One-Hour Postload Plasma Glucose Levels and Diastolic Function in Hypertensive Patients

Angela Sciacquà, MD 1  
Sofia Miceli, MD 1  
Laura Greco, MD 1  
Franco Arturi, MD 1  
Paola Naccarato, MD 1  
Deborah Mazzaferrro, MD 1  
Eliezer J. Tassone, MD 1  
Laura Turano, MD 1  
Francesco Martinò, MD 2  
Giorgio Sesti, MD 1  
Francesco Perticone, MD 1

OBJECTIVE—To address whether glucose tolerance status, and in particular 1-h postload plasma glucose levels, may affect diastolic function in 161 never-treated hypertensive white subjects. Impaired left ventricular relaxation, an early sign of diastolic dysfunction, represents the first manifestation of myocardial involvement in diabetic cardiomyopathy. A plasma glucose value ≥155 mg/dL for the 1-h postload plasma glucose during an oral glucose tolerance test (OGTT) is able to identify subjects with normal glucose tolerance (NGT) at high risk for type 2 diabetes and with subclinical organ damage.

RESEARCH DESIGN AND METHODS—Subjects underwent OGTT and standard echocardiography. Diastolic function was assessed by pulsed Doppler transmitral flow velocity and tissue Doppler imaging. Insulin sensitivity was assessed by Matsuda index.

RESULTS—Among the participants, 120 had NGT, 26 had impaired glucose tolerance (IGT), and 15 had type 2 diabetes. According to the 1-h postload plasma glucose cutoff point of 155 mg/dL, we divided NGT subjects as follows: NGT <155 mg/dL (n = 90) and NGT ≥ 155 mg/dL (n = 30). Those with NGT ≥ 155 mg/dL had higher left atrium dimensions (P < 0.0001) and isovolumetric relaxation time (IVRT) (P = 0.037) than those with NGT <155 mg/dL. By contrast, early/late transmitral flow velocity and all tissue Doppler parameters were significantly lower in those with NGT ≥ 155 mg/dL than in those with NGT <155 mg/dL. At multiple regression analysis, 1-h glucose was the major determinant of left atrium area, IVRT, septal e’, septal e’-to-a’ ratio, lateral e’, and lateral e’-to-a’ ratio.

CONCLUSIONS—The main finding of this study is that 1-h postload plasma glucose is associated with left ventricular diastolic dysfunction. Subjects with NGT ≥155 mg/dL had significantly worse diastolic function than those with NGT<155 mg/dL.

Diabetes Care 34:2291–2296, 2011

Impaired left ventricular relaxation, characterized by reduced early and increased late diastolic flow, is an early sign of diastolic dysfunction. It provides independent prognostic information in the general population, free of clinical signs of heart failure (1), as well as in different clinical settings, including essential hypertension (2), congestive heart failure (3), myocardial infarction (4), and left ventricular hypertrophy (LVH), and in the elderly (5). It represents the first manifestation of myocardial involvement in diabetes (6) and may precede the clinical appearance of diabetes itself (7), suggesting that diastolic dysfunction is not exclusively a complication of diabetes but rather a coexisting condition.

On the other hand, type 2 diabetes (T2D) is recognized, independently of coronary artery disease or hypertension, as an independent risk factor for heart failure that is one of the major causes of cardiovascular morbidity and mortality (8). A possible explanation is that the metabolic abnormalities characterizing T2D may affect the cardiac structure, promoting the LVH and diastolic dysfunction appearance (6). In addition, subjects with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) are characterized by an unfavorable cardiovascular risk profile (9).

Recently, a cutoff of 155 mg/dL for 1-h postload plasma glucose during the oral glucose tolerance test (OGTT) has been shown to be able to identify subjects who are at high risk for T2D (10). Moreover, 1-h postload plasma glucose value is strongly associated with carotid intima-media thickness (IMT) (11) and reduced estimated glomerular filtration rate (eGFR) (12), which are well-established subclinical organ damage and independent predictors for cardiovascular events.

Even if there are several findings demonstrating a strong association between T2D or IGT and diastolic dysfunction, at this moment there are no data supporting the association between postload glucose and diastolic dysfunction. We designed this study to address whether glucose tolerance status, and in particular 1-h postload plasma glucose levels, may affect diastolic function in a group of never-treated hypertensive white subjects.

