

CARDIOVASCULAR MEDICINE

Poor concordance of commonly used echocardiographic measures of left ventricular diastolic function in patients with suspected heart failure but preserved systolic function: is there a reliable echocardiographic measure of diastolic dysfunction?

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Objective: To determine the concordance of different Doppler echocardiographic criteria for "diastolic dysfunction" in patients with suspected heart failure but preserved left ventricular systolic function.

Design: Prospective, descriptive study.

Setting: Outpatient based direct access echocardiography service.

Patients: Consecutive patients referred with suspected heart failure but preserved left ventricular systolic function.

Measurements: Echocardiographic measurements of systolic and diastolic function. Eight published studies giving age and sex specific ranges for measures of diastolic function in healthy subjects were reviewed and the proportion of patients outside the normal limits for each of these published ranges was calculated.

Results: There was very poor concordance between measures with up to a 16-fold difference in the prevalence of diastolic dysfunction in the overall patient cohort. Even for a given measure, there was relatively poor agreement between the published reference ranges. In subsets likely to include patients at high risk of having diastolic dysfunction, an increased prevalence of diastolic dysfunction was not evident with any measure in any patient subset.

Conclusions: Our findings challenge the use of the diagnosis of diastolic heart failure based on the most commonly used echocardiographic criteria. Physicians should be cautious about echocardiographic reports describing diastolic dysfunction and only apply the diagnosis of diastolic heart failure with great care.

There has been tremendous recent interest in the concept of "diastolic dysfunction" as a cause of heart failure.^{1,2} To a great extent this has been fuelled by the finding that many patients with a clinical diagnosis of heart failure have preserved left ventricular systolic function.^{3–7} Diastolic dysfunction is, therefore, frequently proposed as the underlying problem in these patients. This view has been further popularised by the widespread availability of Doppler echocardiography. There are relatively simple measurements that can be made with this technique and that have been advocated (and readily accepted) as indices of diastolic function.^{1,2,8–13} The concordance and, indeed, validity of these indices are relatively poorly documented in humans. Yet, commonly, breathless patients with suspected heart failure are referred for an echocardiogram, which is routinely reported as showing normal systolic function but evidence of diastolic dysfunction. We have taken the most commonly advocated echocardiographic criteria for diastolic function and applied these different measures to a cohort of patients with suspected heart failure referred for transthoracic echocardiography. Our aim was to determine the concordance of different diagnostic criteria for diastolic dysfunction.

METHODS

Patients

The cohort of patients studied was one referred by general practitioners to a direct access echocardiography service

provided by the department of cardiology at the Western Infirmary, Glasgow. Referrals were invited for patients thought to have heart failure and for whom the initiation of an angiotensin converting enzyme inhibitor was being considered. The focus of this analysis was patients with preserved left ventricular systolic function. Patients with left ventricular systolic dysfunction (according to qualitative "eyeball" assessment; see below), significant valvar heart disease, and atrial fibrillation were not studied further. The study was approved by our local committee for medical ethics. Each patient gave written informed consent.

Transthoracic echocardiography

All examinations were performed by a single operator (LC) on an Acuson 128×P10c (Acuson, Berkshire, UK), as previously described.^{14,15} With the patient resting in the left lateral decubitus position M mode, two dimensional, and Doppler ultrasound examinations were carried out.

Left ventricular systolic function was assessed *qualitatively* by the "eyeball" technique from two dimensional images^{16,17} and quantitatively by measurement of ejection fraction and fractional shortening with M mode echocardiography.

Abbreviations: A, peak atrial filling; E, peak rapid filling; IVRT, isovolumetric relaxation time

Ejection fraction was also measured with the Simpson's biplane method.

Pulsed wave Doppler measurements were made at the tips of the mitral valve leaflets in the apical four chamber view. Early diastolic flow (E wave) and atrial contraction (A wave) were measured at the peak velocity. Deceleration time was measured from the peak of the E wave to the point of interception of the baseline. The area under the curve was measured for both E and A waves, representing peak rapid filling and peak atrial filling, respectively. These measurements were then used to estimate the atrial filling fraction, where atrial filling fraction is determined by $A / A + E$.

