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Dyspnoea of cardiac origin in 67 year old men: (1) relation to systolic left ventricular function and wall stress

The study of men born in 1913

KENNETH CAIDAHL,* HENRY ERIKSSON,† MARIANNE HARTFORD,‡ JOHN WIKSTRAND,* INGEMAR WALLENTIN,* KURT SVÄRDSUDD†

From the Gothenburg University Department of Clinical Physiology, Sahlgren's Hospital, Section for Preventive Medicine at the Department of Medicine, Östra Hospital,† and Section of Cardiology at the Department of Medicine 1, Sahlgren's Hospital,‡ Gothenburg, Sweden*

SUMMARY The relation between dyspnoea of presumed cardiac origin and disturbed left ventricular systolic function was studied in a group of 67 year old men from the general population of Gothenburg, Sweden. Forty two men with cardiac dyspnoea were identified and 45 controls were randomly selected from a screened cohort of 644 men. Dyspnoea was graded according to the World Health Organisation standard, and M mode echocardiography, carotid pulse tracing, an apex cardiogram, and phonocardiography were used to evaluate the grade of dyspnoea and its relation to systolic time intervals, left ventricular ejection indices, and wall stress. The dyspnoea grade was significantly related to the left ventricular end systolic dimension, to septal and posterior wall fractional thickening, and to ejection indices such as fractional shortening. The dyspnoea grade was also significantly correlated with the ratio of end systolic wall stress to end systolic volume index. There was a close relation between end systolic wall stress and mean velocity of circumferential fibre shortening adjusted for heart rate. This relation did not clearly show reduced inotropy in the dyspnoeic men. There was no relation between the degree of dyspnoea and the systolic time intervals. Among the systolic variables obtained by echocardiography the only abnormal finding in mild to moderate dyspnoea was an increased end systolic dimension.

The grade of cardiac dyspnoea seemed to be related to the degree of systolic left ventricular dysfunction, which was considerably impaired in severe dyspnoea. In population studies left ventricular end systolic dimension and fractional shortening may provide sufficient information on systolic function without the need to assess variables that are independent of load.

In patients with congestive heart failure a large heart is associated with a poor prognosis,[1] and pronounced left ventricular dilatation identifies a subgroup at high risk.[2] The high mortality from congestive heart failure[3] emphasises the need for early detection and treatment as well as the need for a better understanding of the pathophysiological mechanisms.

New aspects of the non-invasive interpretation of systolic function—for example end systolic wall stress in relation to volume[4] and ejection phase indices[5]—have recently been examined. These indices are less influenced by loading conditions than are the traditional ejection phase indices, and so they may be better estimations of intrinsic myocardial properties and may relate better to symptoms of congestive heart failure.

Most of the current information on systolic cardiac dysfunction has been obtained from clinical studies on small groups of patients with symptoms. We have evaluated regional[6] and diastolic[7] left ventricular function in a random sample of 67 year old men from the general population of Gothenburg, Sweden. The purpose of the present study was to evaluate the relation between dyspnoea of presumed cardiac origin and various indices of systolic cardiac dysfunction in the same study population.

Requests for reprints to Dr Kenneth Caidahl, Department of Clinical Physiology, Sahlgren's Hospital, S-413 45 Gothenburg, Sweden.

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Patients and methods

SCREENED POPULATION

The screened population[8] and the study population[6] have already been described in detail.

In 1980 a third of the male population in the city of Gothenburg born in 1913 (n = 817) was identified in the population register of the city and invited to a screening procedure for the evaluation of various aspects of dyspnoea. Six hundred and forty four men (79%) participated.

Dyspnoea was graded according to the World Health Organisation's modification[9] of the questionnaire that was proposed by the British Medical Research Council's committee on the aetiology of chronic bronchitis. Accordingly, dyspnoea was classified as no shortness of breath (grade 0), shortness of breath when hurrying on level ground or walking up a slight hill (grade 1), shortness of breath when walking with other people of own age on level ground (grade 2), having to stop for breath when walking at own pace on level ground (grade 3), and shortness of breath when washing or dressing (grade 4). The responses were checked by a physician during the interview that accompanied the physical examination.

Information on swollen legs at the end of the day and dyspnoea at night was obtained by interview. Information on chest pain was obtained by Rose's questionnaire.[9] The responses were evaluated by a physician and classified as no angina pectoris, possible angina, or definite angina. For this study, possible angina and definite angina were regarded as angina pectoris. Information on sustained myocardial infarction was obtained from the infarction register covering the city of Gothenburg.[10] Information on chronic bronchitis, asthma, cough, phlegm, and wheeze was obtained by interview. Smoking habits were recorded and total amount of tobacco smoked during life was calculated. One cigarette was assumed to be the equivalent of 1 g of tobacco.

A physical examination was performed by one of three physicians who were trained to make similar clinical judgements. Pulmonary rales and rhonchi were noted. The presence or absence of atrial fibrillation was coded from a standard 12 lead electrocardiogram.

