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Myocardial structure and function by echocardiography in relation to glucometabolic status in elderly subjects from two population-based cohorts: a cross-sectional study

Margret Leosdottir, MD^{1,*}, Ronnie Willenheimer, MD, PhD^{2,3}, Jonathan Plehn, MD⁴, Rasmus Borgquist, MD, PhD⁵, Petri Gudmundsson, BSc, PhD⁶, Tamara B Harris, PhD⁷, Lenore J Launer, PhD⁷, Halldora Bjornsdottir, MD⁸, Peter M Nilsson, MD, PhD², and Vilmondur Gudnason, MD, PhD^{8,9}

¹Dept of Cardiology, Malmö University Hospital, Malmö, Sweden ²Dept of Clinical Sciences, Lund University, Malmö University Hospital, Malmö, Sweden ³Heart Health Group, Malmö, Sweden ⁴Translational Medicine Branch, National Heart, Lung and Blood Institute, NIH, USA ⁵Dept of Cardiology, Lund University Hospital, Lund, Sweden ⁶Department of Biomedical Laboratory Science, Malmö University, Malmö, Sweden ⁷Laboratory of Epidemiology, Demography, and Biometry, Intramural Research Program, NIA, Bethesda, MD, USA ⁸Icelandic Heart Association, Kopavogur, Iceland ⁹University of Iceland, Reykjavik, Iceland

Abstract

Background—Left ventricular (LV) diastolic dysfunction has been associated with impaired glucometabolic status. However, studies of older subjects are lacking. We examined associations between echocardiographic indices of LV diastolic function and LV mass index (LVMI) and glucometabolic status among middle-aged and elderly subjects free from heart disease, hypothesizing that the associations would be comparative to younger cohorts.

Methods—We examined the AGES-RS (Iceland; n=607, 76±6 years) and MPP-RES cohorts (Sweden; n=1519, 67±6 years), evaluating associations with multivariable regression analysis.

Results—In AGES-RS, LVMI was positively correlated with HbA1c (p=0.001). Otherwise, echocardiographic variables were not associated with glucometabolic status. In MPP-RES, LVMI increased with increasing glucometabolic disturbance among both older (70–80 years) and middle-aged (57–69 years) subjects. Among older subjects, HbA1c was positively correlated with two variables reflecting LV diastolic function: late transmitral peak flow velocity (A) (p=0.001) and early transmitral peak flow velocity (E)/early diastolic peak tissue velocity (Em) (p=0.046). In middle-aged MPP-RES subjects, increasing glucometabolic disturbance was correlated with increasing late diastolic peak tissue velocity (Am) (p=0.002) and, after age-adjustment, with increasing A (p=0.001) and decreasing Em/Am (p=0.009). With age-adjustment, Am and A were positively correlated with fasting glucose and HbA1c.

Conclusions—Contrary to our hypothesis, in two independent cohorts of older individuals, associations between glucometabolic status and LV diastolic function were generally weak. This

contrasts with previous reports, as well as with observations among middle-aged subjects in the present study. Changes in LV diastolic function may be more age-related than associated with glucose metabolism in older subjects.

Introduction

Young and middle-aged diabetic patients without known heart disease have echocardiographic signs of left ventricular (LV) diastolic dysfunction and LV hypertrophy, compared to non-diabetic controls.^{1, 2} In non-diabetic subjects, impaired glucose tolerance is related to LV diastolic dysfunction and LV hypertrophy measured by conventional echocardiography/Doppler (CED).^{3–5} Echocardiographic Tissue Doppler Imaging (TDI) has in recent years been proven to sensitively detect early signs of both diastolic and mild systolic LV dysfunction, making echocardiography an increasingly attractive tool to identify patients at risk for developing heart failure (HF).⁶ Indeed, one study of 35 middle-aged, non-diabetic individuals showed a significant association between increasing fasting glucose (FG) and worsening of LV diastolic function assessed by TDI.⁷

The prevalence of both type 2 diabetes mellitus (T2DM) and HF increase with age. Although not as well documented as in younger cohorts, glucometabolic disturbances predict future HF also amongst the elderly.⁸ However, few studies have been published on the relationship between glucose metabolism and LV structure and function measured with CED in otherwise healthy elderly subjects, and these have revealed conflicting results.^{9–11} To our knowledge, there are no reports on the use of TDI to assess any relationship between glucometabolic status and asymptomatic LV diastolic dysfunction in the elderly.