The pulsed Doppler sample was then positioned midway between the mitral valve tips and the aortic outflow track so that isovolumetric relaxation time (IVRT) could be measured between the point of aortic valve closure and mitral valve opening. All of the above measurements were repeated six times and their means calculated for a statistical analysis.

Reference ranges for measures of diastolic function

We conducted an electronic literature search (and a manual search of textbooks) for studies giving age and sex specific ranges for conventional Doppler measures of diastolic function in healthy people. We identified eight studies describing more than 30 subjects.^{9 18–24} These studies included between 32 and 980 unselected participants from the general population. Five had more than 100 participants and seven had more than 80. From the ranges provided, an upper and lower limit of normal was calculated as two standard deviations above or below the normal range reported (appendix 1). The recently published criteria of the European Study Group on Diastolic Heart Failure were also used.¹¹

Proportions of patients with diastolic dysfunction

We then calculated the proportion of our patients who were outside the normal limits for each of the published ranges^{9 18–24} and those advocated by the European Study Group on Diastolic Heart Failure.¹¹ To explore further the value of these measures, we also examined the proportions of measurements that lay outside these normal ranges in four subsets of patients at higher risk of diastolic dysfunction. The subsets were patients with hypertension (defined as a recorded clinical history of hypertension), left ventricular hypertrophy (defined as a septal or posterior wall measurement > 1.1 cm on M mode echocardiography), obesity (defined as a body mass index of > 30.0), and myocardial ischaemia (defined as a history of angina, myocardial infarction, coronary artery bypass grafting, or electrocardiographic changes consistent with a diagnosis of coronary heart disease). Electrocardiographic changes consistent with a diagnosis of coronary heart disease were pathological Q waves, left bundle branch block, and ST segment or T wave abnormalities in ≥ 2 consecutive leads.

RESULTS

Patients

One hundred and forty seven patients with suspected heart failure were referred. Twenty two patients had left ventricular systolic dysfunction. Ten patients had atrial fibrillation alone, two patients had valvar disease alone, and four patients had both atrial fibrillation and valvar heart disease. One hundred and nine patients had suspected heart failure in the absence of left ventricular systolic function, valvar heart disease, or atrial fibrillation. Table 1 summarises characteristics of these 109 patients.

Concordance between different measures of diastolic function

Tables 2 and 3 show the proportion of patients in our study who were more than two standard deviations outside the

Table 1 Patient characteristics and medication

	Mean (SD) or number
Patient characteristics (n = 109)	
Age (years)	71 (11)
Sex (male/female)	34/75
Systolic BP (mm Hg)	152 (23)
Diastolic BP (mm Hg)	85 (11)
Heart rate (beats/min)	74 (16)
Fractional shortening (%)	30 (7)
Ejection fraction (M mode) (%)	56(11)
Ejection fraction (Simpson's biplane) (%)	45(10)
Hypertension	51
Myocardial infarction	12
Coronary artery bypass grafting	7
Pulmonary disease	25
Medication	
Diuretics	85
β Blockers	18
Nitrates	22
Calcium channel blockers	22
ACE inhibitors	6
Aspirin	33
Inhaled β_2 agonists	22
Inhaled corticosteroids	8
Oral hypoglycaemic agents	6
Lipid lowering agents	3
Non-steroidal anti-inflammatory agents	9
Digoxin	4
Warfarin	2

ACE, angiotensin converting enzyme; BP, blood pressure.

published normal ranges for each of the measures of diastolic function used in the individual reference studies. The purpose of these tables is to illustrate the level of concordance between the different measures of diastolic available within the published reference studies.

As can be seen, there was considerable disagreement between measures. For example, based on the data published by Mantero and colleagues,¹⁸ there was a fourfold difference in the prevalence of diastolic dysfunction in the age group 40–49 years, depending on which measure was used (table 3). The proportions varied fivefold and sixfold in the age ranges 50–59 and 60–69 years. In the age group 70–79 years there was a 10-fold difference, with a prevalence of diastolic dysfunction of 4% if the E:A ratio was used versus 39% if an abnormal IVRT was used.