STUDY POPULATION

In the screened population 142 (22%) out of 644 men had dyspnoea grade 1–4. Dyspnoea of cardiac origin was suspected in dyspnoeic men who (*a*) had either angina pectoris or other heart disease, leg oedema at the end of the day, dyspnoea at night, pulmonary rales, or atrial fibrillation and who (*b*) did not have a history of chronic bronchitis, asthma, cough with phlegm and wheeze, or rhonchi at the examination. Forty nine (35%) men with dyspnoea fulfilled these criteria. Four of these men died from ischaemic heart disease before an echocardiographic investigation could be performed, another two declined to participate, and one echocardiographic investigation was not interpretable. Of the 42 men remaining, 20 had grade 1, 12 had grade 2, five grade 3, and five had grade 4 dyspnoea. In the four dyspnoea grade groups digitalis/diuretics/β blockers were given to 9/1/8 (of 20) men with grade 1 dyspnoea, 4/1/6 (of 12) with grade 2 dyspnoea, 3/0/2 (of 5) with grade 3 dyspnoea, and 3/2/0 (of 5) with grade 4 dyspnoea.

Non-dyspnoeic men from the screened population born on day 6 of each month (n = 51) were studied as a control group. Of these 51 men, one died from a non-cardiac cause before the non-invasive investigation, four declined to participate, and one had an echocardiogram that was not interpretable. The remaining control group of 45 men without dyspnoea was divided into two subgroups. There were 14 men (group A) who were not and had not been treated for hypertension, had no atrial fibrillation, no angina pectoris, no myocardial infarction, and had no other known cardiac disease or any akinetic segments on cross sectional echocardiography; the remaining men (n = 31) are called group B. Six men in the control group B were on β blockers (none in group A); nobody in the control groups was on digitalis or diuretics.

No haemodynamically important organic valvar lesions were found by echocardiography or phonocardiography in any of the 87 subjects in the study population. Left ventricular aneurysms were found on cross sectional echocardiography in two men with grade 2 dyspnoea. They were excluded from the M mode echocardiographic study. No left bundle branch blocks were found, but one man with an implanted pacemaker was excluded from measurement of systolic time intervals.

METHODS

Dyspnoeic men and control subjects were investigated in random order and all information was coded blindly.

Systolic and diastolic blood pressures and heart rate were measured after approximately 45 minutes of supine rest. A phonographic method was used with a microphone placed over the brachial artery. The Korotkoff sounds were recorded together with lead II and a calibration signal from a mercury manometer, on a Mingograph. The blood pressure was measured to the nearest 1 mm Hg. The presence of Q waves was noted on a 12 lead electrocardiogram recorded at a speed of 50 mm/s and coded according to the Minnesota Code.[9] The codes 1:3, 1:2, and 1:1

were used and given one, two, and three points respectively.

An upright bicycle exercise test was performed with the load increased by 10 W each minute. At a spirometry test, pulmonary function was measured as vital capacity, and as the ratio of forced expiratory volume during one second to vital capacity. *X* rays of the chest were obtained during inspiration from a frontal, a lateral, and two oblique views. The films were interpreted by two experienced radiologists, who had no other information about the participants. Relative heart volume (ml/m^2 body surface area) was calculated, and venous congestion was estimated and coded as absent or present.

Non-invasive heart measurements

Detailed descriptions of non-invasive heart measurements and recording techniques are given elsewhere.[11-13]

Cross sectional echocardiographic recordings of routine views were stored on a videorecorder with playback and slow motion facilities and analysed for organic valvar disease and left ventricular wall motion disturbances.[6] M mode echocardiographic recordings were obtained at a paper speed of 50 mm/s. A handheld 2·25 MHz transducer was used in combination with either an Irex II or Echoscan 30 ultrasonograph. A simultaneous electrocardiogram (lead II) and a phonocardiographic tracing of the second heart sound was obtained on all M mode recordings.

The following measurements (leading edge to leading edge method) and calculations were made on three beats on the M mode tracings:

(*a*) The left ventricular diameter, interventricular septal thickness, and posterior wall thickness were all measured at end diastole (the electrocardiographic Q wave) and at end systole (the shortest distance between the septum and posterior wall at or before the initial vibrations of the second heart sound).

(*b*) Fractional thickening of the left ventricular wall was calculated as septal and posterior wall increase of thicknesses during systole divided by the corresponding diastolic thicknesses.

(*c*) Fractional shortening was defined as the difference between left ventricular diastolic and systolic dimensions divided by the diastolic dimension. Ejection fraction was calculated according to the cube formula, for reasons discussed elsewhere.[7] The mean velocity of circumferential fibre shortening (mean Vcf) was calculated as fractional shortening divided by left ventricular ejection time. The mean Vcf adjusted for heart rate (mean Vcf_c) was calculated as fractional shortening divided by left ventricular ejection time normalised by the square root of the cardiac cycle length in seconds.[5]

(*d*) Left ventricular meridional end systolic wall stress (10^3dyn/cm^2) was estimated as wall stress = $(1{\cdot}332 \times \text{pressure} \times D)/(4h \times (1 + h/D))$ where D is the left ventricular end systolic dimension and h is the mean of the septal and posterior wall end systolic thicknesses.[12 14] Pressure was obtained by estimating end systolic blood pressure from carotid pulse tracing, where systolic and diastolic blood pressures were assigned to the peak and nadir of the carotid curve, respectively, and end systolic blood pressure was estimated by linear interpolation to the height of the dicrotic notch.[12 15]

(*e*) Left ventricular peak emptying rate and time to peak emptying rate were calculated from the electrocardiographic R wave. Measurements were performed by means of a digitising table (Summagraphics ID-2CTR-TAB17, Connecticut, USA) and a microcomputer (Professional-380, Digital Equipment Corp) with a specially designed computer program.