The aim of the present study was to examine if glucometabolic status is associated with measures of LV diastolic function and LV mass index (LVMI), evaluated by CED and TDI, in two independent population-based cohorts of middle-aged and elderly subjects: the Age Gene/Environment Susceptibility Reykjavik Study (AGES-RS) and the Malmö Preventive Project Re-Examination Study (MPP-RES), hypothesizing that the associations would be comparative to younger cohorts.

Methods

AGES-RS, conducted 2002–2006 in Reykjavik, Iceland, was a prospective cohort study designed to examine risk factors in relation to disease and disability in old age.¹² Birth cohorts of elderly subjects living in Reykjavik, Iceland, were invited to participate, with 5764 subjects attending (attendance rate 71%, 58% women, mean age 76±6 years). The study exam included an extensive questionnaire and a blood draw to measure serum (s-) FG, HbA1c (glycosylated haemoglobin, measured by DCCT standard),¹³ s-insulin, s-creatinine and s-lipid profile (Elecsys 1010 [s-insulin] and Hitachi 912 [other], Roche Diagnostics, Basel, Switzerland). A resting electrocardiogram (ECG) was recorded and blood pressure, heart rate (two separate measurements), height and weight were measured. An echocardiography study was performed on a subsample of approximately 840 individuals, who were randomly selected from the cohort.

The Malmö Preventive Project (MPP, 1974–1992), was a preventive programme with the aim to screen for cardiovascular risk factors, alcohol abuse and breast cancer among inhabitants in Malmö, Sweden, born 1921–1949.¹⁴ In all, 33,346 individuals attended the screening programme. A re-examination, MPP-RES, was conducted during 2002–2006 (72% attendance rate, 63% men, mean age 69±6 years). Laboratory tests included plasma FG, s-lipid profile (Beckman Coulter LX20, Beckman Coulter Inc, Brea, USA) and cystatin-C (automated particle-enhanced immunoturbidimetric method, reagents from

DakoCytomation). HbA1c measurements were conducted in 60% of the subjects with automated HPLC (Variant II from Bio-Rad Laboratories, Munich, Germany). The participants answered a questionnaire and blood pressure, pulse rate, height and weight were measured. In a sample of approximately 1800 participants, echocardiography and ECG recordings were carried out. These subjects were randomly selected from groups defined by glucometabolic status: normal FG (≤ 6.0 mmol/l); impaired FG (IFG); new-onset T2DM; and prevalent DM; with oversampling in groups of subjects with glucometabolic disturbances to ensure sufficient numbers of subjects studied from each group.

The National Bioethics Committee in Iceland and the Icelandic Data Protection Committee approved AGES-RS. The Ethics committee of Lund University, Sweden, approved MPP-RES. Both studies complied with the Declaration of Helsinki. All participants signed an informed consent form.

Various definitions

In MPP-RES, new-onset T2DM was defined by two separate measurements of FG ≥ 7.0 mmol/l or one measurement ≥ 11.1 mmol/l. A single measurement of FG 7.0–11.0 mmol/l was classified as IFG, otherwise defined as FG 6.1–6.9 mmol/l. In AGES-RS, FG was only measured once. Thus a single FG ≥ 7.0 mmol/l was defined as new-onset T2DM and FG 6.1–6.9 mmol/l as IFG.

In both cohorts individuals with a history of DM (by questionnaire or medication) were classified as having prevalent DM regardless of their FG level. In AGES-RS, coronary heart disease was defined as a self-reported diagnosis of myocardial infarction, coronary-artery bypass-graft surgery or percutaneous coronary intervention. In both cohorts, prevalent HF was self-reported by questionnaire. In addition, in MPP-RES, a validated diagnosis of HF acquired from local hospital registries defined prevalent HF. Similarly, a hospital registry diagnosis of myocardial infarction defined prevalent coronary heart disease.

In both AGES-RS and MPP-RES, prevalent valvular disease was defined as 1) aortic stenosis with maximum transvalvular Doppler flow velocity ≥ 3.0 m/s, 2) severe aortic-, 3) mitral- or 4) tricuspid regurgitation.¹⁵ Atrial fibrillation or flutter was considered prevalent if observed during the conduct of the study (by ECG).

