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ORIGINAL ARTICLE

The prognostic value of haemodynamic parameters in the recovery phase of an exercise test. The Finnish Cardiovascular Study

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We tested the hypothesis that the change from the peak to recovery values of systolic arterial pressure ($SAP_{recovery}$) and rate–pressure product ($RPP_{recovery}$) can be used to predict all-cause and cardiovascular mortality, as well as sudden cardiac death (SCD) in patients referred to a clinical exercise stress test. As a part of the Finnish Cardiovascular Study (FINCAVAS), consecutive patients ($n = 2029$; mean age ± SD = 57 ± 13 years; 1290 men and 739 women) with a clinically indicated exercise test using a bicycle ergometer were included in the present study. Capacities of attenuated $SAP_{recovery}$, $RPP_{recovery}$ and heart rate recovery (HRR) to stratify the risk of death were estimated. During a follow-up (mean ± s.d.) of 47 ± 13 months, 122 patients died; 58 of the deaths were cardiovascular and 33 were SCD. In Cox regression analysis after adjustment for the peak level of the variable under assessment, age, sex, use of β-blockers, previous myocardial infarction and other common coronary risk factors, the hazard ratio of the continuous variable $RPP_{recovery}$ (in units 1000 mm Hg × b.p.m.) was 0.85 (95% CI: 0.73–0.98) for SCD, 0.87 (0.78–0.97) for cardiovascular mortality, and 0.87 (0.81 to 0.94) for all-cause mortality. $SAP_{recovery}$ was not a predictor of mortality. The relative risks of having HRR below 18 b.p.m., a widely used cutoff point, were as follows: for SCD 1.28 (0.59–2.81, ns), for cardiovascular mortality 2.39 (1.34–4.26) and for all-cause mortality 2.40 (1.61–3.58). In conclusion, as a readily available parameter, $RPP_{recovery}$ is a promising candidate for a prognostic marker.

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Introduction

An abnormal response of the autonomic nervous system during and after an exercise stress test is believed to be a marker of increased risk of death. Autonomic imbalance is reflected in, for example, the heart rate (HR) profile during and after exercise, which has been shown to associate with all-cause or cardiac mortality during follow-up.[1–4] Furthermore, short-term regulation of blood pressure (~HR × stroke volume × peripheral resistance) is dominated by the autonomic nervous system, and the levels of and changes in systolic arterial pressure (SAP) during the exercise have been found to represent determinants of cardiovascular mortality in several studies.[5,6] Moreover, the recovery of SAP ($SAP_{recovery}$) from the peak to the post-exercise level might mirror changes in the autonomic balance. In that case, $SAP_{recovery}$ could also prove valuable in predicting mortality during follow-up, but earlier studies on this hypothesis have been scarce.[7–9]

Several computed parameters have been derived with the idea that they would integrate several (patho) physiological markers or phenomena into a

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single variable. Such markers have not yet, however, broken through into wide-scale clinical use. Rate pressure product (RPP = HR × SAP) is a simple calculatory parameter based on two variables regulated by the autonomic nervous system. RPP is used as an indicator of myocardial oxygen uptake and coronary blood flow in the exercise test.[10] Moreover, resting and peak RPP during exercise have been linked to cardiovascular mortality,[6,11–18] but the prognostic value of the recovery of RPP ($RPP_{recovery}$) from the peak to the post-exercise level is unknown.

As a part of the Finnish Cardiovascular Study (FINCAVAS), we evaluated the hypothesis that the recovery of two readily available variables, SAP and RPP, can be used to predict all-cause and cardiovascular mortality, as well as sudden cardiac death (SCD) in patients referred to a clinical exercise stress test.

Materials and methods

Study cohort

As described in the detailed study protocol of FINCAVAS,[19] all consecutive patients coming in for a clinically indicated exercise stress test at Tampere University Hospital and willing to participate in the study were recruited between October 2001 and December 2004. A total of 2029 patients (1290 men and 739 women) with technically successful storage of exercise test data were included in the study (Tables 1 and 2). The main indications for the exercise test were a diagnosis of coronary heart disease (CHD, frequency 46%), testing vulnerability to arrhythmia during exercise (21%), evaluations of working capacity (18%) and the adequacy of CHD treatment (16%), in addition to obtaining an exercise test profile prior to an invasive operation (13%) or after a myocardial infarction (8%); some patients had more than one indication. The study protocol was approved by the Ethical Committee of the Tampere University Hospital District (Finland), and all patients gave an informed consent prior to the interview and measurements as stipulated in the Declaration of Helsinki Principles.