(*f*) Measurements from pulse tracings were performed on five beats and the mean values were used. The left ventricular ejection time, the electromechanical interval, the pre-ejection period, and the isovolumic contraction time were measured, as previously described, from the simultaneous recordings of lead II, the phonocardiogram, and the carotid pulse tracing, or apexcardiogram.[11 12]

The electromechanical systole and left ventricular ejection time were related to heart rate. Left ventricular ejection time was therefore adjusted for heart rate according to the regression equation in control group A. The relative left ventricular ejection time was calculated as percentage of the expected normal left ventricular ejection time (control group A). We calculated the relations between pre-ejection period and isovolumic contraction time, on one hand, and left ventricular ejection time and left ventricular ejection time adjusted to heart rate 60 (division by the square root of the cardiac cycle length in seconds) on the other.

STATISTICAL ANALYSIS

Possible relations were tested with Pitman's non-parametric permutation test, which when applied to two groups is equivalent to Fisher's test. We used multiple linear regression technique for multivariate analyses. P values $<0{\cdot}05$ were regarded as statistically significant.

Results

Table 1 shows the characteristics of the four groups (dyspnoea grade 1, 2, and 3 amalgamated). There was a significant relation between dyspnoea grade and weight, body mass index, lifelong tobacco con-

Table 1 *Characteristics (mean (SE)) of control groups and dyspnoeic groups*

	Control groups		*Dyspnoeic groups*		
Dyspnoea grade	*(A)* *0*	*(B)* *0*	*1–3*	*4*	*Relation to dyspnoea grade (0–4) (n = 87)*
Cardiac disease	*−* *(n = 14)*	*+* *(n = 31)*	*+* *(n = 37)*	*+* *(n = 5)*	*p for trend*
Weight (kg)	74 (3)	78 (2)	82 (2)	87 (4)	0·0078
Length (cm)	174 (1)	176 (1)	175 (1)	171 (1)	0·3870
Body mass index (kg/m²)	24 (1)	25 (1)	27 (1)	30 (1)	0·0011
Tobacco consumed (kg)	135 (37)	115 (23)	182 (24)	256 (69)	0·0079
Treated hypertension (%)	0	42	54	40	0·2954
Angina pectoris (%)	0	3	51	40	0·0001
Myocardial infarction (%)	0	16	32	20	0·0494
ECG Q waves (%)	0	16	38	60	0·0011
Atrial fibrillation (%)	0	3	11	20	0·2769
Congestion *x* ray (%)	0	3	11	60	0·0003
Heart size *x* ray (ml/m²)	403 (14)	414 (12)	428 (13)	544 (75)	0·0074
Maximum workload (W)	128 (5)	130 (5)	109 (5)	86 (2)	0·0001
Vital capacity (l)	4·4 (0·2)	4·3 (0·1)	4·0 (0·1)	3·4 (0·2)	0·0003
FEV%	69 (2)	66 (2)	69 (2)	77 (2)	0·0531

ECG, electrocardiographic; FEV%, forced expiratory volume during one second as percentage of vital capacity.

Table 2 *Systolic time intervals (mean (SE))*

	Control groups		*Dyspnoeic groups*		
Dyspnoea grade	*(A)* *0*	*(B)* *0*	*1–3*	*4*	*Relation to dyspnoea grade (0–4) (n = 87)*
Cardiac disease	*−* *(n = 14)*	*+* *(n = 31)*	*+* *(n = 37)*	*+* *(n = 5)*	*p for trend*
Heart rate (beats/min)	59 (2)	63 (3)	61 (2)	76 (7)	0·243
Q-A2 (ms)	417 (7)	412 (6)	411 (6)	366 (8)	0·032
LVET (ms)	315 (6)	303 (6)	299 (5)	272 (19)	0·047
PEP (ms)	102 (3)	110 (3)	112 (3)	94 (12)	0·649
EMI (ms)	38 (5)	42 (3)	42 (3)	40 (6)	0·831
ICT (ms)	64 (6)	67 (3)	69 (4)	54 (13)	0·372
LVET%	100 (1)	98 (1)	96 (1)	97 (6)	0·107
PEP/LVET	0·33 (0·01)	0·37 (0·01)	0·38 (0·01)	0·36 (0·07)	0·469
ICT/LVET	0·20 (0·02)	0·23 (0·02)	0·23 (0·01)	0·21 (0·06)	0·956
PEP/LVET$_c$	0·33 (0·01)	0·36 (0·01)	0·38 (0·01)	0·32 (0·05)	0·721
ICT/LVET$_c$	0·21 (0·02)	0·22 (0·01)	0·24 (0·01)	0·19 (0·05)	0·839

EMI, electromechanical interval; ICT, isovolumic contraction time; LVET, left ventricular ejection time; LVET$_c$, left ventricular ejection time normalised for the square root of the cardiac cycle length; LVET%, left ventricular ejection time as percentage of expected; PEP, pre-ejection period; Q-A2, electromechanical systole.

sumption, angina pectoris, sustained myocardial infarction, Q waves in the electrocardiogram, venous congestion on the *x* ray, maximum workload at the exercise test, and pulmonary vital capacity.

UNIVARIATE ANALYSES

Table 2 shows the systolic time intervals. The grade of dyspnoea correlated significantly only with the total electromechanical systole and the left ventricular ejection time. When left ventricular ejection time was adjusted for heart rate the relation to dyspnoea grade was no longer significant.

Dyspnoea grade was significantly related to left ventricular systolic dimension, septal and posterior wall fractional thickening, ejection indices, the ratio of wall stress to volume index, and peak emptying rate (table 3). To test the ability of the various systolic echocardiographic variables to detect early heart failure, the differences between the group with dyspnoea grade 1–3 and the control group A were tested for the variables shown in table 3. Only the end systolic dimension was found to be significantly ($p < 0·05$) different in the group with dyspnoea grade 1–3 and the control group A.