Echocardiography

For full description of the echocardiography protocol, see the on-line Appendix. In short, CED and TDI were conducted with a 3V2c transducer (Acuson Sequoia, Mountain View, CA, USA; AGES-RS and MPP-RES) or a S3 transducer (Sonos 5500 Philips, Andover, MA, USA; MPP-RES). LV diastolic function was assessed using transmitral pulsed Doppler flow as well as TDI in the four-chamber view.¹⁶ In AGES, a mean of three to five consecutive cycles was used. In MPP, a single cycle was used if the registrations were homogeneous; otherwise a mean of three to five cycles. LV mass calculations were based on two-dimensional end-diastolic measurements in the parasternal long axis view at the level of the mitral tips consistent with M-mode criteria and subsequently indexed for body surface area.¹⁷ For intra- and interobserver variability, see Appendix Table A (online).

Statistical methods

The two cohorts were analyzed individually. Subjects with prevalent coronary heart disease, HF and significant valvular disease were excluded from all calculations. Baseline characteristics are presented as means $\pm$ standard deviations (SD) and percentages. The subject samples were divided into six groups defined by glucometabolic status: 1) FG ≤ 5.0 mmol/l; 2) FG 5.1–5.5 mmol/l; 3) FG 5.6–6.0 mmol/l; 4) IFG; 5) new-onset T2DM and; 6)

prevalent DM. The groups were entered into a multivariable regression analysis and tested against measures of LV diastolic function and structure, with the first group as reference group. The endpoint variables and their definitions are listed in Appendix Table B (online). The regression analyses were first done age adjusted and subsequently fully adjusted. In order to select relevant covariates, the relationship between each covariate and LV function/structure variable was tested in regression analysis. Covariates showing significant correlation with the relevant LV function/structure variable ($p < 0.01$) were then tested for internal correlation (by Spearman's rank test or Pearson's test). If internal correlation was present ($r \geq 0.3$), only the covariate with the strongest correlation to the relevant LV function/structure variable was incorporated into the final multivariable analysis. Covariates tested against each variable were: age, gender, body mass index (BMI), smoking, s-lipids, s-creatinine (AGES-RS) and cystatin C (MPP-RES), systolic and diastolic blood pressure, heart rate, LVMI (only against LV function variables) and use of medication for cardiovascular disease and/or cardiovascular disease risk factors (for list of medications, see Appendix). Atrial fibrillation was also included as a covariate, except in analysis of late diastolic variables where subjects with atrial fibrillation were excluded. Covariates fulfilling the criteria for inclusion in the multivariable analysis for each endpoint are listed in Appendix Table C. Variables with a skewed distribution were naturally log-transformed.

The association between FG, HbA1c and an estimation of insulin resistance, the homeostasis model assessment (HOMA: $s\text{-insulin} \times \text{FG} / 22.5$; AGES-RS only) and the different measures of LV diastolic function and LVMI was tested using the same model as described above.¹⁸ Patients with prevalent DM were excluded as one can expect varying FG, HbA1c and HOMA values for these subjects pending on their treatment. Also, better secondary prevention treatment amongst subjects with DM could in its turn influence the echocardiographic findings, resulting in non-linearity.

The cohorts were first entered as a whole and, subsequently, stratified by gender. In a post-hoc analysis we divided the MPP-RES subjects into middle-aged (≤ 69 years, $n=980$) and elderly (>69 years, $n=539$). All calculations were done in SPSS 16.0 (SPSS Inc, Illinois, USA).

Results

AGES-RS

Table Ia depicts baseline characteristics for the AGES-RS sample by glucometabolic group. Table II illustrates raw mean values ($\pm$ SD) of each LV function/structure variable for the six glucometabolic groups and adjusted p-values from the multivariable analysis for the trend tests (groups 1–5). No significant differences between the individual groups were observed, nor were any of the trend tests statistically significant. The associations between FG, HbA1c and HOMA and LV function/structure variables are shown in Appendix Table D. HbA1c was significantly inversely correlated with Am. With age-adjustment alone, HOMA was positively correlated with transmitral E, transmitral A and E/Em ratio. With men and women analyzed separately, the correlations between HOMA and transmitral A were stronger in men (age-adjustment F -statistic 11.5; $p=0.001$ (men) vs. 4.0; $p=0.048$ (women)) while the correlations between HOMA and transmitral E (age-adjustment 7.6; $p=0.006$) and E/Em (age-adjustment 11.2; $p=0.001$; full adjustment 6.4; $p=0.01$) could only be seen in women. Among men there was a significant trend towards higher Em with worsening glucometabolic status (full adjustment $p=0.008$), a positive correlation between FG and Em (full adjustment 5.3; $p=0.02$), a negative correlation between HOMA index and Em/Am ratio (age-adjustment 12.6; $p=0.001$; full adjustment 10.0; $p=0.002$) and transmitral E/A (age-adjustment 8.4; $p=0.004$; full adjustment 7.3; $p=0.008$), not seen for the whole population.

