

## Risk assessment of left ventricular systolic dysfunction in primary care: cross sectional study evaluating a range of diagnostic tests

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### Abstract

**Objectives** To assess the probability of left ventricular systolic dysfunction without echocardiography in patients from general practice.

**Design** Cross sectional study using multivariate regression models to examine the relation between clinical variables and left ventricular systolic dysfunction as determined by echocardiography.

**Setting** Three general practices in Copenhagen.

**Subjects** 2158 patients aged >40 years were screened by questionnaires and case record reviews; 357 patients with past or present signs or symptoms of heart disease were identified, of whom 126 were eligible for and consented to examination.

**Main outcome measures** Clinical variables that were significantly ( $P < 0.05$ ) related to ejection fraction  $\leq 0.45$  and their predictive value for left ventricular systolic dysfunction.

**Results** 15 patients (12%) had left ventricular systolic dysfunction. The prevalence was significantly related to three questions: does the electrocardiogram have Q waves, left bundle branch block, or ST-T segment changes? ( $P = 0.012$ ); is resting supine heart rate greater than the simultaneous diastolic blood pressure? ( $P = 0.002$ ); and is plasma N-terminal atrial natriuretic peptide  $> 0.8$  nmol/l? ( $P = 0.040$ )? Only one of 60 patients with a normal electrocardiogram had systolic dysfunction (2%, 95% confidence interval 0% to 9%) regardless of response to the other two questions. The risk of dysfunction was appreciable in patients with a yes answer to two or three questions (50%, 27% to 73%).

**Conclusions** A normal electrocardiogram implies a low risk of left ventricular systolic dysfunction. Patients can be identified for echocardiography on the basis of an abnormal electrocardiogram combined with increased natriuretic peptide concentration or a heart rate greater than diastolic blood pressure, or both.

### Introduction

Identification and treatment of patients with left ventricular systolic dysfunction improves survival and reduces morbidity.<sup>1-5</sup> About 3% of the adult population have systolic dysfunction,<sup>6-8</sup> but half of them are

asymptomatic and can be identified only by objective methods, usually echocardiography. Identification consequently rests on selecting the right patients for echocardiography. Patients with a history of ischaemic heart disease are an obvious risk group,<sup>6</sup> but greater sensitivity is achieved by examining anyone with signs suggestive of heart disease. The purpose of the study was to examine how primary care doctors might identify patients at increased risk of systolic dysfunction in order to decide who to refer for echocardiography. We evaluated simple and inexpensive clinical methods that can be used in general practice.

### Subjects and methods

#### Patients

This study is a substudy of a cross-sectional survey that aimed to determine the prevalence of heart failure in general practice. The required population size was calculated as 2200 to give a standard error of about 0.5% on the estimate of heart failure prevalence. We asked the National Health Insurance Register for names and addresses of all patients over 40 years of age who were registered with three general practices on three separate dates in 1993 to 1995. The practices were chosen because they had used the same computer program for case notes (Docbase, Roskilde, Denmark) over two to four years and because they were situated in geographically and socially different areas of Copenhagen. The study was approved by the local ethics committee, and all examined patients gave informed consent.

We included patients with any past or present signs or symptoms of heart disease. Suspected cases were identified within the cross sectional study population by reviewing all general practice case notes and prescription lists and by a mailed questionnaire. We searched and asked for details of past or present palpitations, chest pain, or dyspnoea; treatment for heart disease; referral to coronary care unit; and recognised cardiac abnormalities on previous electrocardiography, chest radiography, or other cardiac imaging. If this screening raised any suspicion of heart disease, patients were given a personal interview, and their hospital discharge letters and hospital records were checked.

We excluded patients who lived in a nursing home, were receiving inpatient or outpatient treatment for advanced heart failure, did not respond to the questionnaire, or could not or refused to be examined.

### Clinical examination

All patients had a physical examination, chest radiography, echocardiography, supine 12 lead electrocardiography, blood pressure measurements, and blood samples taken. OW and JFH independently coded the electrocardiograms using the Minnesota system<sup>9</sup> without knowing the patient's clinical status.

### Echocardiography

Left ventricular ejection fraction was indirectly estimated from the fractional shortening<sup>10,11</sup> or from a nine segment model for assessing wall motion index score.<sup>12,13</sup> Left ventricular systolic dysfunction is indicated by a wall motion index score below 1.5 or a fractional shortening below 0.26—that is, roughly an ejection fraction below 0.45. Left ventricular ejection fraction values were determined from videotapes and photoechocardiograms at the end of the study by OW, who was blinded to other clinical data. The intraobserver and interobserver (CTL *v* OW) standard deviations for a single ejection fraction estimate were equal (0.05 units, coefficient of variation = 8%).