MULTIVARIATE ANALYSES

Fractional shortening and ejection fraction were the two factors from tables 2 and 3 that were most closely related to dyspnoea grade. Fractional shortening was selected for further analysis to find out to what extent systolic variables contribute to the variation in cardiac dyspnoea.

Table 3 *Variables derived from M mode echocardiography (mean (SE))*

	Control groups		*Dyspnoeic groups*		
Dyspnoea grade	*(A)* *0*	*(B)* *0*	*1–3*	*4*	*Relation to dyspnoea grade (0–4)*
Cardiac disease	*–*	*+*	*+*	*+*	*(n = 87)*
	(n = 14)	*(n = 31)*	*(n = 37)*	*(n = 5)*	*p for trend*
Heart rate (beats/min)	60 (3)	62 (3)	61 (2)	81 (5)	0·0780
Left ventricular dimension:					
Diastole (mm)	48·8 (1·1)	51·4 (1·2)	54·6 (1·6)	54·4 (2·6)	0·0620
Systole (mm)	31·8 (0·9)	33·4 (1·3)	37·3 (1·5)	44·1 (3·8)	0·0020
Wall fractional thickening:					
Septum	0·48 (0·09)	0·46 (0·04)	0·45 (0·04)	0·20 (0·09)	0·0276
Posterior wall	0·88 (0·08)	0·82 (0·04)	0·73 (0·04)	0·47 (0·04)	0·0020
Fractional shortening	0·35 (0·01)	0·35 (0·02)	0·32 (0·01)	0·19 (0·04)	0·0002
Ejection fraction	0·71 (0·02)	0·72 (0·02)	0·68 (0·02)	0·46 (0·07)	0·0001
Mean Vcf (circ/s)	1·10 (0·05)	1·18 (0·06)	1·09 (0·04)	0·70 (0·10)	0·0012
Mean Vcf_c (circ/s $s^{0·5}$)	1·12 (0·05)	1·17 (0·05)	1·09 (0·04)	0·64 (0·11)	0·0008
Mean Vcf_{cme} (%)	100 (5)	111 (4)	106 (4)	77 (10)	0·0084
ESWS (10^3dyn/cm^2)	54·6 (5·1)	61·6 (5·1)	59·0 (4·6)	93·8 (14·2)	0·1720
ESWS/ESVI (10^3dyn/cm^2)/(ml/m^2)	3·22 (0·20)	3·12 (0·20)	2·92 (0·26)	1·97 (0·38)	0·0310
ESWS/ESVI × EF (10^3dyn/cm^2)/(ml/m^2)	2·30 (0·16)	2·30 (0·20)	2·11 (0·22)	0·97 (0·39)	0·0159
Peak emptying rate (mm/s)	93·0 (5·2)	101·3 (5·0)	92·3 (3·4)	70·4 (11·9)	0·0298
Time of R wave to peak empyting rate (ms)	150 (15)	163 (9)	162 (8)	194 (18)	0·2388

ESVI, end systolic volume index; ESWS, end systolic wall stress; Vcf, velocity of circumferential fibre shortening; Vcf_c, Vcf adjusted for heart rate; Vcf_{cme}, Vcf measured as percentage of Vcf expected from the end systolic wall stress level (computed from the regression of control group A).

Table 4 *Results of univariate and multivariate analyses of the contribution of clinical and echocardiographical variables to the variance of dyspnoea grade*

	Univariate analysis			*Multivariate analysis*		
	r	*p*	*Proportion of explained variance*	*Additional proportion of explained variance*	*p*	*Cumulative proportion of explained variance*
Angina pectoris	0·51	<0·0001	0·26	0·27*	0·0001	0·27
Pulmonary congestion	0·46	0·0003	0·21	0·19	0·0001	0·46
Fractional shortening	0·41	0·0002	0·17	0·05	0·0058	0·50
Electrocardiographic Q waves	0·39	0·0011	0·15	0·02	0·0835	0·53

*The discrepancy with univariate analysis is the result of eight missing values in the multivariate analysis.

As a first step a multivariate analysis was performed of dyspnoea grade versus a history of angina pectoris, myocardial infarction, tobacco consumption, treatment for hypertension, blood pressure, heart size and pulmonary congestion at *x* ray examination, atrial fibrillation and Q waves in the electrocardiogram, and vital capacity. In this analysis angina pectoris, pulmonary congestion, and Q waves were significantly and independently related to dyspnoea grade, whereas the other factors were not.

The significant factors from the first analysis and fractional shortening were introduced in a new multivariate analysis to test their relation to dyspnoea grade (table 4). All the univariate relations were highly significantly related to dyspnoea grade. The right side of the table shows the multivariate analysis. Each of the variables, except for the Q waves, contributed significantly to the explanation of dyspnoea grade when the other variables were taken into account. The contribution of the Q waves was of borderline significance. About 50% of the variation in dyspnoea grade could be explained by the variables thus tested.

