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Diastolic heart failure in older people

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Abstract

Objectives: to determine the prevalence of diastolic heart failure in older people in the community, identify associated risk factors and measure its impact on function and quality of life.
Design: cross-sectional population-based study.
Methods: a two-stage random sample of 500 subjects was drawn from 5,002 subjects aged 70 years and over living at home. Diastolic heart failure was diagnosed by a panel of three physicians, based on clinical assessment and echocardiographic indicators of diastolic dysfunction.
Main outcome measures: prevalence of diastolic heart failure and its effect on function and quality of life as measured by Nottingham Extended Activities of Daily Living, Hospital Anxiety and Depression and SF-36 questionnaires.
Results: the prevalence of diastolic heart failure was 5.54% (95% CI = 3.71, 7.87) and was higher in women (8.32%) than in men (1.25%), $P = 0.008$. On multivariate analysis of variance, diastolic heart failure was associated with female gender and history of ischaemic heart disease. Subjects with diastolic heart failure had significantly poorer functional status and physical health than those without heart failure.
Conclusions: Diastolic heart failure is relatively common in older people and is associated with adverse affects in older people's lives.

Keywords: *diastolic heart failure, older people, quality of life, activities of daily living*

Introduction

The syndrome of clinical heart failure with normal left ventricular systolic function and in the absence of cardiac valvular lesions often referred to as diastolic heart failure (DHF) is believed to be common in older people. In the Helsinki Ageing Study, 51% of patients aged 75–86 years with clinical heart failure were thought to have DHF [1]. However, the diagnosis of isolated diastolic dysfunction as a cause of heart failure remains controversial. In a study of a direct access echocardiography service, Caruana *et al*. [2] concluded that most patients with suspected heart failure and preserved systolic function were inappropriately labelled as having diastolic heart failure, and in fact had other factors including lung disease causing their symptoms.

Left ventricular diastolic function changes with ageing [3]. This is thought to be due to an increase in myocardial interstitial collagen content [4] and a decrease in sarcoplasmic reticulum function [5]. This therefore gives rise to debates as to whether diastolic dysfunction and DHF are 'normal' in some older individuals. Very little is known about the adverse effects of diastolic dysfunction in older people. No study, to date, has examined the relationship between DHF and function and quality of life in older people.

Most published studies of DHF have been retrospective and practically all were hospital based and, therefore, the prevalence of diastolic heart failure in the community is unknown [6]. Previous epidemiological studies have all relied on a diagnosis of exclusion for DHF and have failed to demonstrate diastolic dysfunction, and have therefore been criticised for overestimating the prevalence of DHF amongst older people. The aims of this study were to determine the prevalence of DHF in older people in the community, identify associated risk factors, and examine the association between DHF and function and quality of life.

Methods

Study design

This was part of a cross-sectional population based study to determine the prevalence of breathlessness and associated cardiovascular diseases in older people in the community [7]. Ethical approval was given by Bro Taf Local Research Ethics Committee and written informed consent was obtained from subjects. Details of the study design and methods have been reported previously [7].

Patients

A modified Medical Research Council (MRC) dyspnoea questionnaire to identify breathlessness was sent to 1404 subjects, randomly selected from general practitioner lists with a total population of 5,002 subjects aged 70 years and over living at home in a South Wales town. Of the responders, a stratified random sample of 250 breathless and 250 non-breathless were invited to attend a study centre for further investigation. Electrocardiogram, transthoracic echocardiogram, lung function tests and clinical examination were performed. Chronic obstructive pulmonary disease was defined as both FEV_1 and the FEV_1/FVC ratio being lower than the lower limits of normal for older people [8]. Obesity was defined as body mass index (BMI) >30 kg/m^2 [9].

Analysis of cardiac function

LV systolic function was assessed by echocardiography (Toshiba SSH-140A) in standard views. All the echocardiograms were analysed independently by 2 of 3 observers, who were blind to the clinical findings. Ejection fraction was measured by M-mode whenever possible, otherwise global LV systolic function was assessed qualitatively as normal or mildly, moderately or severely impaired. Global assessment is practical, and is commonly used to assess LV systolic function, particularly in studies of older people, who tend to be less echogenic [10, 11]. Disagreements between the observers were adjudicated by the third observer.