### N-terminal atrial natriuretic peptide

Concentrations of N-terminal atrial natriuretic peptide were determined from frozen stored plasma samples with a commercial radioimmunoassay (OY NT-pro-ANP <sup>125</sup>I radioimmunoassay, Biotop, Helsinki, Finland). Plasma samples were drawn after 10 minutes' supine rest and analysed within 12 months. The combined between assay and within assay coefficient of variation was 3.7%. The normal range was obtained from 22 patients who, after examination, were concluded to have normal cardiac function. The mean concentration plus 2 SD in these 22 patients was 0.77 nmol/l, so values above 0.8 nmol/l were defined as abnormal.

### Statistical analysis

Predictive markers of left ventricular systolic dysfunction (ejection fraction  $\leq 0.45$ ) were identified by the  $\chi^2$  test with Yates's continuity correction and a multiple linear regression model against the natural logarithm of ejection fraction. The logarithmic transformation was used to weight variables operating on the important lower ejection fraction spectrum. To reduce the risk of chance findings, we maintained only variables that were significant in two equally sized random subsets after sex and systolic dysfunction had been stratified for. Finally, a logistic regression model was used to make a clinically useful algorithm. The computer package Statistica (Statsoft, Tulsa, USA) was used for all calculations, and P values  $< 0.05$  in two sided tests were considered significant. Confidence limits around percentages were derived from the binomial distribution.

## Results

### Study population

We screened 2158 patients from three general practices; the demographic and socioeconomic characteristics were similar to those of the total Copenha-

gen population. About 2.5% (55) had a blank or missing case record. These were coded as cardiac healthy unless the questionnaire indicated otherwise. The questionnaire was returned by 87% (1504/1757) of patients aged 40 to 80 years. But among patients aged over 80 years, 48% (191/401) either did not respond or were resident in nursing homes. Nursing home residents had more heart disease than respondents, but it was often of unknown cause. The prevalence of a history of heart disease was similar in non-respondents and respondents.

We conducted telephone interviews with almost 500 patients. We identified 357 with past or present signs or symptoms of heart disease and deliberately excluded 38 nursing home residents, 36 non-respondents to the questionnaire, and 10 patients with advanced heart failure. In the early stages of the study 21 patients were not invited to participate because of a preliminary decision not to invite patients with a vague indication of heart disease; this decision was dropped in later stages, and 14 such patients were invited. A further 126 patients were excluded for various reasons: 32 declined the invitation, 1 died, 37 were disabled due to various medical and psychosocial conditions, and 56

**Table 1** Characteristics of 126 examined patients with suspected heart disease. Values are numbers (percentages) unless stated otherwise

Findings based on general case notes, discharge letters, and interviews	No (%) of patients
Median age (years)	71
Men	55 (44)
Treated for heart failure in hospital or primary care	43 (34)
Admitted to hospital for any reason	89 (71)
Admitted to hospital for presumptive heart disease	47 (37)
Managed solely by general practice	93 (74)
Managed by consultant physician or cardiologist	33 (26)
Documented heart disease:	64 (51)
Myocardial infarction	31 (25)
Angina pectoris	37 (29)
Atrial fibrillation	11 (9)
Valvular heart disease	4 (3)
Suggestive heart disease:	62 (49)
Unconfirmed myocardial infarction*	16 (13)
Survived "cardiac arrest"	2 (2)
Pacemaker for any reason	7 (6)
Cardiomegaly on radiography	22 (17)
Palpitations or paroxysmal supraventricular tachycardia	24 (19)
Past or present treatment with digoxin	26 (21)
Pulmonary embolism	5 (4)
Past or present diagnosis of cor pulmonale	7 (6)
Current treatment or history of hypertension	69 (55)
Current treatment or history of diabetes	12 (10)
Current treatment or history of pulmonary disease	31 (25)
Past or present smoker	88 (70)
Findings of study clinical examination:	
Mean (SD) N-terminal atrial natriuretic peptide (nmol/l)	0.56 (0.35)
Mean (SD) left ventricular ejection fraction	0.60 (0.13)
New York Heart Association class†:	
Ia	18 (14)
Ib	32 (25)
IIa	35 (28)
IIb	26 (21)
III	15 (12)

\*Electrocardiographic evidence or history suggestive of infarction.