The clinical variables from table 4 were brought together into a clinical score in which the presence of angina, pulmonary congestion, and Q waves in the electrocardiogram were given one point each. Figure 1 shows the mean dyspnoea grade in groups of men

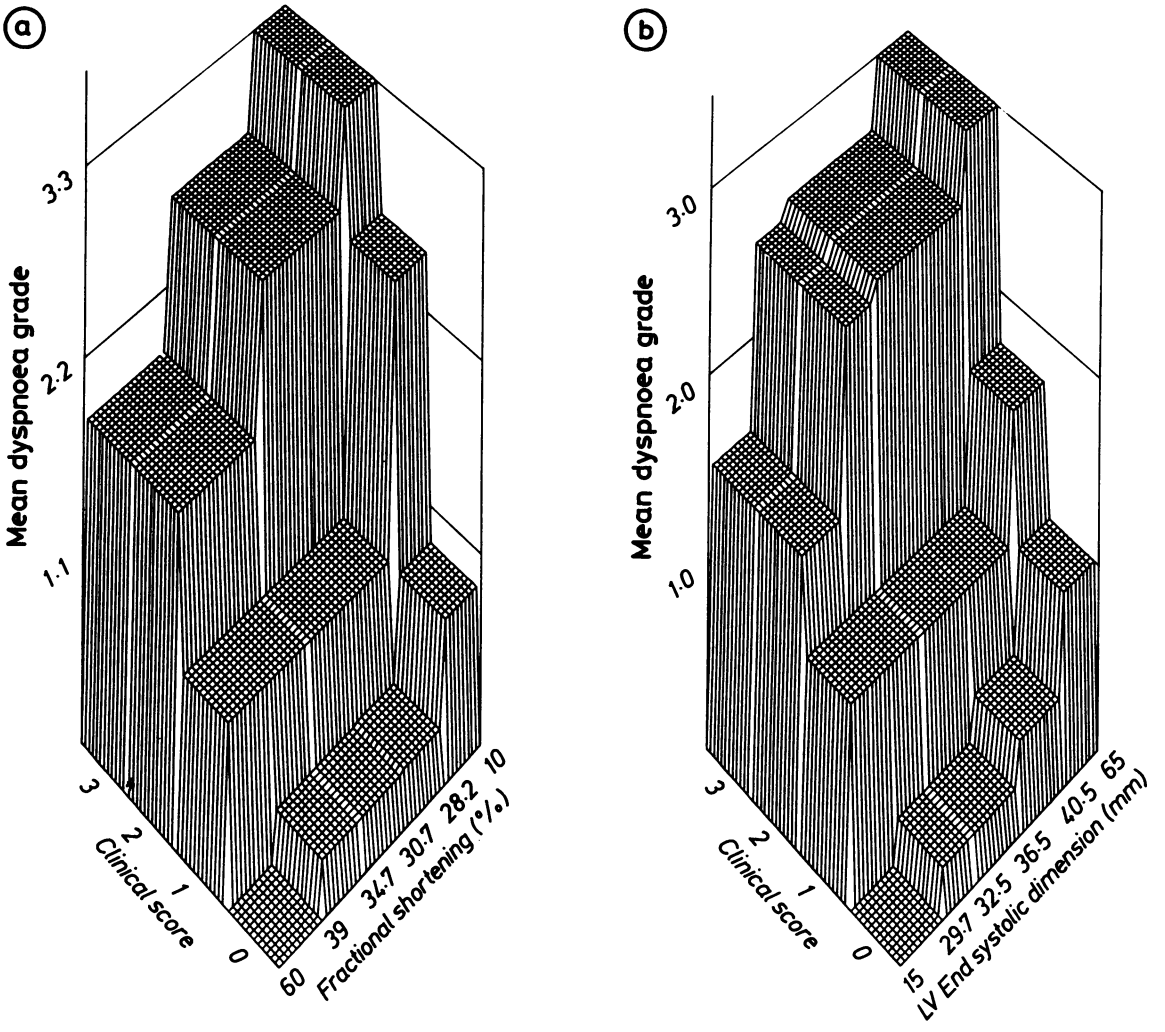

Fig 1 *Mean dyspnoea grade in groups distributed according to clinical involvement and quintiles of fractional shortening (a), or clinical involvement and quintiles of left ventricular (LV) end systolic dimension (b). Clinical involvement was indicated by one point for Q wave in the electrocardiogram, one point for pulmonary congestion on x ray, and one point for a history of angina pectoris. The points were summed as a clinical score. In groups with similar clinical involvement the grade of dyspnoea was related to fractional shortening and end systolic dimension.*

distributed according to the clinical score and fractional shortening (fig 1a) and according to the clinical score and left ventricular end systolic dimension (fig 1b).

LOAD DEPENDENCE

Table 3 shows the end systolic wall stress, the ratio of end systolic wall stress to volume index, and this ratio multiplied by the ejection fraction. Dyspnoea grade was significantly related to the last two ratios but not to end systolic wall stress (despite a high value for wall stress in the group with grade 4 dyspnoea). Figure 2 shows the relation between mean velocity of circumferential fibre shortening adjusted for heart rate (Vcf_c) and end systolic wall stress, where the confidence interval of control group A represents the normal relation between stress and shortening. Only three men (dyspnoea grade 4) had mean Vcf_c values below 2 SD of the value in the control group A. Of these three men, one had a low mean Vcf_c when account was taken of wall stress. We used the regression formula from control group A to calculate