The other reference studies show much the same pattern, with IVRT and deceleration time giving much higher proportions of abnormal results than the other measures. E:A ratio generally gave the lowest prevalence of diastolic dysfunction. The data derived from the reference range of Spirito and colleagues¹⁹ gave another striking example of the discrepancy between prevalence based on E:A ratio and prevalence based on IVRT. For the age range 50–74 years the prevalence of diastolic dysfunction in our patients is 2% with E:A ratio and 35% based on IVRT.

Indeed, even for a given measure, there was relatively poor agreement between the published reference ranges (and, therefore, the proportion outside those ranges). For example, the Framingham study²⁰ reference range for E:A ratio led to a diagnosis of diastolic dysfunction in 1 of 19 (5.3%) of our patients aged 60–69 years, whereas the reference range of Mantero and colleagues¹⁸ for E:A ratio led to this diagnosis in 4 of 19 (21%) of our patients (table 2). For patients aged 40–60 years similar large discrepancies between these two studies were apparent when using atrial filling fraction—that is, 10 of 13 (77%) with the Framingham range versus 0 of 13 (0%) with that of Mantero and colleagues.¹⁸

Table 2 Concordance between the prevalence of diastolic dysfunction using different published reference ranges for individual echocardiographic measures

E:A ratio*		Cardiovascular health study ²²			
Age range (years)	Framingham study ²⁰	Mantero <i>et al</i> ¹⁸	Klein <i>et al</i> ²⁴	Men	Women
40–49	1/5	1/5	1/5	NA	NA
50–59	1/8	0/8	3/8	NA	NA
60–69	1/19	4/19	4/19	1/5†	0/7†
70–79	NA	2/47‡	NA	0/11	4/34
≥70	2/64	NA	2/64§	NA	NA
>80	NA	NA	NA	3/4	5/15
IVRT					
	Mantero <i>et al</i> ¹⁸	Klein <i>et al</i> ²⁴			
40–49	4/5	3/5			
50–59	5/8	0/8			
60–69	4/20	0/20			
70–79	20/51§	NA			
>70	NA	27/67			
AFF					
	Framingham study ²⁰	Mantero <i>et al</i> ¹⁸	Voutilainen <i>et al</i> ²¹		
40–49	3/5	0/5	NA		
50–59	7/8	0/8	NA		
40–60	10/13	0/13	5/13		
>60	NA	NA	8/82		
60–69	7/19	1/19	NA		
70–79	NA	6/46§	NA		
≥70	7/63	NA	NA		
DT					
	Mantero <i>et al</i> ¹⁸	Klein <i>et al</i> ²⁴			
40–49	1/5	1/5			
50–59	0/8	1/8			
60–69	6/20	2/20			
70–79	9/48§	NA			
>70	NA	8/65			

*Bryg *et al*²³ 1/5 30–49 years, 1/22 51–68 years; †65–69; ‡>70; §70–80.

A, peak atrial filling; AFF, atrial filling fraction; DT, deceleration time; E, peak rapid filling; IVRT, isovolumetric relaxation time; NA, not available.

Table 3 Concordance between different indices of diastolic dysfunction

Reference study and patient age range (years)	Measure of diastolic function			
	E:A ratio	IVRT	DT	AFF
<i>Mantero et al</i> ¹⁸				
40–49	1/5	4/5	1/5	0/5
50–59	0/8	5/8	0/8	0/8
60–69	4/19	4/20	6/20	1/19
70–79	2/47	20/51	9/48	6/46
<i>Klein et al</i> ²⁴				
40–49	1/5	3/5	1/5	NA
50–59	3/8	0/8	1/8	NA
60–69	4/19	0/20	2/20	NA
>70	2/64	27/67	8/65	NA
Framingham study ²⁰				
40–49	1/5	NA	NA	3/5
50–59	1/8	NA	NA	7/8
60–69	1/19	NA	NA	7/19
≥70	2/64	NA	NA	7/63
<i>Voutilainen et al</i> ²¹				
40–60	0/15	2/13	NA	5/13
>60	9/81	52/87	NA	8/82
<i>Spirito et al</i> ¹⁹				
30–49	1/5	2/5	0/5	NA
50–74	1/54	21/60	11/56	NA
<i>Cohen et al</i> ⁶				
21–49	0/5	4/6	1/5	NA
≥50	9/91	20/95	11/93	NA

