

Cardiovascular journals

Ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus



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A number of studies indicate that left ventricular diastolic dysfunction represents an early pre-clinical manifestation of diabetic cardiomyopathy. Recent studies suggest that up to 60% of asymptomatic normotensive patients with type II diabetes have diastolic dysfunction when assessed by conventional echocardiography. This diastolic dysfunction can progress to symptomatic heart failure.

This study determines the presence of left ventricular diastolic dysfunction in asymptomatic normotensive patients with type II diabetes. The study utilises conventional Doppler echocardiography at

rest and during a Valsalva manoeuvre. The methodology utilised included tissue Doppler imaging and M-mode echocardiography. Stress electrocardiography excluded significant coronary artery disease in those patients who were noted to have diastolic dysfunction.

Diastolic dysfunction was found in 75% of the patients. Doppler imaging identified more patients with diastolic dysfunction than conventional M-mode cardiography.

Thus, the prevalence of left ventricular diastolic dysfunction in asymptomatic patients with normotension without significant coronary artery disease is much higher than expected. Doppler imaging increases the frequency of diagnosis of diastolic dysfunction.

AMERICAN JOURNAL OF CARDIOLOGY



Asymptomatic diastolic dysfunction in diabetes

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Recent developments in echocardiographic techniques have meant that the ability to detect diastolic dysfunction has improved significantly. Several recent studies using conventional echocardiography in asymptomatic, normotensive patients with type 2 diabetes have shown that up to 60% have diastolic dysfunction.

2 This study aimed to determine left ventricular dysfunction prevalence in asymptomatic, normotensive patients with diabetes mellitus.

3 Sixty-one consecutive patients were studied using Doppler echocardiography at rest and during the Valsalva manoeuvre. Significant valvular disease was excluded using a standard resting echocardiogram, and to exclude significant coronary artery disease in patients with diastolic dysfunction, stress echocardiography was used. Mitral annular velocity and velocity of flow propagation were also assessed, using tissue Doppler imaging and M-mode echocardiography.

4 Results of the combined techniques revealed diastolic dysfunction in 75% of patients. Tissue Doppler echocardiography markedly improved detection of diastolic dysfunction (63%) compared to other techniques.

5 Left ventricular dysfunction prevalence is much greater than thought in this patient group.

Boyer JK, Thanigaraj S, Schechtman KB, Pérez JE (2004) Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus. *American Journal of Cardiology* **93**: 870-75

AMERICAN JOURNAL OF MEDICINE



Management of patients with diabetes and MI

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 Patients with diabetes mellitus and underlying coronary artery disease have a worse prognosis than those without diabetes. To prevent micro- and macrovascular events, a comprehensive multifactorial approach should be used to manage these patients.

2 Immediate management of MI should involve use of fibrinolytic agents, primary percutaneous intervention, or glycoprotein IIb/IIIa inhibitors followed by coronary

angiography (after 24-48 hours) to limit the infarct size.

3 As patients with diabetes have a greater chance of suffering postintervention coronary restenosis, drug-eluting stents may be important.

4 After acute MI aspirin, nitrates, β-blockers and angiotensin converting enzyme (ACE) inhibitors should be given to all patients with diabetes. In the long-term, treatment with ACE inhibitors, β-blockers, lipid-lowering and antiplatelet agents, and glycaemic control decrease mortality.

5 Large randomised clinical trials have shown that maximising the use of lifesaving therapies and tight glycaemic control in MI patients with diabetes reduce mortality rates; however, many therapies are currently underused.

Klein L, Gheorghide M (2004) Management of the patient with diabetes mellitus and myocardial infarction: clinical trials update. *American Journal of Medicine* **116**: S47-S60