Study flow

After an informed consent was signed, the medical history of each patient was collected with a computer-based questionnaire. Thereafter, the subject lay down in the supine position for 10 min. The exercise test was performed using a bicycle ergometer with electrical brakes.

During the test, HR was continuously recorded with electrocardiography, whereas arterial pressure was measured with a brachial cuff every 2 min. The highest HR and SAP values during the exercise were used in the calculation of RPP_{peak}. In the post-exercise phase, HR and SAP in the sitting position

Table 2 Unadjusted percentage of women, frequency of β-blocker use, as well as the prevalence of cardiovascular disease, symptoms, risk factors and death for all participants according to the HRR cutoff point of 18 b.p.m. during the first minute of recovery

	HRR ⩾ 18 b.p.m. (%)	*HRR < 18 b.p.m. (%)*	*P-value*
Women	37	34	0.13
β-Blockers	53	72	0.00
Smoking	27	27	0.85
CHD	35	47	0.00
Prior MI	19	26	0.00
Hypercholesterolaemia	48	55	0.01
Diabetes	10	18	0.00
SCD	1	3	0.03
Cardiovascular death	2	6	0.00
All-cause death	4	13	0.00

Abbreviations: CHD, coronary heart disease; HRR, heart rate recovery; MI, myocardial infarction; SCD, sudden cardiac death.
The *P*-values have been calculated with the χ^2 test.

Table 1 Patient characteristics and exercise test variables for all participants according to the HRR cutoff point of 18 b.p.m. during the first minute of recovery

	HRR ⩾ 18 b.p.m., n = *1498*		*HRR < 18 b.p.m.*, n = *531*		P-*value*
	Mean	*s.d.*	*Mean*	*s.d.*	
Age (years)	55	13	63	12	0.00
BMI (kg/m^2)	27	4	29	5	0.00
Weight (kg)	80	15	83	16	0.00
Height (cm)	171	9	171	9	0.05
HR at rest (b.p.m.)	63	11	66	13	0.00
HR at peak exercise (b.p.m.)	152	23	131	31	0.00
Reached HR of expected maximum (%)	81	13	73	16	0.00
HR at 4 min of the recovery (b.p.m.)	85	17	82	20	0.00
SAP at rest (mm Hg)	135	18	137	20	0.06
SAP at peak exercise (mm Hg)	197	28	180	29	0.00
SAP at 4 min of recovery (mm Hg)	141	21	144	21	0.02

Abbreviations: BMI, body mass index; HR, heart rate; HRR, heart rate recovery; SAP, systolic arterial pressure.
The *P*-values have been derived with the *t*-test for independent samples.

at 4 min post-exercise were used in the calculation of $RPP_{post\text{-}exercise}$. $RPP_{recovery}$ was defined as $RPP_{peak}-RPP_{post\text{-}exercise}$. Similarly, $SAP_{recovery}=SAP_{peak}-SAP_{post\text{-}exercise}$. HRR was calculated as an HR difference at the peak level and 1 min after the exercise.

Follow-up
Death certificates were received from the Causes of Death Register maintained by Statistics Finland in May 2007; this source has been proven reliable.[20] The certificates included causes of death using the 10th revision of the International Classification of Diseases (ICD-10). The diagnosis numbers and certificate texts were used to classify the deaths as all cause, cardiovascular and SCDs (defined as a cardiac death within 24 h after the onset of symptoms).

Statistical analysis
An HRR cutoff point of 18 b.p.m. within the first minute has been suggested by several authors for exercise tests with an abrupt end.[4,] We used the same cutoff point in addition to handling HRR as a continuous variable. Because no previous cutoff points for the decline in SAP and RPP have been published, we used $SAP_{recovery}$ and $RPP_{recovery}$ only as continuous variables.

The *t*-test for independent samples was used to compare continuous patient characteristics and exercise test variables between those with normal and abnormal recovery values (Table 1), and the χ^2 test was applied for dichotomous variables (Table 2).