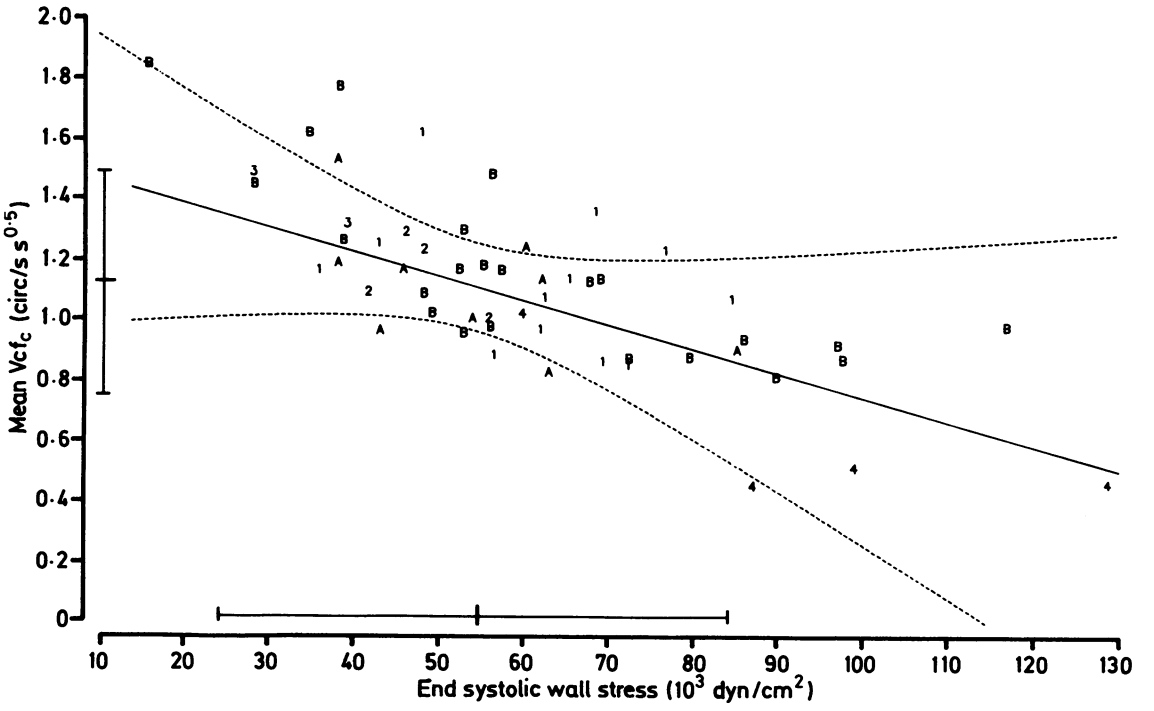

Fig 2 *The relation between mean velocity of circumferential fibre shortening adjusted for heart rate (mean Vcf$_c$) and end systolic wall stress. The curved lines represent 95% confidence limits for control group A. The horizontal line represents mean and confidence interval (± 2 SD) for end systolic wall stress and the vertical line the mean and confidence interval for Vcf$_c$ in the control group A. A shows volunteers in control group A, and B those in control group B; the numbers 1–4 show the corresponding grade of dyspnoea.*

the expected mean Vcf$_c$ from the wall stress value. Table 3 gives the ratios of measured to expected mean Vcf$_c$ as percentages (mean Vcf$_{cme}$).

Discussion

We found impaired systolic function in dyspnoeic men from the general population. Dyspnoea was related not only to fractional shortening and to ejection fraction but to most other echocardiographic indices of systolic function.

In several studies the New York Heart Association functional classification has been used to grade congestive heart failure. The dyspnoea grade applied in this study was found to be more closely related to working capacity, heart size, pulmonary congestion, and other functional variables than the New York Heart Association function classes (unpublished data). Because of this we used the grade of dyspnoea in the present study.

Systolic time intervals have been shown to be of limited value for the study of cardiac function in coronary heart disease.[11] We support this view because we did not find any significant relation between dyspnoea grade and systolic time intervals in the present study. Recently it was suggested that left ventricular ejection time should be corrected for heart rate before calculating ratios—for example to the pre-ejection period.[16] We found, however, that such a recalculation did not affect the relation between dyspnoea grade and time intervals.

The M mode echocardiographic recordings of cardiac dimensions were obtained with a handheld single crystal transducer. Theoretically it is better to use cross sectional echocardiography to guide the positioning of the M mode beam; however, this did not improve either the accuracy or the reproducibility of left ventricular measurements.[17] When it is difficult to obtain a high quality M mode image, a single transducer in the hands of an experienced echocardiographer has advantages because when the echo window is small its smaller size facilitates angulation and the higher repetition frequency of the echo signal improves resolution. Cross sectional echocardiography was used to establish that the M mode tracings were adequate. We

followed the suggestion in a study of wall stress in subjects with coronary artery disease[18] and excluded two men with left ventricular aneurysms. This should have made the indices of the ejection phase more representative. Major dyskinetic areas, which would have considerably limited the representativeness of the M mode recordings, were not found in the remainder of the patients.

The ejection fraction is the most commonly used index of systolic myocardial function. The calculation of ejection fraction from M mode echocardiography is based on assumptions of geometry, because the left ventricular volumes are computed from one ventricular dimension only.[19] We do not consider that the ejection fraction has any advantages over fractional shortening except that it is better known. The correlation between grade of dyspnoea and both these measures was similar, and we used fractional shortening for the multivariate analyses.

Ejection phase indices, although widely used as measures of left ventricular function, have their limitations because they are affected not only by changes in left ventricular contractility but also by changes in preload and afterload.[20 21] This load dependence is especially important in patients with valve dysfunction. In mitral regurgitation, for instance, favourable loading conditions caused by the low impedance leak into the left atrium may serve to maintain ejection indices near normal when the inotropic state is reduced.[4 13 20] On the other hand, in aortic stenosis subnormal fractional shortening may be caused by an increased afterload, and normal values of ejection phase indices may be found postoperatively. In the present study no subject had any signs of haemodynamically important valve disease.