†New York Heart Association class I was subdivided into: Ia (those who exercised regularly) and Ib (those who did not). Likewise, class II was subjectively subdivided into higher (a) or lesser (b) degrees of daily activity.

**Table 2** Characteristics of 15 patients with systolic dysfunction

	Median (range)	Interquartile range
Ejection fraction	0.35 (0.22-0.45)	0.28-0.43
<i>N</i> -terminal atrial natriuretic peptide (nmol/l)	0.72 (0.30-2.39)	0.47-1.33
Age (years)	73 (54-84)	64-77
New York Heart Association class	Ila (Ib-III)	Ib-IIb
Supine heart rate (beats/min)	71 (46-96)	61-85

seemed to be interested but did not turn up for examination. These 126 patients were more likely to be over 80 years of age and less likely to have a registered history of ischaemic heart disease than the 126 patients who were examined. Hypertension, diabetes, chronic obstructive pulmonary disease, and sex were, however, equally distributed in the two groups.

The 126 examined patients were aged 49 to 93 years (5th and 95th percentiles, 53 and 83 years) and considered clinically stable from the case notes. Table 1 shows that 64 patients had good evidence of heart disease and 62 had suggestive evidence. A specialist in internal medicine or cardiology had seen 33 (26%) of the patients once or twice within the past year. Mean ejection fraction was normal, and most patients were in New York Heart Association classes I or II. The prevalence of left ventricular systolic dysfunction was 12% (nine men and six women). Table 2 describes these 15 patients.

**Univariate markers of systolic dysfunction**

Table 3 shows that a normal electrocardiogram indicates a normal systolic function and that systolic dysfunction can occur despite a normal plasma concentration of *N*-terminal atrial natriuretic peptide. The interaction term “heart rate greater than diastolic blood pressure” was superior to both heart rate and blood pressure individually. We initially evaluated “heart rate minus diastolic blood pressure” in the  $\chi^2$  test using various cut off values because we had noted that heart rate and diastolic blood pressure were oppositely

**Table 3** Diagnostic value of different methods to detect left ventricular systolic dysfunction where previous screening brought the unconditional probability of systolic dysfunction to 12%

Type of test	Left ventricular systolic dysfunction		Predictive value		Specificity (%)	Sensitivity (%)	Negative likelihood ratio	P value
	Yes	No	Positive	Negative				
QRS or ST-T changes, or both, on electrocardiography:								
Yes	13	49	21	97	56	87	0.24	0.005
No	2	62						
Treated for congestive heart failure:								
Yes	9	34	21	93	69	60	0.58	0.050
No	6	77						
Confirmed myocardial infarction:								
Yes	7	24	23	92	78	47	0.68	0.073
No	8	87						
<i>N</i> -terminal atrial natriuretic peptide >0.8 nmol/l:								
Yes	6	12	33	92	89	43	0.62	0.006
No	8	95						
Heart rate > diastolic blood pressure:								
Yes	8	15	35	93	86	53	0.55	0.001
No	7	95						

Left ventricular systolic dysfunction is roughly equal to an ejection fraction  $\leq 0.45$ . Minnesota codes for Q wave (1.1-1.3), left bundle branch block (7.1), ST-T abnormalities (4.1-4.4; 5.1-5.4; 9.2) and left ventricular hypertrophy (3.1; 3.3; 3.4) were used.<sup>3</sup>

related to ejection fraction with numerically similar coefficients. A zero difference predicted systolic dysfunction best, hence we used a “greater than” relation. A history of heart failure and myocardial infarction were not as significantly associated with systolic dysfunction. Dyspnoea, chest radiography, and results of the physical examination were not significantly associated with systolic dysfunction ( $P > 0.1$ ).

**Multivariate regression analysis**

The logarithm of ejection fraction was inversely associated with *N*-terminal atrial natriuretic peptide concentration, heart rate, history of myocardial infarction ( $P < 0.001$ ), left bundle branch block in the electrocardiogram ( $P < 0.002$ ), history of heart failure, and Q waves in the electrocardiogram; it was positively associated with diastolic blood pressure and female sex ( $P < 0.05$ ). Sex and history of heart failure were eliminated because they were not significant in both patient subsets. The remaining significant variables were then used to form three clinically useful “yes or no” questions (table 4). Table 5 shows how to combine questions to assess the risk of systolic dysfunction. The probability of systolic dysfunction was very low if the patient had a normal electrocardiogram, regardless of the other questions. The probability increased if an abnormal electrocardiogram was accompanied by another positive answer, with a yes to all three questions being most specific.