Doppler echocardiographic indices of diastolic function were derived from the study of ventricular filling dynamics with precise placement of the pulse-wave Doppler sample volume at the leaflet tips. Mitral inflow interrogation allowed characterisation of LV isovolumic relaxation time (IVRT) defined as time taken from the second heart sound until the opening of the mitral valve, early diastolic filling (E wave), rapidity of pressure equalization between the left ventricle and left atrium during early filling (E deceleration time), and evaluation of atrial contribution to filling (A wave) [12]. The IVRT and E deceleration time were measured in milliseconds (ms), and E wave and A wave in metres per second (m/s).

All data collected were presented to a panel of three physicians. The clinical diagnosis of heart failure syndrome was in accordance with the definition of heart failure proposed by the Task Force on Heart Failure of the European Society of Cardiology [13]. The presence of DHF was diagnosed by consensus panel in accordance with European Study Group recommendations for diagnosis of DHF [14], only when patients fulfilled all of the following criteria:

1. The presence of significant breathlessness (Medical Research Council Grade 3–5) [15, 16] that could not be attributed to chronic obstructive pulmonary disease or asthma or obesity.

and

2. Signs of fluid retention (pulmonary or peripheral); OR signs could be absent if subjects were taking diuretic therapy.

and

3. Normal left ventricular systolic function (ejection fraction $>50\%$ when available or normal on qualitative assessment of LV systolic function) and normal valves on echocardiography, and sinus rhythm on electrocardiography.

and

4. Echocardiographic indicators of diastolic dysfunction, including abnormal E velocity, A velocity, E/A ratio, E deceleration time or IVRT or a combination of any of these using the published normal ranges for measures of diastolic function for older people [12]. Left ventricular hypertrophy defined as septum thickness in diastole >1.2 cm in females and >1.3 cm in males was also considered supportive echocardiographic evidence of diastolic dysfunction [17, 18].

Function and Quality of Life measures

Nottingham Extended Activities of Daily Living (NEADL) index [19], the Hospital Anxiety and Depression Scale (HAD) [20] and short form 36 (SF-36) [21, 22], a generic measure of health status, were administered by an interviewer on home visit. SF-36 scores were aggregated into physical (PCS) and mental (MCS) cumulative summary scores.

Co-morbidity

A structured clinical proforma was used to identify possible risk factors associated with DHF including diabetes mellitus, strokes, transient ischaemic attacks, ischaemic heart disease (history of angina or myocardial infarction) and hypertension.

Statistical analysis

The population prevalence of DHF was estimated from that in the sub-sample, correcting for 2-stage stratified random sampling in the survey design, by utilising survey analysis functions within the statistical package STATA

6.0 [23, 24]. This ensures that both point and interval estimates are valid [24]. Similar methods were used to estimate the population mean scores for the measures of Function and Quality of Life for those with and without DHF as well as the differences between them. Summary scales representing these measures were transformed to percentages of maximum, the HAD scale being inverted for consistency of direction.

To examine the possible risk factors associated with DHF, univariate logistic regression was carried out on patient specific factors including co-morbidities, age and gender. Interactive multivariate logistic regression was done to identify independent risk factors.

Results

Prevalence of DHF

Of the 1404 subjects surveyed, 1169 responded. Of the non-responders, 113 were found to be ineligible because of hospitalisation, move to care home or death, giving an overall response rate in the first stage of 91% of eligible. There were 34 withdrawals including 15 deaths and 19 other valid exclusions, from the sub-sample of 500, leaving 466 in the sub-sample. Three-hundred and fifty-one of these (75.3% of eligible) completed all investigations including echocardiography. We diagnosed DHF in 26 subjects, giving an overall population prevalence of DHF in older people in the community of 5.54% (95% CI = 3.71, 7.87). The mean age of DHF subjects was 77.9 years and 88% were female. The prevalence of DHF was higher in women (8.32%) than in men (1.25%), $P = 0.008$, but did not increase with advancing age.

Echocardiography findings

The echocardiographic abnormalities of those with DHF are summarised in Table 1. Of those with DHF, 21 (81%) patients had analysable transmitral flow Doppler measurements. Sixteen of these had one or more abnormal diastolic parameters using published reference ranges [12]. Echocardiographic left ventricular hypertrophy was found in 58% (Table 1).

Associated factors and co-morbidity

Univariate survey logistic regression was used to examine correlation between DHF and the following factors: age, gender, myocardial infarction (MI), angina, ischaemic heart disease (MI and angina), hypertension, diabetes mellitus, stroke, left bundle branch block on ECG (LBBB), chronic obstructive pulmonary disease, current smoker, and obesity. Five factors were significantly associated with DHF: female gender, myocardial infarction, angina, ischaemic heart disease and hypertension. Advancing age was not associated with DHF.