RESEARCH DESIGN AND METHODS—The study group consisted of 161 outpatients with uncomplicated hypertension, 101 men and 60 women aged 38–65 years (mean ± SD 43.7 ± 11.7 years), participating in the CATanzaro METabolic Risk factors Study (CATOMERIS). All patients were Caucasian and underwent physical examination and review of their medical history. Causes of secondary hypertension were excluded by appropriate clinical and biochemical tests. Other exclusion criteria were history or clinical evidence of coronary or valvular heart disease, congestive heart failure, hyperlipidemia, peripheral vascular disease, chronic...
gastrointestinal diseases associated with malabsorption, chronic pancreatitis, history of any malignant disease, history of alcohol or drug abuse, liver or kidney failure, and treatments able to modify glucose metabolism. No patient had ever been treated with antihypertensive drugs. All subjects underwent anthropometrical evaluation: weight, height, and BMI.

After 12-h fasting, a 75-g OGTT was performed with 0-, 30-, 60-, 90-, and 120-min sampling for plasma glucose and insulin. Glucose tolerance status was defined on the basis of OGTT using the World Health Organization (WHO) criteria. Insulin sensitivity was evaluated using the Matsuda index (insulin sensitivity index [ISI]), calculated as follows: 10,000/\(\sqrt{\text{fasting glucose (millimoles per liter)} \times \text{fasting insulin (millinits per liter)}}\) \(\times \text{[mean glucose \times \text{mean insulin during OGTT}]}\). The Matsuda index is strongly related to euglycemic-hyperinsulinemic clamp, which represents the gold standard test for measuring insulin sensitivity (13). The ethics committee approved the protocol, and informed written consent was obtained from all participants. All of the investigations were performed in accordance with the principles of the Declaration of Helsinki.

**Blood pressure measurements**

Readings of clinic blood pressure were obtained in the left arm of the supine patients, after 5 min of quiet rest, with a mercury sphygmomanometer. A minimum of three blood pressure readings were taken on three separate occasions at least 2 weeks apart. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded at the first appearance (phase I) and the disappearance (phase V) of Korotkoff sounds. Baseline blood pressure values were the average of the last two of the three consecutive measurements obtained at intervals of 3 min. Patients with a clinic SBP \(>140\) mmHg and/or DBP \(>90\) mmHg were defined as hypertensive.

**Laboratory determinations**

Plasma glucose was measured by the glucose oxidation method (Beckman Glucose Analyzer II; Beckman Instruments, Milan, Italy). Triglyceride and total, LDL, and HDL cholesterol concentrations were measured by enzymatic methods (Roche Diagnostics, Mannheim, Germany). Plasma insulin concentration was determined by a chemiluminescence-based assay (Roche Diagnostics).

**Echocardiograms**

Tracings were taken with the patient in a partial left decubitus position, using a VIVID 7 Pro ultrasound machine (GE Technologies, Milwaukee, WI) with an annular phased array 2.5-MHz transducer. Echocardiographic readings were made in random order by the investigator, who had no knowledge of patients’ blood pressure or other clinical data. Only frames with optimal visualization of cardiac structures were considered for reading. The mean values from at least five measurements of each parameter for each patient were computed. Having the same experienced sonographer perform all studies in a dimly lit and quiet room optimized the reproducibility of measurements. Subjects with a left ventricular ejection fraction <50% were excluded from this study. In our laboratory, the intraobserver coefficients of variation during OGTT were 3.85% for posterior wall thickness, 3.7% for interventricular septal thickness, 1.5% for left ventricular internal diameter, and 5.1% for left ventricular mass (LVM).

**M-mode measurements.** Tracings were recorded under two-dimensional guidance, and M-mode measurements were taken at the tip of the mitral valve or just below. Measurements of interventricular septal thickness, posterior wall thickness, and left ventricular internal diameter were made at end diastole and end systole, as recommended by the American Society of Echocardiography (14). LVM was calculated using the Devereux formula and normalized by body surface area (LVMI). The following parameters were evaluated for diastolic function: peak transvalvular flow velocities of each mitral valve leaflet (A, E, a’), and isovolumic relaxation time (IIVRT). The peak A and E wave velocities were measured in the apical four-chamber view, and the sample volume was positioned at the tip of the mitral valve leaflet.