Table 4 Prevalence of diastolic dysfunction in the overall patient group and subsets at high risk of diastolic dysfunction

Reference study and patient age range (years)	Prevalence of abnormal diastolic function				
	All patients	Hypertension	LVH	Obesity	Ischaemia
Framingham study ²⁰ ≥ 70					
E:A	2/64 (3.1%)	1/34 (2.9%)	1/19 (5.3%)	0/18 (0%)	1/26 (3.8%)
AFF	7/63 (11.1%)	2/34 (5.9%)	1/18 (5.6%)	3/17 (18%)	3/26 (11.5%)
Mantero <i>et al</i> ¹⁸ 60–80					
E:A	6/66 (9.1%)	3/35 (8.6%)	2/18 (11%)	1/22 (5%)	4/30 (13%)
AFF	7/65 (11%)	1/35 (2.9%)	1/17 (5.9%)	5/21 (24%)	6/34 (18%)
IVRT	24/71 (34%)	16/38 (42%)	8/20 (40%)	6/24 (25%)	13/33 (39%)
DT	15/68 (22%)	10/36 (28%)	4/18 (22%)	3/23 (13%)	6/33 (18%)
Voutilainen <i>et al</i> ²¹ > 60)					
AFF	8/82 (10%)	4/42 (10%)	4/22 (18%)	3/23 (13%)	5/34 (15%)
IVRT	52/87 (60%)	25/45 (56%)	13/25 (52%)	8/26 (31%)	22/36 (61%)
Klein <i>et al</i> ²⁴ > 70					
E:A	2/64 (3.1%)	0/34 (0%)	1/19 (5.3%)	0/18 (0%)	0/26 (0%)
IVRT	27/67 (40%)	16/36 (44%)	9/21 (43%)	7/19 (37%)	11/27 (41%)
DT	8/65 (12%)	7/34 (21%)	1/19 (5.3%)	2/18 (11%)	3/27 (11%)
Cohen <i>et al</i> ⁹ ≥ 50					
E:A	9/91 (9.9%)	4/44 (9.1%)	3/25 (12%)	1/28 (4%)	3/34 (9%)
IVRT	20/95 (21%)	10/47 (21%)	6/27 (22%)	6/30 (19%)	8/37 (22%)
DT	11/93 (12%)	8/45 (18%)	2/27 (7%)	2/29 (6%)	5/37 (14%)
Spirito <i>et al</i> ¹⁹ 50–74					
E:A	1/54 (2%)	0/26 (0%)	0/14 (0%)	0/22 (0%)	0/19 (0%)
IVRT	21/60 (35%)	11/28 (39%)	5/15 (33%)	9/24 (36%)	8/22 (36%)
DT	11/56 (20%)	8/27 (30%)	2/14 (14%)	4/23 (17%)	5/21 (24%)
European Study Group on Diastolic Heart Failure ¹¹ > 50					
IVRT	45/95 (47%)	18/47 (38%)	14/27 (52%)	15/30 (50%)	16/37 (43%)
E:A+DT	3/91 (3%)	2/45 (4%)	1/25 (4%)	0/29 (0%)	1/35 (3%)

LVH, left ventricular hypertrophy.

We also examined the two more sophisticated criteria advocated by the European Study Group on Diastolic Heart Failure.¹¹ Here, the prevalence of diastolic dysfunction in patients > 50 years of age based on IVRT was 45 of 95 (47%) compared with 3 of 91 (3%) based on their E:A ratio plus the deceleration time criterion (table 4).

Measures of diastolic function in patient subsets at high risk of diastolic dysfunction

Table 4 shows the prevalence of diastolic dysfunction within four patient subsets according to the published normal ranges in our reference studies. Those subsets are believed to include patients at high risk of having diastolic dysfunction. This table is meant to compare the ability of individual measures to identify diastolic dysfunction in these high risk subgroups. As can be seen an increased prevalence of diastolic dysfunction was not evident with any measure in any patient subset.