**Table 4** Multivariate risk of left ventricular systolic dysfunction. Risk is increased if answer is “yes”

Question to assess risk of systolic dysfunction	Odds ratio (95% CI)	P value
Are there QRS or ST-T changes, or both, in the electrocardiogram?	18 (1.9 to 160)	0.012
Is resting supine heart rate (beats/min) > diastolic blood pressure (mm Hg)?	9 (2.4 to 37)	0.002
Is <i>N</i> -terminal atrial natriuretic peptide >0.8 nmol/l ?	5 (1.1 to 20)	0.040

The prevalence of left ventricular systolic dysfunction (ejection fraction  $\leq 0.45$ ) was brought up to 12% by previous screening. Odds ratios were obtained by analysing 120 patients as six had missing values.

**Discussion**

We evaluated a range of simple diagnostic tests to assess the risk of left ventricular systolic dysfunction in 126 patients from primary care with past or present signs or symptoms of heart disease. A normal electrocardiogram was the only clinically useful test to rule out systolic dysfunction with a sufficiently high accuracy. No single test could diagnose systolic dysfunction. Combined use of heart rate, diastolic blood pressure, and *N*-terminal atrial natriuretic peptide concentration in patients with an abnormal electrocardiogram, however, was accurate enough to be used to identify patients who should or should not be referred for echocardiography. Those with “yes” to all questions may be treated as if they have systolic dysfunction while waiting for the results of echocardiography, since they almost certainly will have it.

The electrocardiogram was the most useful test in this stable population from primary care. This has also been found true for patients referred for open access echocardiography,<sup>14</sup> in a general population,<sup>15</sup> and in referred patients with chest pain,<sup>16</sup> dyspnoea,<sup>17</sup> and

**Table 5** Probability of systolic dysfunction for different combinations of answer to questions. Prevalence of systolic dysfunction was brought up to 12% by previous screening

Answers to questions: abnormal ECG?/ heart rate > diastolic pressure?/Increased atrial natriuretic peptide?*	No with left ventricular dysfunction/No with combination of answers	Prevalence (%) of left ventricular dysfunction (95% CI)	Risk of left ventricular dysfunction	Ejection fraction	
				Mean (SD)	Range
(a) No/—/—	1/60	1.7 (0 to 9)	Very low	0.63 (0.11)	0.30-0.87
(b) Yes/ no/ no	3/40	8 (2 to 20)	Low	0.59 (0.12)	0.27-0.83
(c) Yes/ no/ yes	2/7	28 (4 to 70)	Moderate	0.51 (0.08)	0.40-0.62
(d) Yes/ yes/ no	4/9	44 (14 to 79)	Moderate	0.53 (0.17)	0.33-0.83
(e) Yes/ yes/ yes	4/4	100 (27 to 100)	High	0.29 (0.06)	0.22-0.35
(c)-(e) combined	10/20	50 (27 to 73)	Moderate to high	0.47 (0.15)	0.22-0.83
Missing values†	1/6			0.63 (0.13)	0.43-0.76

\*Questions were: are there QRS or ST-T changes, or both, in the electrocardiogram? Is resting supine heart rate (beats/min) > diastolic blood pressure (mm Hg)? Is *N*-terminal atrial natriuretic peptide > 0.8 nmol/l?

†Six patients were excluded from analysis because of missing values for *N*-terminal atrial natriuretic peptide. One of these patients had systolic dysfunction and a normal electrocardiogram, which would have doubled the prevalence of systolic dysfunction in combination (a) to 3.3% (95% confidence interval 0.4% to 12%).

myocardial infarction.<sup>18, 19</sup> As in a recent study of stable myocardial infarction patients from primary care,<sup>20</sup> we found that a single measurement of plasma *N*-terminal atrial natriuretic peptide could not discriminate between minor degrees of systolic dysfunction and preserved systolic function. Measuring brain natriuretic peptide instead would probably not have changed our conclusions, since it has only a slightly higher association with systolic dysfunction than *N*-terminal atrial natriuretic peptide.<sup>15, 20, 21</sup> The close relation between heart rate and blood pressure gives reason for a joint assessment. Although the combined variable was highly significant (tables 3 and 4), it should be used with caution until it has been validated in other settings.