**RESULTS**—Of 161 patients examined by OGTT, 120 had normal glucose tolerance (NGT), 26 had IGT, and 15 had newly diagnosed T2D. A 1-h postload plasma glucose cutoff point of 155 mg/dL during OGTT was used to stratify NGT subjects into two groups: 90 patients with 1-h postload plasma glucose \(<155\) mg/dL (NGT \(<155\)) and 30 individuals with 1-h postload plasma glucose \(\geq155\) mg/dL (NGT \(\geq155\)). Table 1 shows the demographic, clinical, and biochemical characteristics of the four study groups.

There were no significant differences among groups for sex, age, BMI, SBP, DBP, and total cholesterol. From the first to the fourth group, there was a significant increase of triglyceride (\(P=0.002\)) and a significant reduction of HDL cholesterol (\(P=0.034\)). Obviously, a progressive increase of fasting and 1-h and 2-h postload glucose parallels the worsening...
Table 1—Anthropometric, hemodynamic, and biochemical characteristics of the study population according to glucose tolerance

|                  | NGT <155 | NGT ≥155 | IGT     | T2D     | P     |
|------------------|----------|----------|---------|---------|-------|
| n                | 90       | 30       | 26      | 15      |       |
| Male/female      | 54/36    | 22/8     | 18/8    | 7/8     | 0.373*|
| Age (years)      | 41.9 ± 12.5 | 44.7 ± 11.6 | 47.1 ± 11.3 | 48.1 ± 6.7 | 0.090 |
| BMI (kg/m²)      | 28.5 ± 4.1 | 28.1 ± 4.7 | 29.1 ± 5.1 | 29.8 ± 5.6 | 0.624 |
| SBP (mmHg)       | 129.9 ± 13.4 | 131.3 ± 9.7 | 131.6 ± 9.2 | 134.0 ± 4.3 | 0.602 |
| Triglycerides (mg/dL) | 113.2 ± 10.7 | 80.1 ± 8.4 | 83.7 ± 10.3 | 86.1 ± 6.2 | 0.186 |
| Fasting glucose (mg/dL) | 87.5 ± 7.9 | 91.2 ± 9.2 | 94.4 ± 10.6 | 108.2 ± 10.2 | <0.0001 |
| 1-h glucose (mg/dL) | 119.6 ± 23.7 | 176.2 ± 21.2 | 179.5 ± 33.2 | 239.3 ± 18.9 | <0.0001 |
| 2-h glucose (mg/dL) | 100.8 ± 17.9 | 113.5 ± 14.3 | 156.8 ± 13.7 | 248.2 ± 18.1 | <0.0001 |
| Fasting insulin (μU/mL) | 11.1 ± 6.2 | 15.5 ± 9.1 | 13.7 ± 7.3 | 23.9 ± 8.1 | <0.0001 |
| 1-h insulin (μU/mL) | 77.9 ± 37.2 | 139.8 ± 70.1 | 129.1 ± 115.3 | 101.3 ± 24.0 | <0.0001 |
| 2-h insulin (μU/mL) | 57.6 ± 34.1 | 103.6 ± 55.1 | 153.1 ± 105.9 | 149.6 ± 30.5 | <0.0001 |
| MATSUDA index/ISI | 89.2 ± 38.2 | 49.1 ± 20.7 | 54.8 ± 45.5 | 28.2 ± 11.9 | <0.0001 |
| Total cholesterol (mg/dL) | 197.5 ± 38.4 | 195.7 ± 31.5 | 211.1 ± 24.6 | 201.1 ± 37.1 | 0.325 |
| HDL cholesterol (mg/dL) | 50.5 ± 12.5 | 45.1 ± 12.7 | 45.7 ± 14.8 | 41.9 ± 13.6 | 0.034 |
| Triglycerides (mg/dL) | 113.2 ± 61.4 | 139.2 ± 87.8 | 134.5 ± 65.3 | 187.2 ± 100.3 | 0.002 |

Data are means ± SD unless otherwise indicated. *χ² test.

of glucose tolerance (P < 0.0001). Fasting and postload insulin values were higher in the NGT ≥155 group and IGT subjects in comparison with those in the NGT <155 group and diabetic patients, respectively. All of these parameters account for the reduction of MATSUDA index/ISI.