Combination of measures of diastolic function

Table 5 shows the prevalence of diastolic dysfunction defined as an abnormality of any one of the measures of diastolic function used in the study concerned. While such an approach obviously increased the prevalence of diastolic dysfunction, it did not enhance differentiation between the high risk subsets and the overall patient group.

DISCUSSION

There is ever growing interest in the concepts of diastolic dysfunction and diastolic heart failure.¹⁻⁷ Though a number of measurements have been proposed (and accepted) as indices of diastolic function, the concordance of these indices has not been examined. We, therefore, set out to examine just how much agreement there really is between the most commonly used echocardiographic measures of diastolic function. Using published reference ranges, we have applied each of these measures to a single cohort of consecutive

Table 5 Prevalence of diastolic dysfunction (any index within reference study) in the overall patient group and subsets at high risk of diastolic dysfunction

Reference study and patient age range (years)	Prevalence of abnormal diastolic function				
	All patients	Hypertension	LVH	Obesity	Ischaemia
Framingham study ²⁰ > 70					
E:A or AFF	8/63 (13%)	3/34 (9%)	2/18 (11%)	3/17 (18%)	4/25 (16%)
Mantero <i>et al</i> ¹⁸ 60–80					
E:A or AFF or IVRT or DT	36/65 (56%)	20/35 (57%)	11/17 (65%)	10/21 (48%)	20/30 (67%)
Klein <i>et al</i> ²⁴ > 70					
E:A or IVRT or DT	26/63 (41%)	15/34 (44%)	8/19 (42%)	7/17 (41%)	10/25 (40%)
Cohen <i>et al</i> ⁹ > 50					
E:A or IVRT or DT	25/90 (28%)	22/44 (50%)	7/25 (28%)	5/28 (18%)	16/34 (47%)
Spirito <i>et al</i> ¹⁹ 50–74					
E:A or IVRT or DT	24/54 (44%)	13/26 (50%)	5/14 (36%)	9/22 (41%)	7/19 (37%)
European Study Group on Diastolic Heart Failure ¹¹ > 50					
IVRT or E:A+DT	44/91 (48%)	20/44 (45%)	13/25 (52%)	13/27 (48%)	17/34 (50%)

patients referred for echocardiographic investigation of suspected heart failure.^{9 18–24} We also specifically examined subsets of patients believed to be at high risk of diastolic dysfunction (that is, patients with hypertension, left ventricular hypertrophy, obesity, and myocardial ischaemia).^{1–7} Obviously, if each of these indices is a true measurement of diastolic function then they should generally identify the same patients with abnormal diastolic function. Furthermore, they should each identify a greater proportion of patients at high risk of abnormal diastolic function as having diastolic dysfunction. We found neither of these things. There was very poor concordance between measures with up to a 16-fold difference in prevalence in the overall patient cohort, depending on what measure of diastolic function was used. There was also little difference in the proportion of patients with abnormal diastolic function in the overall cohort and the high risk subsets.

As we have reported previously, even the two recently recommended echocardiographic criteria of the European Study Group on Diastolic Heart Failure give widely discordant prevalences. These criteria do not seem at all discriminating when the high risk patient subsets are examined.^{11 25–27} Almost identical findings (and a similar conclusion) have recently been reported by Cahill and colleagues.²⁶

What are the implications of these findings? These results suggest that, based on the available reference ranges in the literature, none of the commonly used echocardiographic measures of diastolic function are reliable. They neither agree with each other nor identify patients at high risk of diastolic dysfunction *individually*.

These conclusions, however, are greatly influenced by one index, the IVRT, which appears to over-diagnose diastolic dysfunction and which may be an invalid measure of diastolic function.²⁸

Other indices may be influenced by loading conditions and, therefore, pharmacological treatment. It is important to point out, however, that this is unavoidable in “real world”, elderly patients, who often have a number of concomitant medical problems and take a variety of medications. Indeed, these are just the type of breathless patients sent for echocardiographic examination and who are often subsequently labelled as having diastolic dysfunction.