The hazard ratios and relative risks implied by recovery values with regard to all-cause and cardiovascular deaths, as well as SCD were estimated with a Cox proportional hazards model using the following covariates: the peak level of the variable under assessment, sex, age, body mass index (BMI), daily smoking (no/yes), use of β-blockers (no/yes), prior diagnoses of CHD (no/yes), myocardial infarction (no/yes), diabetes (no/yes) and hypercholesterolaemia (no/yes). The statistical analyses were performed with the SPSS release 14.0 for Windows (SPSS Inc, Chicago, IL, USA). All statistical tests were two-tailed and used an α-level of <0.05.

Results

During the follow-up period of 47 ± 13 months (mean ± s.d.), there were 122 deaths (6.0% of the population), 58 (2.9%) of which were classified as cardiovascular deaths and 33 (1.6%) further as SCD (Figure 1). Patient characteristics, exercise test variables and the number of deaths for those with HRR $\geqslant$18 b.p.m. ($n=1498$) and HRR $<$18 b.p.m. ($n=531$) are given in Tables 1 and 2.

Mortality and recoveries in HR, SAP and RPP
In Cox regression with adjustments for the peak level of the variable to be assessed, sex, age, BMI, smoking, use of β-blockers, and prior diagnoses of CHD, myocardial infarction, diabetes and hypercholesterolaemia, the hazard ratios of the continuous variable $RPP_{recovery}$ (in units 1000 mm Hg × b.p.m.) were statistically significant for all the three categories of death (Table 3). The continuous variable $SAP_{recovery}$ did not predict any type of mortality (Table 4).

The relative risks of HRR when applying the cutoff point of 18 b.p.m. were 1.28 for SCD (95% confidence interval 0.59–2.81, $P=0.53$), 2.39 for

Table 3 Adjusted hazard ratios and relative risks for sudden cardiac, cardiovascular and all-cause death in the Cox regression models with $RPP_{recovery}$

	SCD				*Cardiovascular mortality*				*All-cause mortality*			
	RR	*95% CI*		P-*value*	*RR*	*95% CI*		P-*value*	*RR*	*95% CI*		P
		Lower	*Upper*			*Lower*	*Upper*			*Lower*	*Upper*	
$RPP_{recovery}$ (1000 b.p.m. per mm Hg)	0.85	0.73	0.98	0.02	0.87	0.78	0.97	0.01	0.87	0.81	0.94	<0.001
RPP_{peak} (1000 b.p.m. per mm Hg)	1.03	0.91	1.16	0.64	1.01	0.92	1.10	0.86	1.02	0.96	1.08	0.51
Age (years)	0.99	0.96	1.03	0.60	1.02	0.99	1.05	0.13	1.04	1.02	1.06	0.00
Sex (M/F)	0.14	0.03	0.60	0.01	0.35	0.17	0.73	0.01	0.55	0.36	0.84	0.01
BMI (kg/m^2)	0.95	0.87	1.03	0.21	0.94	0.88	1.00	0.05	0.94	0.89	0.98	0.00
Smoking (no/yes)	1.08	0.49	2.38	0.84	0.85	0.47	1.53	0.59	0.64	0.43	0.96	0.03
Diabetes (no/yes)	0.68	0.28	1.63	0.39	0.69	0.37	1.30	0.26	0.80	0.51	1.28	0.36
β-Blocker (no/yes)	0.49	0.15	1.58	0.23	0.51	0.23	1.17	0.11	0.83	0.52	1.33	0.43
CHD (no/yes)	1.02	0.36	2.88	0.97	1.09	0.51	2.34	0.82	1.66	0.98	2.81	0.06
Prior MI (no/yes)	0.57	0.22	1.46	0.24	0.56	0.28	1.12	0.10	0.60	0.35	1.02	0.06
Hypercholesterolaemia (no/yes)	0.88	0.42	1.85	0.73	1.43	0.84	2.42	0.18	1.22	0.84	1.75	0.29

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; F, female; RR, hazard ratio/relative risk; M, male; MI, myocardial infarction; RPP_{peak}, peak rate–pressure product during exercise; $RPP_{recovery}$, recovery of rate–pressure product; SCD, sudden cardiac death.