Echocardiographic parameters and glucose tolerance

Echocardiographic parameters for the study population, according to glucose tolerance groups, are reported in Table 2. T2D patients had the highest LVMI value (P = 0.020), and clinically relevant, NGT ≥155 subjects showed an LVMI value not significantly different from IGT patients (P = 0.691) but significantly higher than NGT <155 subjects (P = 0.042).

It is interesting to note that the left atrium volume and IVRT values significantly increased from the first to the fourth group (P < 0.0001) and that NGT ≥155 subjects showed both parameters significantly higher than NGT <155 subjects (P < 0.0001 for left atrium and P = 0.037 for IVRT). Moreover, left atrium dimensions increased from the IGT group and T2D patients; NGT ≥155 subjects showed an IVRT value similar to that of IGT subjects (P = 0.120). By contrast, E-to-A ratio significantly decreased from the first to the fourth group (P < 0.0001), and it was significantly lower in NGT ≥155 than in NGT <155 subjects. No significant differences among groups were observed for the DT duration (P = 0.391).

E-to-e’ ratio significantly increased from the first to the fourth group (P < 0.044) and in NGT ≥155 subjects was significantly higher than in NGT <155 subjects (P < 0.036) and similar to that of diabetic patients. All remaining tissue Doppler parameters were significantly decreased from the first to the fourth group, confirming the progressive impairment of left ventricular diastolic dysfunction from the first to the fourth group of glucose tolerance. It is important to remark that NGT ≥155 subjects had the same characteristics observed in IGT and T2D patients.

Correlational analysis

A linear regression analysis was performed to test the correlation between echocardiographic parameters and different covariates (Table 3). One-hour postload glucose was linearly correlated with IVRT (r = 0.426; P < 0.0001) and left atrium volume (r = 0.366; P = 0.001)

Table 2—LVMI and echocardiographic parameters of left ventricular diastolic function according to glucose tolerance

|                  | NGT <155 | NGT ≥155 | IGT     | T2D     | P     |
|------------------|----------|----------|---------|---------|-------|
| n                | 90       | 30       | 26      | 15      |       |
| LVMI (g/m²)      | 90.5 ± 21.1 | 99.5 ± 19.9 | 97.2 ± 23.2 | 108.4 ± 16.7 | 0.020 |
| Left atrium volume/BSA (mL/m²) | 15.8 ± 4.2 | 18.7 ± 4.6 | 19.4 ± 3.7 | 20.5 ± 3.6 | <0.0001 |
| E-to-A ratio     | 1.3 ± 0.4 | 1.0 ± 0.3 | 0.9 ± 0.2 | 0.9 ± 0.7 | <0.0001 |
| DT (ms)          | 185.6 ± 48.8 | 201.6 ± 64.3 | 194.2 ± 44.5 | 201.9 ± 49.6 | 0.391 |
| IVRT (ms)        | 107.5 ± 24.6 | 120.5 ± 40.1 | 116.1 ± 20.1 | 152.3 ± 38.1 | <0.0001 |
| Tissue Doppler parameters |       |         |         |         |       |
| Septal e’ (cm/s) | 12.2 ± 3.1 | 9.6 ± 3.3 | 8.9 ± 3.6 | 7.9 ± 1.5 | <0.0001 |
| Septal e’-to-a’ | 1.4 ± 0.5 | 0.9 ± 0.5 | 0.7 ± 0.4 | 0.7 ± 0.2 | <0.0001 |
| Lateral e’ (cm/s) | 13.1 ± 3.9 | 10.7 ± 3.5 | 8.4 ± 3.3 | 9.2 ± 2.6 | <0.0001 |
| Lateral e’-to-a’ ratio | 1.7 ± 1.3 | 1.0 ± 0.6 | 0.9 ± 0.5 | 0.8 ± 0.4 | <0.0001 |
| E-to-e’ ratio    | 10.8 ± 3.6 | 12.4 ± 3.5 | 13.8 ± 6.3 | 12.3 ± 3.2 | 0.044 |