LVMI was positively significantly associated with FG (age-adjustment) and HbA1c (full adjustment) (Appendix Table D). In the gender-specific analysis this correlation was only significant among the women and for HbA1c only (age-adjustment 8.5; $p=0.004$; full adjustment 9.2; $p=0.003$).

MPP-RES

Baseline characteristics for the MPP-RES cohort are presented in Table Ib. Table III shows raw mean values ($\pm$ SD) and adjusted between-groups' trends of LV function/structure variables for the six glucometabolic groups. With higher glucometabolic group, i.e. increasing glucometabolic disturbance, there was a significant trend towards increasing LV diastolic dysfunction, by means of increased Am (full adjustment) and transmitral A (full adjustment) and reduced Em/Am (age-adjustment). A significant trend towards increasing transmitral E with higher glucometabolic group was also seen (full adjustment). In the gender-specific analysis the trends for the transmitral variables were stronger in men, while the trends in TDI variables were stronger in women. Associations between FG and HbA1c and LV function/structure variables are shown in Appendix Table E. We observed positive associations between FG and Am, transmitral A and transmitral E in the age-adjusted models, but these were attenuated or disappeared in the fully adjusted models. Weaker associations were generally seen with HbA1c. No gender differences were observed. Analyzing the whole cohort, there was a significant trend toward increasing LMVI with increasing glucometabolic disturbance (age-adjustment). FG was positively correlated with LVMI (age-adjustment). In the gender specific analysis the between-groups' trend was only seen in women (full adjustment).

In the MPP-RES post-hoc age-stratified analysis (middle-aged and older subgroups) the significant trends of increasing LV diastolic dysfunction with increasing glucometabolic disturbance observed for the whole cohort remained significant for Am (full adjustment), Em/Am (age-adjustment) and transmitral A (age-adjustment) in the middle-aged subgroup but not in the older subgroup (Appendix Table F). Likewise, the age-adjusted positive correlation between FG and Am, transmitral A and transmitral E remained significant only in the middle-aged subgroup (Appendix Table G). The between-groups difference in LVMI was seen in both age groups but the trend towards increasing LVMI with increasing glucometabolic disturbance (full adjustment) and association between FG and LVMI (age-adjustment), on the other hand, remained significant only in the older subgroup. The association between HbA1c and transmitral A was stronger in the older subgroup (full adjustment). In the gender-stratified analyses the observed associations remained significant most often among younger men who comprised the largest group (younger men $n=772$, younger women $n=208$, older men $n=279$, older women $n=260$). P-values were generally of borderline significance (0.02–0.04).

Discussion

In this cross-sectional analysis of a large, population-based cohort of elderly Caucasian individuals, with validation in another independent cohort of similar size and age distribution, we examined whether glucometabolic status was associated with LV diastolic function and LVMI. This is, to our knowledge, the first study examining these relationships in elderly non-diabetic subjects as well as the first study using TDI to compare LV diastolic function in elderly diabetic subjects to non-diabetic controls. Contrary to our current finding in the middle-aged subgroup in MPP-RES as well as previous reports in younger subjects, in AGES-RS and in the older subgroup in MPP-RES we observed only few and weak associations between glucometabolic status and LV diastolic function. A positive association between glucometabolic status and LVMI was seen in middle-aged and older subjects (both cohorts), although remaining significant for women only in fully adjusted models.