Interactive modelling using multivariate logistic regression suggested that DHF was independently associated only with female gender [odds ratio = 10.92 (1.96, 60.87), $P = 0.007$], history of ischaemic heart disease [odds ratio = 7.91 (2.59, 24.13), $P < 0.001$] and weakly with history of hypertension [odds ratio = 2.21 (0.78, 6.25)]. There was a high degree of colinearity between these cardiovascular factors and the most parsimonious model included only female gender (12.17 (2.21, 67.00)) and ischaemic heart disease (9.66 (3.46, 26.93)).

Associations between DHF and function and quality of life

The 26 subjects with DHF had impaired function and poorer health as measured by lower scores in SF36-PCS (25.4 *versus* 41.8%, $P < 0.001$) and total NEADL (67.2% *versus* 83.1%, $P < 0.001$) respectively, compared with 285 subjects with no DHF or LVSD (Figure 1). DHF subjects also scored significantly worse in HAD (72.6% *versus* 82.0%, $P = 0.002$), compared with those with no DHF or LVSD but there was no difference in SF36-MCS (51.2% *versus* 54.1%, $P = 0.321$) (Figure 1).

Subjects with DHF had impairments in function and quality of life similar to that found in patients with systolic heart failure (Table 2) and stroke survivors in the same population (Table 3). There were no significant differences between these three groups in mean age, 77.9 years in DHF, 78.7 years in stroke survivors and 78 years in systolic heart failure ($P > 0.5$). There were more women in the DHF group (88%) compared with stroke (46%) and systolic heart failure (57%), ($P < 0.0001$).

Table 1. Abnormal indices of diastolic function in patients with diastolic heart failure

Diastolic function parameters	Number of patients with abnormal indices/(%)
Mitral valve E (m/s) > 0.9 or < 0.3	4 (15%)
Mitral valve A (m/s) > 0.9	12 (46%)
E:A ratio < 0.5	2 (8%)
Mitral E dec time (ms) > 280	5 (19%)
Left ventricular hypertrophy	15 (58%)

Table 2. Function and quality of life mean % scores in subjects with DHF and systolic heart failure

	Population mean percentage scores with 95% CI		
Scale	Subjects with DHF (*n* = 26)	Systolic heart failure (*n* = 28)	*P* values
SF36-PCS	25.4 (22.9, 27.9)	29.4 (25.6, 33.1)	0.067
SF36-MCS	51.2 (45.5, 56.8)	50.8 (49.2, 55.3)	0.995
NEADL	67.2 (62.5, 71.9)	67.5 (61.3, 73.7)	0.996
HAD (inverted)	72.6 (66.9, 78.4)	74.6 (68.8, 80.4)	0.641

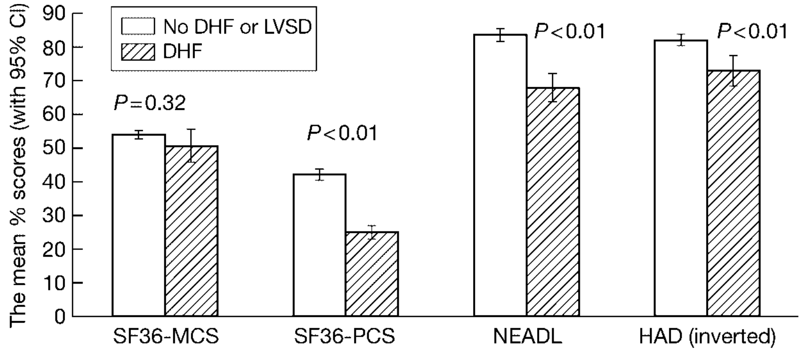

Figure 1. The mean % scores in subjects with DHF and those with no DHF or LVSD

Discussion

Chronic heart failure is a community problem affecting mainly older people, the mean age of CHF patients living at home or in long-term care being 74 years [25]. The prevalence of CHF rises from < 1% in people aged under 65 to 10–20% in the over 80s [26, 27].

In DHF the ventricle is unable to fill to its normal volume at normal pressure in diastole to produce an adequate cardiac output despite the presence of normal ventricular systolic function. In this community-based study, we found a prevalence of diastolic heart failure of 5.54% in people aged over 70 living at home. Interestingly, this is similar to the prevalence of 4.2% for heart failure with normal systolic function in the Helsinki Ageing Study, though diastolic function was not measured [1].