Data are means ± SD unless otherwise indicated. BSA, body surface area.
Linear regression analysis (R/P) between diastolic function parameters and different covariates

|                      | Left atrium volume/BSA | E-to-A ratio | DT | IVRT | Septal e′ | Septal e′-to-a′ ratio | Lateral e′ | Lateral e′-to-a′ ratio | E-to-e′ ratio |
|----------------------|------------------------|--------------|----|------|-----------|------------------------|-----------|------------------------|--------------|
| Age (years)          | 0.275/<0.0001         | -0.332/<0.0001 | 0.063/0.215 | 0.215/0.003 | -0.278/<0.0001 | -0.231/0.002 | -0.122/0.062 | -0.105/0.092 | 0.141/0.037 |
| SBP (mmHg)           | 0.073/0.179           | -0.022/0.389  | -0.064/0.209 | 0.196/0.006 | -0.146/0.032 | -0.129/0.052  | 0.113/0.077 | 0.051/0.261 | 0.175/0.014 |
| DBP (mmHg)           | -0.068/0.194          | -0.016/0.421  | -0.148/0.31  | 0.077/0.167 | -0.042/0.300 | -0.059/0.229  | 0.048/0.274 | 0.011/0.445 | -0.023/0.386 |
| BMI (kg/m²)          | -0.021/0.377          | 0.069/0.194   | -0.014/0.431 | -0.060/0.226 | -0.004/0.247 | -0.101/0.101  | -0.117/0.069 | 0.001/0.493 | 0.075/0.172 |
| Fasting glucose (mg/dL) | 0.031/0.350         | -0.153/0.026  | 0.092/0.122 | 0.253/0.001 | -0.296/<0.0001 | -0.271/<0.0001 | -0.208/0.044 | -0.110/0.082 | 0.030/0.352 |
| 1-h glucose (mg/dL)  | 0.366/0.001           | -0.238/0.001  | 0.202/0.001 | 0.426/<0.0001 | -0.389/<0.0001 | -0.502/<0.0001 | -0.427/<0.0001 | -0.384/<0.0001 | 0.161/0.020 |
| 2-h glucose (mg/dL)  | 0.111/0.080           | -0.218/0.003  | 0.077/0.184 | 0.014/0.431 | -0.074/0.087  | -0.144/0.001  | -0.421/<0.0001 | -0.386/0.001 | 0.019/0.436 |
| Fasting insulin (μU/mL) | -0.044/0.291         | 0.035/0.331   | 0.170/0.016 | 0.249/0.001 | -0.196/0.006 | -0.284/<0.0001 | -0.219/0.003 | -0.169/0.016 | 0.019/0.407 |
| 1-h insulin (μU/mL)  | 0.021/0.397           | -0.040/0.306  | 0.122/0.062 | 0.134/0.045 | -0.080/0.157 | -0.218/0.003  | -0.241/0.001 | 0.151/0.028 | 0.072/0.181 |
| 2-h insulin (μU/mL)  | 0.063/0.213           | -0.078/0.162  | 0.105/0.092 | 0.137/0.041 | -0.180/0.011 | -0.252/0.001  | -0.233/0.001 | -0.160/0.022 | 0.130/0.050 |
| Matsuda/ISI          | -0.070/0.188          | 0.088/0.134   | -0.136/0.043 | -0.104/0.094 | 0.177/0.012  | 0.290/<0.0001  | 0.300/<0.0001 | 0.187/0.009 | 0.045/0.284 |
| LVMi (g/m²)          | 0.181/0.011           | -0.139/0.039  | 0.046/0.280 | 0.202/0.005 | -0.289/<0.0001 | -0.362/<0.0001 | -0.159/0.022 | -0.079/0.159 | 0.143/0.035 |

BSA, body surface area; DT, deceleration time.

CONCLUSIONS—This study confirmed that 1-h postload glucose and diastolic function parameters are independent predictors of left atrial volume, IVRT, and DT, explaining 25.6% of their variation, respectively. Age and e′-to-a′ ratio were the first predictor of left atrial volume, followed by e′-to-e′ ratio, explaining 8.3% of its variation. The variables explaining 14.8% of IVRT, 10.2% of DT, and 12.9% of the study population, showed that the worsening of glucose intolerance was associated with left atrium dysfunction. This result suggests that the worsening of glucose intolerance may be an independent predictor of left atrium dysfunction.