It can also be argued that at least some of these indices quantify slightly different aspects of diastolic function and that all of them should be measured to detect diastolic dysfunction—that is, that an abnormality of any one is sufficient for this diagnosis.^{28 29} This is the conceptual approach recently adopted by Zile and colleagues,²⁹ who made invasive haemodynamic and Doppler ultrasound measurements in 63 patients with a clinical diagnosis of heart failure and echocardiographic left ventricular hypertrophy. Of these 63, 79% had an abnormal relaxation time constant and 92% a left ventricular end diastolic pressure of > 16 mm Hg (both taken as haemodynamic yardstick diagnostic criteria for diastolic dysfunction). Zile and colleagues then calculated the proportions of patients with a variety of Doppler measures of diastolic function outside their “normal” range. These were 38% for IVRT, 48% for E:A ratio, and 64% for deceleration time; at least one index was abnormal in 94% of patients. We also examined this approach and found that, in the subset of patients with left ventricular hypertrophy, up to 65% (range 11–65%, mean 39%) of our patients had diastolic dysfunction, depending on the criteria used. Our criteria for defining “abnormal” (> 2 standard deviations outside the upper and lower limits of age and sex specific normal ranges) were, however, more stringent than those of Zile and colleagues²⁹ and this may, at least in part, account for the lower abnormal proportion of patients in our

study. Our patients also had a primary care rather than secondary care diagnosis of heart failure and probably had a less advanced condition than those studied by Zile and colleagues.²⁹ Whether this approach is a valid one, however, is open to question. If, as Brutsaert²⁸ has argued so cogently, IVRT is not a valid Doppler measure of diastolic function, then our conclusion about the prevalence of diastolic dysfunction, using the approach of Zile and colleagues,²⁹ would have to be revised (as, almost certainly, would the conclusion of these other authors).

Clearly, there are invasive haemodynamic, nuclear, and magnetic resonance measures of diastolic function, as well as newer echocardiographic ones that may be reliable.^{13 30–34} The purpose of this study was, however, to test the validity of those most commonly used at present and advocated by expert groups. The other measures are not in general use and most remain research tools. One group has attempted to validate a complex combination of Doppler techniques: mitral inflow (before and at peak Valsalva), Doppler tissue imaging of mitral annular imaging, and pulmonary venous flow.^{34 35} Unfortunately, even in the population studied (all were referred for evaluation of either angina or heart failure), the predictive accuracy of any of these indices alone or in combination was suboptimal. This group subsequently used these same Doppler measures in a sample of the general population.³⁵ In that study, almost 30% of the general population were felt to have diastolic dysfunction.³⁵ Interestingly, in another population based study in Germany, which used the European Study Group echocardiographic criteria, only 11.1% were found to have diastolic abnormalities.²⁷ We believe that these Doppler techniques require further validation in appropriate populations before diastolic abnormalities are diagnosed.

Though it can be argued that our group of patients was relatively small, it did represent a reasonably large, consecutive series of patients with suspected heart failure and a high prevalence of hypertension and coronary heart disease—exactly the patient group where a diagnosis of diastolic heart failure is often inferred. Our findings challenge the use of this diagnosis based on echocardiographic criteria, especially as this group of patients typically has a number of other potential explanations for their symptoms (obesity, pulmonary disease, myocardial ischaemia) amenable to specific management.¹⁵ Physicians should be cautious about echocardiographic reports describing diastolic dysfunction and only apply the diagnosis of diastolic heart failure with great care, after thorough assessment to evaluate other possible diagnoses.^{12 15} Even then, a diagnosis of “heart failure with preserved left ventricular systolic function” or “preserved left ventricular ejection fraction heart failure” may be more accurate, if less succinct.

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APPENDIX 1: DOPPLER ECHOCARDIOGRAPHY NORMAL RANGES CALCULATED FROM REFERENCE STUDIES