Table 4 Adjusted hazard ratios and relative risks for sudden cardiac, cardiovascular and all-cause death in the Cox regression models with $SAP_{recovery}$

	SCD				*Cardiovascular mortality*				*All-cause mortality*			
	RR	*95% CI*		P-*value*	*RR*	*95% CI*		P-*value*	*RR*	*95% CI*		P-*value*
		Lower	*Upper*			*Lower*	*Upper*			*Lower*	*Upper*	
$SAP_{recovery}$ (mm Hg)	0.99	0.97	1.01	0.28	0.99	0.97	1.00	0.15	0.99	0.98	1.00	0.21
SAP_{peak} (mm Hg)	0.99	0.97	1.01	0.21	0.99	0.97	1.00	0.08	0.99	0.98	1.00	0.01
Age (years)	1.00	0.97	1.04	0.86	1.03	1.01	1.06	0.01	1.05	1.03	1.07	0.00
Sex (M/F)	0.18	0.05	0.61	0.01	0.33	0.17	0.67	0.00	0.50	0.33	0.77	0.00
BMI (kg/m^2)	0.98	0.90	1.06	0.58	0.96	0.90	1.02	0.20	0.95	0.91	0.99	0.03
Smoking (no/yes)	0.96	0.45	2.04	0.91	0.82	0.46	1.44	0.48	0.64	0.44	0.95	0.02
Diabetes (no/yes)	0.66	0.28	1.59	0.36	0.69	0.37	1.30	0.26	0.76	0.47	1.20	0.24
β-Blocker (no/yes)	0.44	0.14	1.38	0.16	0.46	0.20	1.02	0.05	0.78	0.49	1.23	0.28
CHD (no/yes)	0.99	0.36	2.72	0.98	1.08	0.51	2.29	0.83	1.59	0.94	2.69	0.08
Prior MI (no/yes)	0.61	0.24	1.58	0.31	0.58	0.29	1.18	0.14	0.62	0.37	1.06	0.08
Hypercholesterolaemia (no/yes)	0.87	0.41	1.81	0.70	1.47	0.88	2.46	0.15	1.25	0.87	1.80	0.22

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; F, female; RR, hazard ratio/relative risk; M, male; MI, myocardial infarction; SAP_{peak}, peak systolic arterial pressure during exercise; $SAP_{recovery}$, recovery of systolic arterial pressure; SCD, sudden cardiac death.

cardiovascular mortality (1.34–4.26, $P=0.003$) and 2.40 for all-cause mortality (1.61–3.58, $P<0.001$). HRR as a continuous variable produced a significant hazard ratio for all-cause mortality 0.971 (0.954–0.988, $P<0.001$), but not for cardiovascular (0.987 0.961–1.013, $P=0.32$) or sudden cardiac (0.981, 0.949–1.015, $P=0.27$) mortality.

Discussion

The exercise stress test is a routine tool in the diagnostics and follow-up of CHD, as well as in determining cardiovascular status prior to a major procedure. In addition, the merits of the exercise test as a prognostic means have been increasingly recognized during the last two decades.[21] It remains a continuous challenge to develop new approaches and enhance the existing techniques to screen large general cardiovascular patient populations—not only those at a particularly high risk—for increased risk of cardiac death. Because the exercise stress test is a widespread and relatively inexpensive tool, it will be of special interest if the applicability of the test can be expanded from evaluating the prevailing cardiovascular status to cardiovascular prognosis.

Several markers of vagal tone and autonomic imbalance at rest have been connected to cardiovascular events and mortality: elevated resting HR, impaired HR variability, decreased baroreflex sensitivity,[22,23] and so on. During exercise, HR and SAP increase steadily because of the gradual activation of the sympathetic and concomitant deactivation of parasympathetic nervous system. HRR after exercise is considered to be a function of the reactivation of the parasympathetic nervous system, which is important primarily during the first minute after exercise. HRR has been used as a predictor of overall and cardiovascular mortality in studies with various types of patients: healthy subjects and those with or without CHD.[1,3,8,24] Our unselected hospital population that comprises consecutive patients coming in for a clinically indicated clinical exercise test repeated this finding when using the cutoff point of 18 b.p.m. at 1 min after an abrupt discontinuation of the exercise.