Thus, variables reaching statistical significance, 3.2 years, fasting glucose (P = 0.001), 1-h postload glucose (P = 0.001), and e′-to-a′ ratio (P = 0.001), were inserted in a stepwise multivariate regression model to determine the independent predictors of left atrium function. The variables explained 25.6% of the study population, explaining 14.8% of IVRT, 10.2% of DT, and 12.9% of the study population, showing that the worsening of glucose intolerance may be a predictor of left atrium dysfunction.
of other cardiovascular heart diseases such as hypertension or atherosclerotic ischemic coronary disease (16,17). The development of diabetic cardiomyopathy is likely multifactorial involving several mechanisms including metabolic disturbances, endothelial dysfunction, coronary microvascular impairment, modification in the extracellular matrix, and sympathetic hyperactivity (16,17). All of these factors contribute to the increase of ventricular stiffness, promoting cardiac structure abnormalities such as left ventricular remodeling or hypertrophy. Cardiac fibrosis causes an imbalance between extracellular matrix deposition and degradation within the heart resulting in excessive fibroblast proliferation. In addition, ventricular fibrosis causes progressive stiffening of the ventricular wall resulting in ventricular dysfunction, increase in end diastolic pressure, and atrial dilatation.

Some of these effects could be related to chronic hyperglycemia that induces, in diabetic patients, nonenzymatic glycation of circulating and cellular membrane proteins, leading to the formation of advanced glycation end products (AGEs) and, through protein kinase C activation, to reactive oxygen species production with increased oxidative stress (18). AGEs accumulation, in the myocardium and arteral wall, makes irreversible and stable links with collagen polymers, leading to fibrosis development with reduction of ventricular compliance and increase of LVM, as observed in animal models of IGT (19). Moreover, under chronic hyperglycemia condition, there is an increased turnover of free fatty acids, with a shift of myocardial metabolism toward the oxidation of the latter, with intracellular accumulation of intermediate products that lead, via increased oxidative stress, to deleterious effects (20). In keeping with this, our results, obtained in NGT subjects, confirm that these modifications begin early, at a clinically silent phase, and support reconsideration of the notion that NGT subjects are a homogeneous group with a low cardiovascular risk profile.

The activation of both the renin-angiotensin-aldosterone system and sympathetic nervous system is another important mechanism potentially involved in activation of cardiac fibroblasts and collagen production (21), leading to fibrosis and likely subsequent to the development of diastolic dysfunction. Finally, we should not ignore the role of coronary microcirculation abnormalities that may lead to myocardial cell injury and reactive fibrosis/hypertrophy. Of interest, the impairment of coronary microcirculation, occurring without obstructive atherosclerotic lesions on epicardial coronary arteries, induces a reduction of coronary flow reserve, as demonstrated in type 1 diabetic patients (22) and hypertensive subjects (23). The reduction of coronary flow reserve seems to be a direct consequence of elevated glycemia (24). Thus, equally interesting are the results reported by Scognamiglio et al. (25) showing that postprandial hyperglycemia induces myocardial perfusion defects in T2D patients, secondary to deterioration in microvascular function causing a decrease in myocardial blood flow.

The most clinically relevant information from this study, is that there is a statistically significant and direct correlation between 1-h postload plasma glucose and diastolic dysfunction in NGT hypertensive patients. This has an important clinical implication considering its negative prognostic impact in hypertensive patients. Our data have allowed us to identify a new early predictor of subclinical organ damage and emphasize the importance of performing an OGTT in all subjects affected by essential hypertension, paying attention not only to 2-h but also to 1-h postload plasma glucose values, which are more strongly associated with diastolic dysfunction, in order to better stratify the global cardiovascular risk in hypertensive patients.

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

A.S. and S.M. researched data and wrote the manuscript. L.G. and F.A. researched data and reviewed and edited the manuscript. P.N. and D.M. analyzed the data and edited the manuscript. E.J.T. researched data and reviewed and edited the manuscript. L.T. and P.M. contributed to the discussion and reviewed and edited the manuscript. G.S. and F.P. designed the study, wrote the manuscript, contributed to the discussion, and reviewed and edited the manuscript.

