The prevalence of left ventricular diastolic filling abnormalities in patients with suspected heart failure

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Aims It is reported that one third of patients with heart failure have normal left ventricular systolic function, and may or may not have left ventricular diastolic dysfunction. We sought to define the prevalence of left ventricular diastolic filling abnormalities in a large unselected group of patients, unlike the diagnosis by exclusion in the small highly selected groups of patients studied previously.

Methods and results Patients were referred by general practitioners to an open-access echocardiography service for assessment of possible heart failure. Echocardiography included a Doppler study of transmitral flow at the tips of the mitral leaflets and calculation of an E/A ratio. Of 534 patients referred and assessed, 371 patients had normal systolic function and a measurable E/A ratio. These were compared with age-adjusted reference ranges to give 9 above the reference range and 19 below. This is only 10 more than would be expected if our patients were normal. In the same group of patients we found 96 cases of left ventricular systolic dysfunction, or 52 amongst the 423 with a measurable E/A ratio.

Conclusion Either left ventricular diastolic filling abnormalities are very much less common than previously supposed or the E/A ratio is almost useless for their detection.

Key Words: Heart failure, echocardiography, diastolic filling abnormalities.

Introduction

In recent years there has been much interest in the possibility that heart failure can be caused by diastolic as well as systolic mechanisms. Systolic and diastolic dysfunction probably often coexist; whether isolated diastolic dysfunction causes heart failure remains controversial.

In 1983, Echeverria et al.[1] studied 50 heart failure patients to find that 40% had a normal ejection fraction. In 1984, Dougherty et al.[2] studied 188 patients having radionuclide ventriculography to find that 36% had a normal ejection fraction. In 1985, Soufer et al.[3] studied 74 heart failure patients to find that 42% had intact systolic function. In 1989, Aguirre et al.[4] studied 151 heart failure patients to find that 34% had normal systolic function. Wong et al.[5] studied 54 elderly patients admitted with heart failure to find that 41% had normal systolic function. In 1990, Aronow et al.[6] studied 166 elderly heart failure patients in long-term care to find that 41% had a normal ejection fraction. In 1991, Ghali et al.[7] studied 82 patients admitted with heart failure to find that 28% had preserved systolic function. Forman et al.[8] studied 32 elderly nursing home patients on digoxin in sinus rhythm to find that 72% had a normal ejection fraction. More recently, in 1995, Andersson et al.[9] studied 275 heart failure patients to find that 34% had normal end-diastolic diameter and ejection fraction. Again, McDermott et al.[10] studied 298 patients hospitalized with heart failure to find that 31% had normal systolic function.

The above studies cover 1370 patients with heart failure, 491 of whom (36%) were found to have normal systolic function, and were thereby implied to have diastolic dysfunction. The subject has been even more comprehensively reviewed recently[11]. These findings have not gained universal acceptance because of the limitations of the studies. The patients have been highly selected, non-consecutive, hospital-based and mostly American. The patients have therefore been mostly male, elderly, and often largely African American. Furthermore, diastolic dysfunction has usually been
presumed on the basis of absence of systolic dysfunction, rather than determined in its own right. This begs the question of whether or not such patients actually have heart failure at all, let alone whether or not they have diastolic dysfunction as a mechanism. With this in mind, we set out to examine the prevalence of left ventricular diastolic filling abnormalities in a large, consecutive and representative group of patients.

Methods

An open-access echocardiography service was set up in this hospital, the details of which have been well documented[12]. In short, general practitioners were invited to refer patients suspected of having heart failure, in case they might benefit from treatment with an angiotensin converting enzyme (ACE) inhibitor. Referrals for evaluation of murmurs alone were not encouraged, and few such patients were referred. We were primarily interested in identification of patients with systolic dysfunction but we sought to examine left ventricular diastolic filling as well.

Echocardiography was performed by a dedicated echocardiography technician using an Accuson XP10 or Hewlett Packard 1500, and the results were reported by a cardiologist experienced in echocardiography. Standard views were obtained with the patient relaxed in the left lateral decubitus position. In the absence of valvular regurgitation, systolic function was considered to be significantly impaired if fractional shortening by M-mode was less than 25%. In addition (and if quantitative measurements were not possible) a qualitative overall assessment of systolic function as normal or impaired by 2D was made. Doppler echocardiography included a pulsed-wave study of the spectrum of trans-mitral flow velocities recorded from the apical four-chamber view with the sample window positioned at the tips of the mitral valve leaflets. The ultrasound beam was aligned with transmitral flow to minimize the angle of incidence, and studies were eliminated if this angle was >30°. Doppler was recorded at a sweep speed of 100 mm/s. When a consistent waveform was obtained, it was ‘frozen’, and the outline traced to obtain the peak early diastolic inflow velocity coincident with the E wave, the peak late diastolic inflow velocity coincident with the A wave (measured from baseline), and the ratio of the former to the latter (E/A ratio). This method is well described previously[13].