DIABETIC MEDICINE

Cerebral infarction carotid risk factors in type 2 diabetes

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

- Common carotid artery intima-media thickness (IMT) is a marker for early atherosclerosis; thickening is associated with cardiovascular and cerebrovascular disease.
- This study aimed to evaluate the use of the carotid artery restrictive index (RI) and pulsatility index (PI) in estimating cerebral infarction risk in type 2 diabetes.
- In this cross-sectional survey 382 patients with diabetes, of which 40 had a history of cerebral infarction, and 110 controls underwent ultrasonography of the common carotid artery to determine IMT, RI and PI. For patients with diabetes, a Second Manifestations of ARterial disease (SMART) atherosclerosis risk score was calculated.
- Compared to controls, mean IMT, PI and RI values were greater for those with diabetes, significantly so in individuals with a previous cerebral infarction (IMT $P < 0.005$, PI $P < 0.01$, RI $P < 0.05$).
- SMART risk scores showed weak but significant correlations with increasing IMT, and PI and RI scores.
- IMT and PI were shown to be independent risk factors for cerebral infarction using the multiple logistic model. Patients with IMT scores < 1.0 and PI < 2.00 were at greater risk of developing cerebral infarction.
- PI, RI and IMT measurements are useful when estimating the risk of previous cerebral infarction in type 2 diabetes. The value of these measurements in assessing future infarction risk in this group is currently unknown.

Nakatou T, Nakata K, Nakamura A, Itoshima T (2004) Carotid haemodynamic parameters as risk factors for cerebral infarction in type 2 diabetic patients. *Diabetic Medicine* **21**: 223–29

ANTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY

Vascular damage in diabetes: enhanced P2X₇ activity

Readability	✓
Applicability to practice	✓✓
WOW! factor	✓✓

- This investigation measured P2X₇ receptor expression and function in fibroblasts from skin biopsies from patients with and without diabetes.
- Functional assays, reverse transcription polymerase chain reaction, fluorescence-activated cell sorter and immunoblocking were used to measure P2X₇ receptor expression.

- Enhanced P2X₇-mediated responses, higher basal levels of spontaneous fibronectin secretion and apoptosis were found in fibroblasts from individuals with diabetes.
- Increased pericellular ATP concentration in these patients was attributed to the high fibronectin and apoptosis levels, with release of three times as much ATP into the supernatants as those without diabetes.
- Enhanced P2X₇ activity and higher ATP release characterised fibroblasts from people with type 2 diabetes.

Solini A, Chiozzi P, Morelli A, et al (2004) Enhanced P2X₇ activity in human fibroblasts from diabetic patients: a possible pathogenic mechanism for vascular damage in diabetes. *Arteriosclerosis, Thrombosis, and Vascular Biology* **24**: 1–7

CIRCULATION

Suppression of atherosclerosis in diabetes

Readability	✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

- This study compared the effect of iberisartan, an angiotensin II subtype 1 (AT₁) receptor blocker, with amlodipine (an antihypertensive) on diabetes-induced plaque formation in mice. The mice were randomised to no treatment, iberisartan or amlodipine for 20 weeks.

- There was an increase in plaque area and complexity in the aorta associated with diabetes.
- Iberisartan attenuated development of atherosclerosis, whereas amlodipine did not.
- AT₁ receptor blockade but not calcium-channel antagonism improves atherosclerosis in diabetes. This is further evidence that in diabetes-associated atherosclerosis a pivotal role is played by the vascular renin-angiotensin system.

Candido R, Allen TJ, Lassila M, et al (2004) Iberisartan but not amlodipine suppresses diabetes-associated atherosclerosis. *Circulation* **109**: 1536–42

ANTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY

Oxidative stress, insulin resistance and CVD

Readability	✓✓
Applicability to practice	✓✓
WOW! factor	✓✓

- The risk of cardiovascular disease is increased by insulin resistance, impaired glucose tolerance and diabetes. Oxidative stress accompanies all three conditions and this paper hypothesises that oxidative stress is the

pathogenic mechanism linking insulin resistance, and dysfunction of β -cells and the endothelium.

- The authors suggest that their hypothesis helps explain why using compounds with intracellular antioxidant activity, such as calcium-channel blockers, statins, ACE inhibitors and AT₁ receptor antagonists, to treat cardiovascular risk results in the possible reduction in onset of new diabetes cases.

Ceriello A, Motz E (2004) Is oxidative stress the pathogenic mechanism underlying insulin resistance, diabetes and cardiovascular disease? The common soil hypothesis revisited. *Arteriosclerosis, Thrombosis, and Vascular Biology* **24**: 816–23

‘Measurement of the pulsatility index of the common carotid artery is useful, together with intima-media thickness, in estimating the risk of previous cerebral infarction in type 2 diabetic patients’

‘Diabetes-associated atherosclerosis is ameliorated by angiotensin II subtype 1 receptor blockade but not by calcium-channel antagonism.’

‘Diabetes is a potent, independent risk factor for mortality in patients hospitalised with heart failure.’