Diastolic function

The majority of prior studies in younger and middle-aged subjects, examining if DM and/or continuous measures of glucometabolic status are related to LV diastolic function, have found similar changes in CED/TDI measures of LV diastolic function: a decrease in transmitral E and Em, a compensatory increase in transmitral A and Am, a subsequent decrease in E/A and Em/Am, increase in E/Em and left atrial enlargement.^{7, 19} Disturbed relaxation of the LV myocardial wall is likely to explain these echocardiographic changes.¹⁹ There are few prior studies in elderly subjects on the relationship between glucose metabolism and LV diastolic function measured with CED, and none where TDI has been applied.^{9–11} These have not shown as consistent results as among younger subjects. In the Uppsala Study of 70-years old men, and in the Cardiovascular Health Study (CHS) in elderly free-living individuals 65–103 years of age, FG and/or measures of insulin resistance were positively correlated to transmitral E and A.^{9, 10} Karvounis and colleagues found reduced transmitral E and E/A and increased transmitral A in elderly (mean age 67 years) diabetic subjects compared to age- and gender-matched controls.¹¹ The only published study on the association between FG and TDI measures of LV diastolic function in middle-aged non-diabetic subjects found clear and significant correlations between FG and Em (negative), Am (positive) and Em/Am (negative), despite a small cohort of 35 subjects.⁷

In our study, neither CED nor TDI measures of LV diastolic function differed significantly among glucometabolic groups in the AGES-RS cohort. Some associations were observed between measures of LV diastolic function/LVMI and continuous measures of glucometabolic status, but only in age-adjusted models. In MPP-RES, we observed a significant trend of increasing Am, transmitral A and transmitral E, and decreasing Em/Am with increased glucometabolic disturbance (by groups and continuous measures). However, in our sub-analysis of middle-aged and older subjects, this trend was attenuated in the older subgroup, remaining significant only in the middle-aged group. Thus, in our two cohorts of elderly subjects, there were generally weak associations between glucometabolic status and CED or TDI measures of LV diastolic function.

Interestingly, the changes in LV diastolic function seen amongst younger and middle-aged diabetic subjects are similar to typical age-related changes of LV diastolic function.^{19–21} Apart from LV diastolic dysfunction, ageing is associated with increasing LV mass and left atrial diameter, and with decreasing longitudinal LV systolic function (measured by TDI), whereas LVEF is usually preserved.^{20, 21} Hence, one possible explanation to the prior inconclusive findings on the association between glucometabolic status and myocardial function amongst elderly subjects, as well as to the findings of the present study, is that age-related changes in myocardial function and structure might overshadow the effects of glucose metabolism in older subjects. This hypothesis is supported by differences in HF incidence between subjects with and without diabetes, where incidence ratios fall from approximately 5.4/1 in middle-age to 1.2/1 in old age.²² Our observations from the post-hoc analysis based on age also supports this hypothesis, as the significant trend of increased LV diastolic dysfunction with worsening glucometabolic status was much stronger in the middle-aged subgroup.

Left ventricular hypertrophy

An association between worsening glucose tolerance and increased LV hypertrophy has been documented in younger and middle-aged pre-diabetic subjects.^{3, 23} However, it is still debated whether this association is independent of BMI, especially in non-diabetic subjects, and studies in older subjects are sparse.^{24, 25} In our study, LVMI was positively associated with HbA1c in AGES-RS. In MPP-RES, we observed a positive association between LVMI and FG in the older subgroup (age-adjusted only) and an increased LVMI in the upper

glucometabolic groups compared to the reference group (both age strata). However, this might be explained by a markedly low LVMI in the reference groups (Appendix Table F). Compared to the second groups, which also had normal FG (5.1–5.5 mmol/l), only middle-aged IFG and new-onset diabetic subjects had significantly increased LVMI. Thus, contrary to previous studies in younger and middle-aged subjects, and in parallel with LV diastolic function in the present study, no clear trends towards increased LV hypertrophy with worsening glucometabolic status were observed in elderly subjects.

Gender issues

In both cohorts we observed gender differences in LV diastolic function measures, with some associations remaining significant among men while others remained significant among women. In the post-hoc age-stratified analysis in MPP-RES the associations between LV diastolic dysfunction and increased glucometabolic disturbance were most often significant among younger men, but the associations were generally weak and the younger men comprised by far the largest group, increasing the likelihood of the observed differences being power-related. There was a stronger association between increasing glucometabolic disturbance and increasing LVMI among women in both cohorts. This is consistent with previous echocardiography findings and the fact that women with glucometabolic disorders run a greater risk of cardiovascular disease and HF than men.^{23, 26}

The major strength of the present study is our finding of reproducible results in two independent cohorts. The large size of the cohorts also strengthens the assumption that the findings, although mostly negative, are true and not due to insufficient statistical power. Attendance rates were high in both studies and the study samples represented different parts of northern Europe, suggesting that the results are applicable at least to these populations.

