQ scores had progressively lower risks of death; with the lowest tertile for VSAQ

Figure 2



Age-adjusted relative risks for all-cause mortality using the VSAQ, expressed in tertiles (*P* for trend <.001). The 95% CIs for the 5 to 8 METs and >8 METs groups were 0.96 to 1.16 and 1.02 to 1.13, respectively.

score as the referent group (<5 METs), the age-adjusted relative risks across tertiles of VSAQ scores were 1.0, 0.54 (≥5-8 METs), and 0.22 (>8 METs; $P < .001$ for trend; Figure 2). The relative risks associated with exercise capacity predicted by the VSAQ demonstrated that the highest VSAQ tertile (>8 METs) was associated with a >75% reduction in mortality risk.

Discussion

In the present study, we assessed the prognostic value of a brief self-administered symptom questionnaire (VSAQ) among patients referred for exercise testing for clinical reasons. We were interested in whether the VSAQ was an independent predictor of death and whether it was as strong a marker of risk as other established cardiovascular risk factors. We observed that the VSAQ strongly predicted mortality in our patient population, with an approximate 10% reduction in mortality per increment in VSAQ score. In a multivariate analysis, the VSAQ outperformed established risk factors such as smoking, diabetes, hypertension, and hyperlipidemia (Table IV). The risk of death from any cause in subjects whose VSAQ score was <5 METs was roughly 4-fold that of subjects whose VSAQ score was >8 METs (Figure 2). These findings suggest that there is significant prognostic value in simply having a patient subjectively assess their functional capabilities based on their own assessment of symptoms and activity tolerance. Such information may be particularly useful in situations where maximal exercise testing is not available.

Not surprisingly, peak METs achieved on the treadmill more strongly predicted mortality than the VSAQ score. This is in accordance with the growing body of data demonstrating that exercise capacity powerfully pre-

Table V. Correlations between VSAQ and measured or estimated METs from previous studies

	N	Measured METs	Estimated METs
Myers et al[12]	212	–	0.81
Rankin et al*[13]	97	0.57	–
Myers[18]	337	0.42	0.59
Pierson et al[22]	198	0.66	–
Zaheer, 2003† (CHF)	105	0.50	0.82
Maeder, 2005* ‡	41	0.46	0.52
McAuley (current study)	321	0.56	0.68

CHF, chronic heart failure.
*Modified VSAQ.
†Abstract, *Med Sci Sports Exerc* 2003;35(suppl):S352.
‡Maeder M, Wolber T, Atefy R, et al. Impact of the exercise mode on exercise capacity: bicycle testing revisited. Chest 2005;128:2804-11.

dicts outcomes in patients referred for exercise testing.[1,3-5,29,30] Thus, the VSAQ is not an appropriate surrogate for the exercise test in terms of estimating prognosis; in addition, as with any questionnaire, the VSAQ lacks the high yield of symptomatic, hemodynamic, and diagnostic information provided by the exercise test. Thus, in addition to its other applications (eg, developing ramp rates for individualized exercise protocols),[13] the VSAQ may be considered a useful risk assessment tool when exercise testing is not available.

Predicting health outcomes using surrogate measures of exercise capacity

Exercise capacity is commonly used clinically to gauge therapy, assess the efficacy of various interventions, and establish activity recommendations for patients with cardiovascular disease. In addition, in several recent studies performed among both clinically referred and asymptomatic populations, exercise capacity has been shown to be a more powerful predictor of mortality than other established risk factors for cardiovascular disease.[3-5] This is a departure from the past in which the diagnostic and prognostic value of the test generally focused on the ST segment.[4,29,30]

Insurers, clinicians, and regulatory agencies are increasingly relying upon patient outcomes to evaluate and improve patient care. Because of the additional time and costs associated with maximal exercise testing, surrogate measures of exercise tolerance have been widely used, particularly in multicenter pharmaceutical trials. Various questionnaires have been used to estimate tolerance of symptoms, assess disability, and evaluate the effectiveness of therapy. However, few such studies have been performed in which patients were followed for outcomes. The concept that an indirect and subjective estimate of exercise tolerance using a questionnaire could significantly contribute to the risk paradigm in patients with cardiovascular disease has a number of important clinical applications. These include

(1) providing a simple inexpensive alternative when exercise testing is unavailable or not feasible because of financial or physical limitations, time constraints, or increased patient risk, (2) serving as an end point in clinical trials, and (3) utilization in disease management or quality assessment/improvement programs.

Previous studies

The VSAQ has been used along with strength and body composition measures to predict outcomes among 200 patients undergoing coronary bypass surgery. Cook et al[22] observed that patients with both a high percentage of body fat and a low VSAQ score were at higher risk for at least one serious event (mortality or surgical complication over 3 months) and were associated with longer postoperative hospital stays. Pierson et al[21] similarly used the VSAQ to estimate functional capacity before and after coronary bypass surgery. The VSAQ correlated well with peak oxygen consumption per unit time ($\dot{V}O_2$; $r = 0.66$) and was a better predictor of 1-year exercise capacity than other clinical and postoperative variables, including the performance of regular aerobic exercise. Correlations ranging from 0.42 to 0.82 between the VSAQ and either measured METs or estimated METs have been reported in the literature (Table V). It is not known if the VSAQ predicts mortality in persons not referred for exercise testing. If so, the VSAQ could have much wider applications in patients presenting with symptoms typical of cardiovascular disease.

Limitations

The VSAQ has been shown to underestimate achieved exercise capacity by approximately 10% and 30% in the oldest and youngest age groups, respectively.[13,18] Moreover, it is likely that the correlation between the VSAQ and exercise capacity we observed might have been higher had we used an interview rather than a self-administered approach. For example, the DASI correlated highly (0.80) with measured peak $\dot{V}O_2$, but the correlation was only 0.58 when self-administered.[12] Exercise capacity was estimated on the basis of speed and grade of the treadmill in our study. Although this method is the most common measure of exercise capacity, directly measured peak oxygen uptake is the most accurate and reproducible measure of exercise tolerance.[31]

Any effort to predict mortality by assessing physical activity or using clinical or demographic data should be considered population-specific. The present population differed from those of previous studies in that only men referred for exercise testing for clinical reasons were included. Thus, the VSAQ was targeted toward a clinical population; many of whom were limited by symptoms, medications, and other factors related to cardiovascular disease. Therefore, our results generally apply only to patients who reach a symptom-limited end point. Other questionnaires may have greater utility in asymptomatic populations.

Conclusions

A brief self-administered symptom questionnaire that is routinely used to individualize the exercise test at our institution strongly predicted all-cause mortality in heterogeneous patients referred for the test for clinical reasons. This observation suggests that a low-cost time-saving instrument such as a simple questionnaire can contribute significantly to the risk paradigm in cardiovascular disease. Moreover, the VSAQ has the potential to serve as a surrogate end point in clinical trials, in addition to having utility for patient management and quality assessment.

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