Study	Age range (years)	E:A ratio	IVRT	DT	AFF	E:A+DT
Framingham study ²⁰ (n = 127)	20–29	0.98–3.18			0.14–0.34	
	30–39	0.95–2.55			0.15–0.35	
	40–49	0.92–1.96			0.23–0.35	
	50–59	0.73–1.85			0.22–0.38	
	60–69	0.51–1.55			0.23–0.47	
	≥70	0.26–1.42			0.24–0.60	
	All ages	0.32–2.48			0.15–0.47	
	Cardiovascular health study ²² (n = 980)	Overall (>65)	0.64–1.56			
Women						
65–69		0.50–1.62				
70–74		0.50–1.42				
75–79		0.52–1.28				
>80		0.48–1.12				
Men						
65–69		0.52–1.64				
70–74		0.44–1.48				
75–79		0.47–1.39				
Mantero ¹⁸ (n = 288)	20–29	0.9–2.9	41.2–94.8	97.2–194.4	0.04–0.44	
	30–39	0.9–2.5	45.3–97.7	94.2–283.8	0.07–0.47	
	40–49	0.8–2.0	49.0–97.8	93.2–218.8	0.10–0.50	
	50–59	0.6–1.8	51.7–102.9	87.5–222.3	0.14–0.54	
	60–69	0.6–1.4	51.0–107.8	103.5–241.1	0.17–0.57	
	70–80	0.2–1.4	44.7–117.5	86.5–269.7	0.19–0.59	
	Voutilainen ²¹ (n = 93)	<40	1.0–3.0	101–177		0.11–0.35
40–60		0.6–1.8	100–204		0.20–0.48	
>60		0.76–0.84	112–216		0.27–0.63	
All		0.3–2.7	99–199		0.08–0.56	

Study	Age range (years)	E:A ratio	IVRT	DT	AFF	E:A+DT
Klein ²⁴ (n = 117)						
	<50	0.7–3.1	54–98	139–219		
	>50	0.5–1.7	56–124	138–282		
	20–29	0.8–3.6	49–93	144–220		
	30–39	0.9–2.5	63–95	138–214		
	40–49	0.8–2.4	53–105	131–223		
	50–59	0.9–1.7	52–124	157–245		
	60–69	0.6–1.4	60–128	132–296		
	>70	0.2–1.8	56–116	135–303		
European Study Group on Diastolic Heart Failure ¹¹ (review)						
			Age <30			Age <50
			IVRT >92			E:A <1.0
			Age 30–50			DT >220
			IVRT >100			Age >50
			Age >50			E:A <0.5
			IVRT >105			DT >280
Cohen ⁹ (n = 107)						
	21–49	1.9 (0.7–3.1*)	76 (54–98*)	179 (139–219*)		
	≥50	1.1 (0.5–1.7*)	90 (56–124*)	210 (138–282*)		
Bryg ²³ (n = 32)						
	24–29	0.92–3.04				
	30–49	0.80–2.24				
	51–68	0.25–1.89				
Spirito ¹⁹ (n = 86)						
	20–29	1.3–4.1	48–96	158–278		
	30–49	0.8–3.2	56–104	166–274		
	50–74	0.4–2.0	60–108	155–287		

Ranges calculated (normal ranges ± 2 SDs from mean and *occasional 95% confidence intervals.
A, peak atrial filling; AFF, atrial filling fraction; DT, deceleration time; E, peak rapid filling; IVRT, isovolumetric relaxation time.

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Vasovagal syncope interrupting sleep?

C T P Krediet, D L Jardine, P Cortelli, A G R Visman, W Wieling

Clinical data are reported for 13 patients who were referred with recurrent loss of consciousness at night interrupting their sleep. Most of the patients were women (10 of 13) with a mean age of 45 years (range 21–72 years). The histories were more consistent with vasovagal syncope than with epilepsy. This was supported by electroencephalographic and tilt test results. More polysomnographic monitoring data are required to confirm the diagnosis of vasovagal syncope interrupting sleep. This will be difficult because, although the condition may not be rare, the episodes are usually sporadic.

(*Heart* 2004;**90**:e25) www.heartjnl.com/cgi/content/full/90/5/e25

Acute myocardial infarction caused by thrombotic occlusion at a stent site two years after conventional stent implantation

T Hayashi, A Kimura, K Ishikawa

Two cases of acute myocardial infarction caused by thrombotic occlusion at the conventional stented site two years after stenting are described. Late thrombotic stent occlusion may be caused by atherosclerotic regression, sustained inflammatory reaction, and inhibition of proliferation of neointima. Cardiologists must be aware of the potential for late thrombosis following even conventional stent implantation.

(*Heart* 2004;**90**:e26) www.heartjnl.com/cgi/content/full/90/5/e26