This study has some limitations. Being a cross-sectional study, conclusions to be drawn are limited and causality cannot be determined. Although subjects with prevalent coronary heart disease and HF were excluded from all calculations, a large portion of the study subjects was taking prescription drugs affecting cardiac function so despite adjustments the possibility of bias cannot be excluded. As only one measurement of FG was performed in AGES and as oral glucose tolerance tests were not performed in either study, missed diagnoses of T2DM are possible. A survival bias cannot be excluded, with diabetic individuals suffering cardiovascular complications either not reaching high age or being too sick to participate in a cohort study. Finally, on account of multiple testing, borderline p-values (0.03–0.05) should be interpreted with caution.

In conclusion, contrary to previous reports in younger subjects as well as to our own findings among middle-aged individuals, we found generally weak associations between glucometabolic status and echocardiographic measures of LV diastolic function and LV mass in two large independent population-based cohorts of elderly persons. Thus, although a survival bias might contribute to these findings, age-related changes in LV structure and function might be more important than glucose metabolism in older subjects and these should be explored as potentially explaining the observed results. As such, using echocardiography to screen for preclinical glucometabolic-related myocardial dysfunction in asymptomatic older populations might be questioned. Further studies of a prospective design, taking different age-strata into account, are needed answer these questions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Baseline characteristics for AGES-RS (1a) and MPP-RES (1b) subjects, by glucometabolic groups.

1a.	New-onset				Prevalent			
	FG ≤5.0	5.1–5.5	5.6–6.0	IFG	DM	DM	DM	DM
Number	82	218	144	82	23	59		
Age (years ±SD)	77±6	75±6	75±6	76±6	76±5	76±6		
Sex (% men)	78%	68%	50%	60%	48%	46%		
BMI (kg/m ²)	25.1±4.1	26.8±3.9	27.0±4.1	29.0±4.6	29.0±5.1	29.5±5.6		
Systolic BP (mmHg)	143±23	142±21	142±18	142±20	148±16	144±21		
Diastolic BP (mmHg)	74±9	74±9	75±9	74±9	80±9	73±8		
Total cholesterol*	6.0±1.1	6.0±1.0	5.8±1.0	6.1±1.1	6.0±1.4	5.3±1.3		
HDL cholesterol*	1.71±0.42	1.63±0.47	1.59±0.43	1.57±0.39	1.44±0.42	1.37±0.31		
Triglycerides*	1.01±0.48	1.11±0.47	1.12±0.48	1.36±0.56	1.73±0.81	1.45±0.60		
Current smoker	6%	11%	11%	9%	4%	9%		

1b.	New-onset				Prevalent			
	FG ≤5.0	5.1–5.5	5.6–6.0	IFG	DM	DM	DM	DM
Number	134	224	213	436	152	360		
Age (years ±SD)	69±5	67±6	66±6	66±6	67±6	68±6		
Sex (% men)	41%	62%	66%	78%	78%	72%		
BMI (kg/m ²)	26.1±3.3	26.9±3.8	26.9±3.6	28.5±4.0	30.3±4.9	29.4±4.4		
Systolic BP (mmHg)	143±18	142±20	146±16	150±20	156±23	148±19		
Diastolic BP (mmHg)	83±10	83±10	85±10	87±10	89±10	83±10		
Total cholesterol*	5.8±0.9	5.7±0.9	5.7±1.1	5.7±1.1	5.8±1.2	5.0±1.0		
HDL cholesterol*	1.6±0.4	1.4±0.4	1.4±0.4	1.3±0.4	1.2±0.3	1.3±0.4		
Triglycerides*	1.1±0.5	1.2±0.6	1.3±0.8	1.5±0.9	2.1±1.6	1.6±1.0		
Current smoker	19%	17%	19%	20%	23%	14%		

* mmol/L.

BMI, body mass index; BP, blood pressure; DM, diabetes mellitus; IFG, impaired fasting glucose; SD, standard deviation.

Table II

Results from the multivariable regression analyses for the AGES-RS cohort.