Caruana *et al.* [2] highlighted that alternative diagnoses to heart failure with normal systolic function such as obesity and lung disease commonly account for breathlessness. In our study we rigorously excluded all patients with significant lung disease or obesity. Patients with chronic atrial fibrillation were also excluded in case they had arrhythmia-induced breathlessness. We also demonstrated some evidence of diastolic dysfunction on echocardiography before reaching a diagnosis of DHF. We have probably, if anything, underestimated the prevalence of DHF as we required all patients to have significant breathlessness with MRC grade 3–5 and we effectively excluded people who could have DHF and co-morbidities such as obesity, atrial fibrillation and chronic lung disease.

However the diagnosis of DHF remains fraught with difficulty. We have attempted to apply the European Study Group criteria for the diagnosis of DHF [14], but one of the main limitations of our study is our reliance on indices of Doppler mitral inflow to assess ventricular diastolic function. As DHF progresses, the E velocity increases following the initial reduction, which gives rise to a 'normal' E velocity, E/A ratio and IVRT, often referred to as pseudonormalisation [28]. This limits the use of these parameters in diagnosing diastolic dysfunction, as using these parameters alone, one will miss moderately severe DHF. We therefore used echocardiographic evidence of LVH as an additional indicator of DHF [17, 18].

For more accurate characterization of diastolic function, a combined analysis of pulmonary venous and mitral inflow velocity profile preferably with Valsalva manoeuvre is preferable [28–30]. These measurements were not unfortunately feasible in our study due to time constraints imposed by our wish to keep the study protocol as short as possible for community dwelling older people. Hopefully, newer echocardiographic techniques such as tissue Doppler imaging may prove more accurate in the diagnosis of diastolic dysfunction [31].

The European Study Group criteria for diagnosis of DHF are of limited clinical use because of the third criterion, the requirement to demonstrate evidence of abnormal left ventricular relaxation, filling, diastolic distensibility or diastolic stiffness. Because of the limitations of currently available doppler indices, as discussed above, demonstrating objective evidence of diastolic dysfunction can require invasive techniques including cardiac catheterisation to measure pressure and volume [32]. It is obviously not feasible to subject all patients with chronic heart failure to this invasive procedure. In the context of these difficulties, Vasan and Levy propose a scheme for the definition of definite, probable or possible DHF [32] as illustrated in Table 4, which relies on cardiac catheterisation to provide evidence of 'definite' DHF. According to this classification, subjects in our study would have 'probable DHF'.

Our data convincingly demonstrate that subjects with DHF have significant impairments in function and quality of life. The impairments in function and quality of life in DHF subjects in our study were similar to those found

Table 3. Function and quality of life mean % scores in subjects with DHF and in stroke survivors

	Population mean percentage scores with 95% CI		
Scale	Stroke Survivors (n=26)	DHF (n=26)	P values
SF36-PCS	30.6 (25.1, 36.0)	25.4 (22.9, 27.9)	0.083
SF36-MCS	53.6 (49.0, 58.2)	51.2 (45.5, 56.8)	0.236
NEADL	68.8 (64.4, 73.2)	67.2 (62.5, 71.9)	0.853
HAD (inverted)	75.1 (69.4, 80.8)	72.6 (66.9, 78.4)	0.752

Table 4. Classification of DHF by Vasan and Levy [32]

Definite DHF	Probable DHF	Possible DHF
Definite evidence of clinical heart failure	Definite evidence of clinical heart failure	Definite evidence of clinical heart failure
AND	AND	AND
Objective evidence of normal LV systolic function within 72 hours of heart failure event	Objective evidence of normal LV systolic function within 72 hours of heart failure event	Objective evidence of normal LV systolic function, but not at the time of heart failure event
AND	AND	AND
Objective evidence of LV diastolic dysfunction	Lack of objective evidence of LV diastolic dysfunction	Lack of objective evidence of LV diastolic dysfunction

in stroke survivors (Table 3). This finding is important in emphasising that DHF is associated with adverse effects in older people's lives. Currently, the debate on what is 'normal' in terms of diastolic function in healthy ageing is clouded by confusion between statistical normality and clinical/biological normality. A more fruitful approach might be to identify the level of diastolic dysfunction associated with adverse effects in terms of mortality and morbidity in older people. A mortality follow up of the subjects in our study population is currently underway to better characterize the natural history and prognosis of DHF.

In conclusion, DHF is relatively common in older people in the community with female gender and ischaemic heart disease being the most important associated risk factors. DHF is associated with substantial adverse effects in function and quality of life, making it a very real syndrome in the elderly.

Key Points

- Diastolic heart failure is relatively common in older people.
- It is more common in women than in men.
- Diastolic heart failure is associated with significant impairments in function and quality of life.

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