Various alternative approaches have been proposed to overcome the fact that ejection phase indices depend upon loading conditions.[4 5 22] In most cases these are based on the relation between end systolic pressure or wall stress (measures of afterload) and ejection phase indices or end systolic dimension or volume.[4 5 15] The relation between afterload and ejection phase indices such as fractional shortening or mean velocity of circumferential fibre shortening is useful when studying the individual contractility to load matching.[5 12 15] The mean velocity of circumferential fibre shortening is augmented by an accelerated heart rate,[23] but the mean velocity of circumferential fibre shortening corrected for heart rate may be the measure of contractile performance that is least dependent upon preload.[5] The relations described are comparatively independent of preload, take account of the afterload, and are sensitive to the inotropic state.[4 24] The various relations have been used to evaluate contractile reserve in patients after cardiac transplantation,[25] to study the cardiac function in sickle cell anaemia with reduced afterload[26] and in hypertensive heart disease with an increased afterload,[12] and to evaluate the left ventricular mechanics in dilated cardiomyopathy[27] and in patients receiving antineoplastic agents.[28] Such indices have also been used to show that the hyperkinesia in hyperthyroidism is the result of augmented contractility rather than altered loading (or chronotropic) conditions,[29] and that the contractile state in young athletes is normal despite a considerable increase in left ventricular mass and irrespective of the type of exercise.[30] The ratio of end systolic wall stress to volume has been used to predict preoperatively the outcome of valve replacement.[4] Incorporation of ejection fraction into this index has been claimed to improve prognostic accuracy.[22]

In the present study two of the various proposed "load independent indices" were applied. Their correlations with the grade of dyspnoea were similar. The ratio of end systolic wall stress to volume correlated with the grade of dyspnoea, and the addition of ejection fraction to the formula had no appreciable effect. The relation between mean velocity of circumferential fibre shortening corrected for heart rate and dyspnoea grade was not improved by taking account of the level of wall stress. Three men (dyspnoea grade 4) had abnormal mean velocity of circumferential fibre shortening corrected for heart rate (below two standard deviations of the mean value of the control group A), and one of them seemed to have a reduced mean velocity of circumferential fibre shortening corrected for heart rate in relation to the wall stress level, indicating a noncompensated depressed inotropic state.

Consideration of preload and afterload is important, particularly in valve disease, and in pharmacological or other interventions aiming at the treatment or investigation of, for example, preload reserve. In a study of patients treated with doxorubicin, variables that are independent of load, such as the wall stress/fractional shortening relation, were regarded as useful for the early detection of left ventricular dysfunction.[28] In the present study such indices were not helpful in detecting early cardiac dysfunction, as judged by their relation with presumed cardiac dyspnoea. Pharmacological intervention to alter afterload during the investigation might have yielded some additional information and led to an early diagnosis of heart failure. The additional value of such an approach is not obvious,[28] however, and interventions in epidemiological studies are neither practicable or ethical.

Early systolic dysfunction causing dyspnoea seemed to be most effectively demonstrated by the end systolic dimension. The end systolic dimension was the only one of the variables tested that was

significantly different in the control group A and the group with grade 1–3 dyspnoea. In this small group this variable was a better indicator of early systolic dysfunction than fractional shortening (and ejection fraction). The reason may be that any increase in systolic dimension was accompanied by an increase in diastolic dimension, thereby reducing the decrease of fractional shortening.

We conclude that the group with grade 4 dyspnoea made an important contribution to the relation between dyspnoea grade and echocardiographic variables. The group with grade 1–3 dyspnoea essentially seemed to have a well functioning ventricle. The only significant difference was an increase in end systolic dimension; heart rate, wall stress, and fractional shortening were normal (table 3). On the other hand, the group with grade 4 dyspnoea showed increased heart rate and wall stress and reduced fractional shortening. These considerable differences between those with grade 1–3 dyspnoea and those with grade 4 dyspnoea might indicate pathophysiological or haemodynamic differences between the groups. One explanation is that the influence of diastolic dysfunction is greater in early heart failure (grade 1–3). Because it has recently been suggested that diastolic abnormalities might be important in congestive heart failure when systolic function is normal we evaluated diastolic function in a separate study.[7]

Valve disease and severe untreated hypertension are the major mechanisms that alter the load in congestive heart failure; neither was present in this study population. Thus the loading conditions were not imposed externally but were brought about mainly by mechanisms generated to compensate for impaired myocardial function. Fractional shortening seems to be an appropriate simple measure of contractility in a population in whom clinical and noninvasive data indicate that congestive heart failure is caused by coronary artery disease. An increased end systolic dimension may be an even earlier sign of abnormal systolic function. Although several complex variables of systolic function have emerged during recent years, these indices do not necessarily add much information in population studies. Also, they do not lead to earlier detection of cardiac failure than simple measures such as end systolic dimension or fractional shortening.

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References

1 Weber KT, Ratshin RA, Janicki JS, Rackley CE, Russell RO. Left ventricular dysfunction following acute myocardial infarction. A clinicopathologic and hemodynamic profile of shock and failure. *Am J Med* 1973;**54**:697–705.

2 Nestico PF, Hakki A-H, Iskandrian AS. Left ventricular dilatation. Prognostic value in severe left ventricular dysfunction secondary to coronary artery disease. *Chest* 1985;**88**:215–20.