	FG ≤5.0	5.1–5.5	5.6–6.0	IFG	New-onset DM	Prevalent DM	p for trend A	F
Em (cm/sec)	7.8±1.5	8.1±1.7	8.0±1.7	7.9±1.5	7.8±1.7	8.1±2.9	0.8	0.5
Am (cm/sec)	10.8±1.8	10.9±2.0	11.0±2.0	11.2±2.1	10.7±1.8	11.0±2.3	0.6	0.4
Em/Am	0.74±0.18	0.76±0.22	0.74±0.20	0.71±0.14	0.71±0.16	0.74±0.21	0.2	0.3
Transmitral E (cm/sec)	72.3±17.9	70.8±16.9	72.9±17.6	75.8±20.3	72.3±22.1	75.9±18.7	0.2	0.3
Transmitral A (cm/sec)	82.3±21.8	80.8±20.0	82.0±19.1	86.9±24.4	81.4±15.0	89.1±26.0	0.1	0.4
E/A	0.90±0.21	0.90±0.25	0.91±0.26	0.88±0.21	0.85±0.27	0.90±0.35	0.3	0.6
E/Em	9.7±2.8	9.2±2.9	9.6±3.0	9.8±3.2	9.5±2.8	10.0±3.0	0.4	0.97
LA diameter (mm/m ²)	2.14±0.36	2.09±0.28	2.11±0.34	2.07±0.29	2.09±0.26	2.10±0.29	0.3	0.1
L VMI (g/m ²)	151±52	154±44	168±55	169±55	187±56	171±44	0.06	0.4

Raw (unadjusted) mean values and standard deviations of LV diastolic function parameters and L VMI for the six glucometabolic groups from AGES-RS. Age (A) and fully (F) adjusted p-values for trends are also shown. Definitions of LV function and structure variables can be seen in Appendix Table B.

Table III

Results from the multivariable regression analyses for the MPP-RES cohort.

	FG ≤5.0	5.1–5.5	5.6–6.0	IFG	New-onset DM	Prevalent DM	p for trend	
Em (cm/sec)	7.6±2.5	7.9±2.8	8.4±2.8	8.2±2.8	8.2±2.7	7.4±2.6	A	F
Am (cm/sec)	10.8±2.7	11.6±2.8 ^{*A, *F}	12.4±2.7 ^{‡A, ‡F}	12.3±2.8 ^{§A, §F}	12.2±3.0 ^{‡A, ‡F}	11.3±2.8 ^{*F}	0.0002	0.0004
Em/Am	0.72±0.24	0.68±0.21 ^{*A}	0.68±0.18 ^{‡A, *F}	0.68±0.19 ^{‡A, ‡F}	0.68±0.18 ^{*A}	0.65±0.18 ^{‡A, ‡F}	0.006	0.3
Transmitral E (cm/s)	72.2±16.0	68.2±14.7 ^{*A}	70.1±14.9	70.2±17.4 ^{‡A}	74.5±16.9	73.6±17.9 ^{‡A, *F}	0.04	0.02
Transmitral A (cm/s)	78.7±16.8	76.3±16.5	76.0±15.2	78.5±17.3	81.0±17.6 ^{*A}	85.1±18.5 ^{§A, §F}	0.0002	0.03
E/A	0.95±0.26	0.92±0.24	0.95±0.27	0.92±0.24	0.95±0.26	0.89±0.24	0.2	0.8
E/Em	10.6±4.1	9.5±3.3	9.1±3.5	9.4±4.0	10.1±3.9	11.0±4.2	0.2	0.9
LAD (mm/m ²)	20.6±2.7	20.8±2.7	20.5±2.7	20.7±2.7	20.6±2.6	21.1±2.6	0.5	0.6
LVMI (g/m ²)	148±41	170±52 ^{§A, ‡F}	168±42 ^{‡A, *F}	176±45 ^{§A, *F}	178±49 ^{‡A}	182±54 ^{§A}	0.001	0.7

Raw (unadjusted) mean values and standard deviations (SD) of LV diastolic function parameters and LVMI for the six glucometabolic groups from MPP-RES. Age (A) and fully (F) adjusted p-values for trends are also shown. Significant age (A) and fully (F) adjusted between-group differences are denoted by footnotes (with the first group (FG ≤5.0) as reference group).

* p<0.05;

[‡] p<0.01;

[§] p<0.001;

[§] p<0.0001.