AMERICAN JOURNAL OF CARDIOLOGY

Metabolic view of diabetic cardiomyopathy

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The risk of developing cardiovascular diseases is greater in patients with diabetes than the general population.

2 The metabolic abnormalities hypothesis is one of several that

attempt to explain the increased vulnerability in those with diabetes.

3 Cardiac metabolism is altered in diabetes and is expressed in diminished glucose utilisation, lower rates of lactate oxidation and increased fatty acid usage.

4 Cardiac amino acid disturbances may be important as they result in reduced energy reserves and abnormalities of qualitative and quantitative contractile protein, so this may be a relevant future research area.

Avogaro A, de Kreutzenberg SV, Negut C, Tiengo A, Scognamiglio R (2004) Diabetic cardiomyopathy: a metabolic perspective. *American Journal of Cardiology* **93**: (Suppl) 13A–16A

AMERICAN JOURNAL OF CARDIOLOGY

Early diabetic cardiomyopathy

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Diabetic cardiomyopathy is characterised by contractile function defects without significant coronary artery disease or systemic hypertension.

2 Contractile depression begins as early as a week after the induction of diabetes in animal models. Diabetes is also associated with poor cardiac amino acid

catabolism and exercise-induced left ventricular (LV) overload.

3 In up to 40% of cases there is impaired LV ejection fraction augmentation, which is caused by defective contractile recruitment. Exercise-induced LV overload is worsened if the amino acid supply is increased in addition to conventional therapy.

4 These observations may be useful when optimising a dietary or supplemental approach to prevent progressive myocardial dysfunction.

Scognamiglio R, Avogaro A, Negut C, Piccolotto R, de Kreutzenberg SV, Tiengo A (2004) Early myocardial dysfunction in the diabetic heart: current research and clinical applications. *American Journal of Cardiology* **93**: (Suppl) 17A–20A

AMERICAN JOURNAL OF MEDICINE

Diabetes in diastolic heart failure

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Preserved left ventricular systolic function (diastolic heart failure, DHF) is seen in about 40% of patients with heart failure (HF). Diabetes is a major risk factor, as is a high HbA_{1c} level.

2 Studies have found that functional, biochemical and morphologic myocardial abnormalities are present with diabetes. These abnormalities may

result in impaired left ventricular diastolic function, and lead to DHF with preserved left ventricular function.

3 Short-term management of symptoms is with nitrates and diuretics, while in the long term underlying disorders can be treated with ACE inhibitors, β-blockers, aldosterone antagonists and calcium-channel blockers.

4 The efficacy of treatment regimens for diabetic patients with DHF are currently unknown because there are no completed large randomised clinical trials analysing this patient group.

Piccini JP, Klein L, Gheorghide M, Bonow RO. New insights into diastolic heart failure: role of diabetes mellitus. *American Journal of Medicine* **116**: S64–S75

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Influence of diabetes on the risk of CHF death

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 In patients with congestive heart failure (CHF) diabetes is a common co-morbidity. The influence of diabetes on long-term mortality in these patients is analysed in this study.

2 The survival data used was from 5548 patients hospitalised with new or worsening CHF who were followed-up for between five and eight years. Patients had been screened, using an echocardiogram in 95% of cases, between 1993 and 1995 for entry into the Danish Investigations of Arrhythmia and Mortality on Dofetilide (DIAMOND).

3 Of the patients included in the study 900 (16%) had a history of diabetes, of which 41% were female.

4 During the follow-up 3975 patients died – 3200 (70%) patients without diabetes and 775 (84%) with (risk ratio of 1.5 for patients with diabetes, P<0.0001).

5 A multivariate analysis of the data found that there was a significant interaction between diabetes and gender, with a mortality risk ratio of 1.7 in women and 1.4 in men (P<0.0001).

6 Both depressed and normal left ventricular systolic function had a similar effect on mortality in patients with diabetes.

7 In patients hospitalised with CHF, diabetes is an important and independent risk factor for mortality. This risk is further increased if the patient with diabetes is female.

Gustafsson I, Brendorp B, Seibæk M, et al (2004) Influence of diabetes on a diabetes-gender interaction on the risk of death in patients hospitalised with congestive heart failure. *Journal of the American College of Cardiology* **43**: 771–77

‘The effects of different diabetic treatment regimens on heart failure with normal systolic function are unknown and remain subject to future investigation.’