#### Application of results

Our results are robust because the two independent regression models minimised risk of finding significant variables by chance and because we used unbiased ejection fraction values and a clinically relevant study population for screening. We would probably have identified more variables with a higher significance if we had studied more patients and used a more reproducible measurement of ejection fraction than echocardiography. The algorithm will probably identify fewer false positive results if applied to a hospital outpatient population, where the prevalence of systolic dysfunction is higher. This screening method needs to be compared with other screening methods in a prospective randomised controlled trial with different samples of patients; the trial should incorporate a health economic evaluation. Other screening methods could be simplified echocardiography,<sup>22</sup> computerised heart auscultation, or new biochemical markers.

Congestive heart failure and left ventricular systolic dysfunction are not identical. In patients with ongoing symptoms suspected by a general practitioner to be due to heart failure, plasma brain natriuretic peptide concentration seems to be a useful indicator of which patients require further clinical assessment.<sup>23</sup> Screening for stable systolic dysfunction, however, should be targeted at patients with symptoms or signs suggestive of heart disease,<sup>6, 15</sup> hypertension, or diabetes, who are easily identified in general practice.

Our algorithm could considerably improve the identification of patients with systolic dysfunction in primary care. However, not everyone with left ventricular systolic dysfunction in the community would be identified. Firstly, some patients with systolic dysfunction may not have complained of or have been

#### Key messages

- Early treatment of left ventricular systolic dysfunction reduces morbidity, but diagnosis relies on echocardiography
- This study examines methods for assessing the risk of left ventricular systolic dysfunction in patients from primary care with past or present signs or symptoms of heart disease
- Risk can be assessed by three factors: QRS or ST-T changes in the electrocardiogram; increased plasma concentration of *N*-terminal atrial natriuretic peptide; and tachycardia (supine resting heart rate > diastolic blood pressure)
- Risk of systolic dysfunction was very low in patients with normal electrocardiographic results
- Risk was high in patients who had an abnormal electrocardiogram in combination with at least one other abnormal result

registered with cardiac symptoms in general practice. Secondly, many patients over 80 years of age were unwilling to attend hospital for examinations, and a home echocardiographic service would probably have identified more patients.<sup>24</sup>

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Contributors: OWN initiated and coordinated the primary study hypothesis, discussed core ideas, designed the protocol, collected the data, performed the analyses, and wrote the paper. JFH discussed core ideas and design and participated in clinical analyses and writing of the paper. JH discussed core ideas and design and participated in statistical analyses and writing the paper. CTL supervised the echocardiography, participated in a reproducibility study, and edited the paper. JS analysed natriuretic peptide and edited the paper. OWN and JFH will act as guarantors.

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## Evaluation of the effectiveness of an educational intervention for general practitioners in adolescent health care: randomised controlled trial

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website  
*extra*

*The sample size calculation and a chart showing the flow of participants through the trial appears on the BMJ's website*

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### Abstract

**Objective** To evaluate the effectiveness of an educational intervention in adolescent health designed for general practitioners in accordance with evidence based practice in continuing medical education.

**Design** Randomised controlled trial with baseline testing and follow up at seven and 13 months.

**Setting** Local communities in metropolitan Melbourne, Australia.

**Participants** 108 self selected general practitioners.

**Intervention** A multifaceted educational programme for 2.5 hours a week over six weeks on the principles of adolescent health care followed six weeks later by a two hour session of case discussion and debriefing.

**Outcome measures** Objective ratings of consultations with standardised adolescent patients recorded on videotape. Questionnaires completed by the general practitioners were used to measure their knowledge, skill, and self perceived competency, satisfaction with the programme, and self reported change in practice.

**Results** 103 of 108 (95%) doctors completed all phases of the intervention and evaluation protocol. The intervention group showed significantly greater improvements in all outcomes than the control group at the seven month follow up except for the rapport and satisfaction rating by the standardised patients.

104 (96%) participants found the programme appropriate and relevant. At the 13 month follow up most improvements were sustained, the confidentiality rating by the standardised patients decreased slightly, and the objective assessment of competence further improved. 106 (98%) participants reported a change in practice attributable to the intervention.

**Conclusions** General practitioners were willing to complete continuing medical education in adolescent health care and its evaluation. The design of the intervention using evidence based educational strategies proved an effective and quick way to achieve sustainable and large improvements in knowledge, skill, and self perceived competency.

### Introduction

The patterns of health need in youth have changed noticeably over the past three decades. Studies in the United Kingdom, North America, and Australia have shown that young people experience barriers to health services.<sup>1-3</sup> With the increase in a range of youth health problems, such as depression, eating disorders, drug and alcohol use, unplanned pregnancy, chronic illness, and suicide, there is a need to improve the accessibility and quality of health services to youth.<sup>3-6</sup>

In the Australian healthcare system general practitioners provide the most accessible primary health