Poor decrease of SAP after the exercise has been linked to CHD or the severity of myocardial ischaemia,[25,26] stroke[27] and myocardial infarction,[28] but the previous studies on mortality have yielded conflicting results. In one of these previous studies, abnormal post-exercise SAP response stratified the all-cause mortality in patients ($n=217$) after an acute myocardial infarction.[9] However, two other studies, with either 12 379 low-risk[7] or 2428 consecutive adult patients,[8] did not support this finding, which is consistent with our results: we did not find an association between $SAP_{recovery}$ and overall, cardiovascular or sudden cardiac mortality. Given the impact of the large studies, $SAP_{recovery}$ does not seem to be applicable in risk stratification. The peak-level SAP reached significance for all-cause mortality: the higher the peak SAP, the lower the risk of death. This has also been found in earlier reports,[29] suggesting that better trained subjects exhibit a higher SAP response to exercise.[29]

To the best of our knowledge, this is the first report of the value of $RPP_{recovery}$ in prognostics. Because no previous cutoff points were available, we used only $RPP_{recovery}$ as a continuous variable. This parameter had an inverse relation with all three types of end points used: the greater the drop in RPP, the lower the risk of death. This is clearly supported by Figure 1, where the prevalence of death is clearly higher in the quintile with lowest than highest $RPP_{recovery}$. It deserves to be mentioned

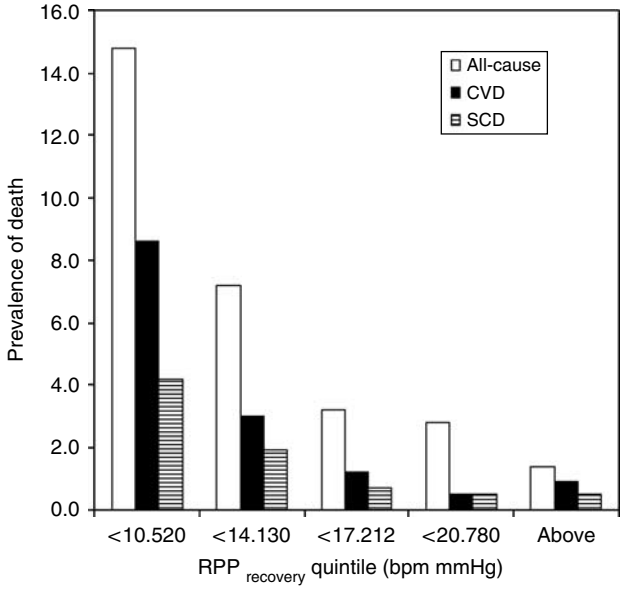

Figure 1 Prevalence (%) of unadjusted all-cause and cardiovascular (CVD) mortality, as well as sudden cardiac death (SCD) for the $RPP_{recovery}$ quintiles.

that $RPP_{recovery}$ emerged as the sole haemodynamic parameter with a statistically significant hazard ratio for SCD. There are many possible mechanisms to explain why delayed decrease in RPP after the exercise would be an indicator of increased mortality. Both HR and blood pressure are adjusted by several mechanisms, but the autonomic nervous system is the dominant regulator in acute changes. Autonomic dysfunction or abnormalities in vasoreactivity may thus cause low $RPP_{recovery}$. Moreover, $RPP_{recovery}$ may reflect aerobic capacity and physical fitness, which have been linked to prognosis.

Because we used no cutoff points for RPP or SAP, the demographic data presented are divided by HRR at 18 b.p.m. The groups with HRR of at least 18 b.p.m. and <18 b.p.m. differ from each other regarding several known cardiovascular risk factors (Tables 1 and 2). Therefore, we used many covariates to clarify the importance of each of these risk factors as determinants of poorer prognosis (Table 3). In the models with $RPP_{recovery}$, sex and $RPP_{recovery}$ were the only statistically significant independent risk factor for SCD and cardiovascular death, whereas BMI, age and smoking status appeared as significant covariates in addition to $RPP_{recovery}$ and sex for all-cause mortality. Surprisingly, age was a prognostic marker only for all-cause mortality. This is probably due to the duration of follow-up. Smoking and BMI had a paradoxical negative association with all-cause mortality; however, smoking and BMI had a positive link to mortality if they were the only covariates in the model.

One disparity between our study groups was the use of β-blockers (Table 2). Medication with the β-blockers causes reduced increase in HR and SAP, and thus reduced maximal RPP. The medication status upon the exercise test depends on the indication the test is performed for. Our patients with a clinically indicated exercise test were tested, for example, to evaluate working capacity (18% of the tests) and the adequacy of CHD treatment (16%). These tests are performed with the prevailing medications, whereas those tested for CHD diagnostics (46%) enter the test after discontinuing their β-blockers for at least 5 days. We used the β-blocker status as a covariate in the Cox regression analyses, but it did not prove to be a significant risk factor in any of the models.