Results

Five hundred and thirty-four patients were referred and assessed in the first 12 months of the service. Four hundred and seventy-four out of 534 patients were in sinus rhythm with a normal heart rate and so had a potentially measurable E/A ratio. Four hundred and twenty-three out of 474 patients had an actually measurable E/A ratio. Three hundred and seventy-one out of 423 patients had normal systolic function. There were thus 371 patients with normal systolic function and a measurable E/A ratio.

As reported previously, the E/A ratio was highly age-dependent. Figure 1 illustrates which of our cases were within and which above or below the age-adjusted reference ranges derived from Framingham[14] and endorsed by Feigenbaum[13]. Thus when age is taken into account, nine out of 371 cases emerged above the reference range and 19 out of 371 cases emerged below.

Figure 1 Age in years vs E/A ratio (dots = within reference range, crosses = outside reference range).
Given that the age-adjusted reference ranges are 95% confidence limits, nine out of 371 cases would be expected to be above the reference range and nine out of 371 cases would be expected to be below, even if there was no significant difference between normals and our patients suspected of having heart failure by their general practitioners.

**Discussion**

The E/A ratio is one of the most widely quoted echocardiographic indices of left ventricular diastolic filling. Our findings confirm the previously reported relationship between age and the E/A ratio and emphasize the importance of making adjustment for this. It is potentially misleading to regard E/A reversal (i.e., a wave bigger than E wave, E/A ratio less than unity) as abnormal on its own, we therefore sought to correlate our results as closely as possible with age. We found that out of 371 patients, nine had an E/A ratio which was high for their age, and 19 had an E/A ratio which was low for their age. However, this is an excess of only 10 cases over what might be expected even if our patients were normal. In contrast, we found that 96 out of the whole 534 patients, or 52 out of the 423 patients with a measurable E/A ratio had systolic dysfunction. Even though we found that relatively few of our patients suspected of having heart failure had systolic dysfunction compared with previous studies, we looked at and found that very much fewer had an abnormal E/A ratio. It is therefore questionable to what extent the E/A ratio was indicative of any significant abnormality at all amongst our patients. Indeed, we must conclude that either 'diastolic dysfunction' is very much less common than previously supposed, or the E/A ratio is almost useless for the diagnosis of left ventricular diastolic filling abnormalities. The latter might be considered to be self-evident, but that does not stop many physicians, specialists as well as generalists, using the term 'E:A reversal' as if it was meaningful.

Previous studies have taken patients with an established diagnosis of heart failure and have defined diastolic dysfunction as absence of systolic dysfunction, but our study has taken a large population of patients who may or may not have heart failure (but are quite likely to have it), and sought to define the prevalence of systolic dysfunction, and left ventricular diastolic filling abnormalities as well. We have almost certainly failed to detect some cases of diastolic dysfunction, but others have equally certainly diagnosed diastolic dysfunction in cases where it is not extant (perhaps heart failure is not either).

We may have failed to detect some left ventricular diastolic filling abnormalities because of the phenomenon of pseudonormalization, where the filling pattern is assumed to be in transition from an abnormal relaxation pattern with a low E/A ratio to a restrictive pattern with a high E/A ratio, and therefore has a normal pattern with a normal E/A ratio. It is obviously impossible to detect these cases without some other index of left ventricular diastolic filling. On the other hand, this is probably a small problem compared to assumption of diastolic dysfunction on the basis of exclusion of systolic dysfunction alone.

We have excluded by necessity patients with atrial fibrillation and patients in whom an E/A ratio was unmeasurable for other reasons. It is possible that a number of these may have had undetected diastolic dysfunction. There is an obvious pathophysiological association between left ventricular diastolic filling abnormalities and atrial fibrillation. There is an obvious empirical association between an unmeasurable E/A ratio and obesity, and this is a condition itself which has been associated with left ventricular diastolic filling abnormalities. On the other hand, we did not exclude patients with ischaemic heart disease, hypertension and diabetes, each of which is also associated with left ventricular diastolic dysfunction. That we have not corrected for these, if anything, implies that we may have underestimated the extent to which the E/A ratio failed to reveal significant abnormality amongst our patients.

The most significant limitation of our study is the choice of a single echocardiographic variable only, the E/A ratio, and omission of others, such as isovolumic relaxation time, deceleration time, deceleration rate, etc. This is justified by the fact that the E/A ratio is one of the easiest, quickest and most reproducible to perform, and therefore suitable for rapid frequent elicitation in a large number of cases, as we have done. Furthermore, it is one of the most frequently quoted indicators of diastolic dysfunction, often without critical appraisal, and therefore worthy of further careful study. Whilst we would like to avail ourselves of the opportunity to examine other echocardiographic features of left ventricular diastolic filling abnormalities in a similar context, we feel that our results are significant enough to be worthy of a wider audience as they stand.

This study was supported, in part, by a grant from MSD (U.K.). We thank Lynn Fenn and Gillian Reid for their help in performing a number of echocardiograms. We thank the general practitioners who referred their patients to this service.

**References**