3 Franciosa JA. Epidemiologic patterns, clinical evaluation, and the long-term prognosis in chronic congestive heart failure. *Am J Med* 1986;**80**(suppl 2B): 14–21.

4 Carabello BA, Spann JF. The uses and limitations of end-systolic indexes of left ventricular function. *Circulation* 1984;**69**:1058–64.

5 Colan SD, Borow KM, Neumann A. Left ventricular end-systolic wall stress-velocity of fiber shortening relation: a load-independent index of myocardial contractility. *J Am Coll Cardiol* 1984;**4**:715–24.

6 Caidahl K, Svärdsudd K, Eriksson H, Wilhelmsen L. Relation of dyspnoea to left ventricular wall motion disturbances in a population of 67-year-old men. *Am J Cardiol* 1987;**59**:1277–82.

7 Caidahl K, Eriksson H, Hartford M, *et al.* Dyspnoea of cardiac origin in 67 year old men: (2) relation to diastolic left ventricular function and mass. The study of men born in 1913. *Br Heart J* 1988;**59**:329–38.

8 Eriksson H, Caidahl K, Larsson B, *et al.* Cardiac and pulmonary causes of dyspnoea—validation of a scoring test for clinical-epidemiological use. The study of men born in 1913. *Eur Heart J* 1987;**8**: 1007–14.

9 Rose GA, Blackburn H, Gillum RF, Prineas RJ. *Cardiovascular survey methods.* (Monograph No 56.) 2nd ed. Geneva: World Health Organisation, 1982: 123–68.

10 Elmfeldt D, Wilhelmsen L, Tibblin G, Vedin JA, Wilhelmsson CE, Bengtsson C. Registration of myocardial infarction in the city of Göteborg, Sweden. *J Chronic Dis* 1975;**28**:173–86.

11 Wikstrand J, Berglund G, Wilhelmsen L, Wallentin I. Value of systolic and diastolic time intervals. Studies in normotensive and hypertensive 50-year-old men and in patients after myocardial infarction. *Br Heart J* 1978;**40**:256–67.

12 Hartford M, Wikstrand JCM, Wallentin I, Ljungman SMG, Berglund G. Left ventricular wall stress and systolic function in untreated primary hypertension. *Hypertension* 1985;7:97–104.

13 Caidahl K, Larsson S, Südow G, Wallentin I, Angelhed JE, Olsson SB. Conservative surgery for mitral valve prolapse with regurgitation: clinical follow-up and noninvasive assessment. *Eur Heart J* 1987;**8**:384–94.

14 Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. *J Clin Invest* 1975;**56**:56–64.

15 Borow KM, Green LH, Grossman W, Braunwald E. Left ventricular end-systolic stress-shortening and stress-length relations in humans. Normal values and sensitivity to inotropic state. *Am J Cardiol* 1982;

50:1301–8.

16 Sundberg S. Influence of heart rate on systolic time intervals. *Am J Cardiol* 1986;**58**:1144–5.

17 Devereux RB, Liebson PR, Horan MJ. Recommendations concerning use of echocardiography in hypertension and general population research. *Hypertension* 1987;**9**(suppl II):97–104.

18 Strauer BE. *Hypertensive heart disease*. Berlin: Springer-Verlag, 1980:7–11.

19 Teichholtz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence or absence of asynergy. *Am J Cardiol* 1976;**37**:7–11.

20 Ross J Jr. Cardiac function and myocardial contractility: a perspective. *J Am Coll Cardiol* 1983;**1**:52–62.

21 Ross J Jr. Mechanisms of cardiac contraction. What roles for preload, afterload and inotropic state in heart failure? *Eur Heart J* 1983;**4**(suppl A):19–28.

22 Breisblatt W, Goodyer AVN, Zaret BL, Francis CK. An improved index of left ventricular function in chronic mitral regurgitation. *Am J Cardiol* 1986; **57**:1105–8.

23 DeMaria AN, Neumann A, Schubart PJ, Lee G, Mason DT. Systematic correlation of cardiac chamber size and ventricular performance determined with echocardiography and alterations in heart rate in normal persons. *Am J Cardiol* 1979;**43**:1–9.

24 Marsh JD, Green LH, Wynne J, Cohn PF, Grossman W. Left ventricular end-systolic pressure-dimension and stress-length relations in normal human subjects. *Am J Cardiol* 1979;**44**:1311–7.

25 Borow KM, Neumann A, Arensman FW, Yacoub MH. Left ventricular contractility and contractile reserve in humans after cardiac transplantation. *Circulation* 1985;**71**:866–72.

26 Denenberg BS, Criner G, Jones R, Spann JF. Cardiac function in sickle cell anemia. *Am J Cardiol* 1983; **51**:1674–8.

27 Laskey WK, St John Sutton M, Zeevi G, Hirshfeld JW, Reichek N. Left ventricular mechanics in dilated cardiomyopathy. *Am J Cardiol* 1984;**54**:620–5.

28 Borow KM, Henderson IC, Neuman A, *et al*. Assessment of left ventricular contractility in patients receiving doxorubicin. *Ann Intern Med* 1983;**99**: 750–6.

29 Feldman T, Borow KM, Sarne DH, Neumann A, Lang RM. Myocardial mechanics in hyperthyroidism: importance of left ventricular loading conditions, heart rate and contractile state. *J Am Coll Cardiol* 1986;7:967–74.

30 Colan SD, Sanders SP, Borow KM. Physiologic hypertrophy: effects on left ventricular systolic mechanics in athletes. *J Am Coll Cardiol* 1987;**9**:776–83.