The standard exercise stress test with a bicycle has certain advantages compared with treadmill tests.[10,30] One of these is the easier measurement of blood pressure during exertion. On the other hand, the present study is subject to some limitations. We included all patients scheduled for a clinical exercise stress test at a university setting, and the population comprises patients with a wide spectrum of ages, life styles, histories and statuses of cardiac disease. The impact of the heterogeneity is diminished if not eliminated by using several covariates in the analysis.

In conclusion, the readily available parameter $RPP_{recovery}$ is a promising candidate for a prognostic marker. The validity of this variable needs to be tested further in other exercise stress test populations, before a more widespread clinical use of the markers can be recommended. $SAP_{recovery}$ does not seem to serve as a prognostic tool.

What is known about the topic
- Levels of and changes in systolic arterial pressure and heart rate during an exercise test are associated with mortality.
- Suppressed heart rate recovery, an index of parasympathetic re-activation after the exercise phase, is a predictor of mortality.
- Peak rate–pressure product (heart rate × systolic arterial pressure) during exercise is a prognostic marker.

What this study adds
- Recovery of rate–pressure product after the exercise phase is linked to cardiovascular and all-cause mortality, as well as sudden cardiac death independently of traditional risk factors.
- Recovery in systolic arterial pressure is not associated with any of the three types of mortality.

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Conflict of interest

The authors do not have any conflict of interest.