References
1. Mogelvang R, Sogaard P, Pedersen SA, et al. Cardiac dysfunction assessed by echocardiographic tissue Doppler imaging is an independent predictor of mortality in the general population. Circulation 2009;119:2679–2685
One-hour postload glucose and diastolic function

2. Schillaci G, Pasqualini L, Verdecchia P, et al. Prognostic significance of left ventricular diastolic dysfunction in essential hypertension. J Am Coll Cardiol 2002;39:2005–2011

3. Hansen A, Haass M, Zugck C, et al. Prognostic value of Doppler echocardiographic mitral inflow patterns: implications for risk stratification in patients with chronic congestive heart failure. J Am Coll Cardiol 2001;37:1049–1055

4. Cserigó, Bolognese L, Buonamici P, et al. Prognostic implications of restrictive left ventricular filling in reperfused anterior acute myocardial infarction. J Am Coll Cardiol 2001;37:793–799

5. Aurigemma GP, Gottdiener JS, Shemanski L, Gardin J, Kitzman D. Predictive value of systolic and diastolic function for incident congestive heart failure in the elderly: the cardiovascular health study. J Am Coll Cardiol 2001;37:1042–1048

6. Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheller RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA 2003;289:194–202

7. Stahrenberg R, Edelmann F, Mende M, et al. Association of glucose metabolism with diastolic function along the diabetic continuum. Diabetologia 2010;53:1331–1340

8. Zhou L, Deng W, Zhou L, et al. Prevalence, incidence and risk factors of chronic heart failure in the type 2 diabetic population: systematic review. Curr Diabetes Rev 2009;5:171–184

9. Ilercil A, Devereux RB, Roman MJ, et al. Relationship of impaired glucose tolerance to left ventricular structure and function: the Strong Heart Study. Am Heart J 2001;141:992–998

10. Abdul-Ghani MA, Abdul-Ghani T, Ali N, DeFronzo RA. One-hour plasma glucose concentration and the metabolic syndrome identify subjects at high risk for future type 2 diabetes. Diabetes Care 2008;31:1650–1655

11. Succurro E, Marini MA, Arturi F, et al. Elevated one-hour post-load plasma glucose levels identifies subjects with normal glycaemic tolerance but early carotid atherosclerosis. Atherosclerosis 2009;207:245–249

12. Succurro E, Arturi F, Lugara M, et al. One-hour postload plasma glucose levels are associated with kidney dysfunction. Clin J Am Soc Nephrol 2010;5:1922–1927

13. Matsuda M, DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 1999;22:1462–1470

14. Chetlin MD, Armstrong WF, Aurigemma GP, et al; American College of Cardiology; American Heart Association; American Society of Echocardiography. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guideline (ACC/ AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). Circulation 2003;108:1146–1162

15. Naghli SF, Appleton CP, Gillette TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009;22:107–133

16. Galderisi M. Diastolic dysfunction and diabetic cardiomyopathy: evaluation by Doppler echocardiography. J Am Coll Cardiol 2006;48:1548–1551

17. Dinh W, Lankisch M, Nickl W, et al. Insulin resistance and glycemic abnormalities are associated with deterioration of left ventricular diastolic function: a cross-sectional study. Cardiovasc Diabetol 2010;9:63–74

18. Bardi G, Dicembrini I, Cresci B, Rotella CM. Inflammation markers and metabolic characteristics of subjects with 1-h plasma glucose levels. Diabetes Care 2010;33:411–413

19. Watts GF, Marwick TH. Ventricular dysfunction in early diabetic heart disease: detection, mechanisms and significance. Clin Sci (Lond) 2003;105:537–540

20. Singleton JR, Smith AG, Russell JW, Feldman EL. Microvascular complications of impaired glucose tolerance. Diabetes 2003;52:2867–2873

21. Sartori M, Ceolotto G, Papparella I, et al. Effects of angiotensin II and insulin on ERK1/2 activation in fibroblasts from hypertensive patients. Am J Hypertens 2004;17:604–610

22. Schalkwijk CG, Stehouwer CD. Vascular complications in diabetes mellitus: the role of endothelial dysfunction. Clin Sci (Lond) 2005;109:143–159

23. Galderisi M, Cicala S, Caso P, et al. Coronary flow reserve and myocardial diastolic dysfunction in arterial hypertension. Am J Cardiol 2002;90:860–864

24. Srinivasan M, Herrero P, McGill JB, et al. The effects of plasma insulin and glucose on myocardial blood flow in patients with type 1 diabetes mellitus. J Am Coll Cardiol 2005;46:42–48

25. Scognamiglio R, Negut C, De Kreutzenberg SV, Tiengo A, Avogaro A. Postprandial myocardial perfusion in healthy subjects and in type 2 diabetic patients. Circulation 2005;112:179–184