References

1 Jouven X, Empana JP, Schwartz PJ, Desnos M, Courbon D, Ducimetiere P. Heart-rate profile during exercise as a predictor of sudden death. *N Engl J Med* 2005; **352**: 1951–1958.
2 Elhendy A, Mahoney DW, Khandheria BK, Burger K, Pellikka PA. Prognostic significance of impairment of heart rate response to exercise: impact of left ventricular function and myocardial ischemia. *J Am Coll Cardiol* 2003; **42**: 823–830.
3 Vivekananthan DP, Blackstone EH, Pothier CE, Lauer MS. Heart rate recovery after exercise is a predictor of mortality, independent of the angiographic severity of coronary disease. *J Am Coll Cardiol* 2003; **42**: 831–838.
4 Shetler K, Marcus R, Froelicher VF, Vora S, Kalisetti D, Prakash M *et al.* Heart rate recovery: validation and methodologic issues. *J Am Coll Cardiol* 2001; **38**: 1980–1987.
5 Allison TG, Cordeiro MA, Miller TD, Daida H, Squires RW, Gau GT. Prognostic significance of exercise-induced systemic hypertension in healthy subjects. *Am J Cardiol* 1999; **83**: 371–375.
6 Ciaroni S, Delonca J, Righetti A. Early exercise testing after acute myocardial infarction in the elderly: clinical evaluation and prognostic significance. *Am Heart J* 1993; **126**: 304–311.
7 Ellis K, Pothier CE, Blackstone EH, Lauer MS. Is systolic blood pressure recovery after exercise a predictor of mortality? *Am Heart J* 2004; **147**: 287–292.
8 Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. *N Engl J Med* 1999; **341**: 1351–1357.
9 Kato K, Saito F, Hatano K, Noda S, Tsuzuki J, Yokota M *et al.* Prognostic value of abnormal postexercise systolic blood pressure response: prehospital discharge test after myocardial infarction in Japan. *Am Heart J* 1990; **119**: 264–271.
10 Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J *et al.* Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001; **104**: 1694–1740.
11 Elhendy A, Modesto KM, Mahoney DW, Khandheria BK, Seward JB, Pellikka PA. Prediction of mortality in patients with left ventricular hypertrophy by clinical, exercise stress, and echocardiographic data. *J Am Coll Cardiol* 2003; **41**: 129–135.
12 Elhendy A, van Domburg RT, Vantrimpont P, Poldermans D, Bax JJ, van Gelder T *et al.* Prediction of mortality in heart transplant recipients by stress technetium-99 m tetrofosmin myocardial perfusion imaging. *Am J Cardiol* 2002; **89**: 964–968.
13 Elhendy A, Schinkel AF, van Domburg RT, Bax JJ, Valkema R, Poldermans D. Risk stratification of patients after myocardial revascularization by stress Tc-99m tetrofosmin myocardial perfusion tomography. *J Nucl Cardiol* 2003; **10**: 615–622.
14 Elhendy A, Schinkel AF, Van Domburg RT, Bax JJ, Poldermans D. Prediction of cardiac death in hypertensive patients with suspected or known coronary artery disease by stress technetium-99m tetrofosmin myocardial perfusion imaging. *J Hypertens* 2003; **21**: 1945–1951.
15 Schinkel AF, Elhendy A, Bax JJ, van Domburg RT, Huurman A, Valkema R *et al.* Prognostic implications of a normal stress technetium-99m-tetrofosmin myocardial perfusion study in patients with a healed myocardial infarct and/or previous coronary revascularization. *Am J Cardiol* 2006; **97**: 1–6.
16 Dekany M, Nyolczas N, Reif E, Fiok J, Vandor L, Paksy A. Prognostic value of simple exercise test parameters in patients with dilated cardiomyopathy. *Acta Cardiol* 1995; **50**: 45–52.
17 Prakash M, Myers J, Froelicher VF, Marcus R, Do D, Kalisetti D *et al.* Diagnostic exercise tests on 4000 consecutive men. *Am Heart J* 2001; **142**: 127–135.
18 Villella M, Villella A, Barlera S, Franzosi MG, Maggioni AP. Prognostic significance of double product and inadequate double product response to maximal symptom-limited exercise stress testing after myocardial infarction in 6296 patients treated with thrombolytic agents. GISSI-2 Investigators. Grupo Italiano per lo Studio della Sopravvivenza nell-Infarto Miocardico. *Am Heart J* 1999; **137**: 443–452.
19 Nieminen T, Lehtinen R, Viik J, Lehtimäki T, Niemelä K, Nikus K *et al.* The Finnish Cardiovascular Study (FINCAVAS): characterising patients with high risk of cardiovascular morbidity and mortality. *BMC Cardiovasc Disord* 2006; **6**: 9.
20 Pajunen P, Koukkunen H, Ketonen M, Jerkkola T, Immonen-Räihä P, Kärjä-Koskenkari P *et al.* The validity of the Finnish Hospital Discharge Register and Causes of Death Register data on coronary heart disease. *Eur J Cardiovasc Prev Rehabil* 2005; **12**: 132–137.
21 Lauer MS. Exercise electrocardiogram testing and prognosis. Novel markers and predictive instruments. *Cardiol Clin* 2001; **19**: 401–414.
22 Wichterle D, Simek J, La Rovere MT, Schwartz PJ, Camm AJ, Malik M. Prevalent low-frequency oscillation of heart rate: novel predictor of mortality after myocardial infarction. *Circulation* 2004; **110**: 1183–1190.
23 Curtis BM, O'Keefe Jr JH. Autonomic tone as a cardiovascular risk factor: the dangers of chronic fight or flight. *Mayo Clinic Proc* 2002; **77**: 45–54.
24 Watanabe J, Thamilarasan M, Blackstone EH, Thomas JD, Lauer MS. Heart rate recovery immediately after treadmill exercise and left ventricular systolic dysfunction as predictors of mortality: the case of stress echocardiography. *Circulation* 2001; **104**: 1911–1916.
25 McHam SA, Marwick TH, Pashkow FJ, Lauer MS. Delayed systolic blood pressure recovery after graded exercise: an independent correlate of angiographic coronary disease. *J Am Coll Cardiol* 1999; **34**: 754–759.
26 Hashimoto M, Okamoto M, Yamagata T, Yamane T, Watanabe M, Tsuchioka Y *et al.* Abnormal systolic blood pressure response during exercise recovery in patients with angina pectoris. *J Am Coll Cardiol* 1993; **22**: 659–664.
27 Kurl S, Laukkanen JA, Rauramaa R, Lakka TA, Sivenius J, Salonen JT. Systolic blood pressure response to exercise stress test and risk of stroke. *Stroke* 2001; **32**: 2036–2041.

28 Laukkanen JA, Kurl S, Salonen R, Lakka TA, Rauramaa R, Salonen JT. Systolic blood pressure during recovery from exercise and the risk of acute myocardial infarction in middle-aged men. *Hypertension* 2004; **44**: 820–825.
29 Gupta MP, Polena S, Coplan N, Panagopoulos G, Dhingra C, Myers J *et al.* Prognostic significance of systolic blood pressure increases in men during exercise stress testing. *Am J Cardiol* 2007; **100**: 1609–1613.
30 Mundal R, Kjeldsen SE, Sandvik L, Erikssen G, Thaulow E, Erikssen J. Exercise blood pressure predicts mortality from myocardial infarction. *Hypertension* 1996; **27**: 324–329.