SUPPLEMENTAL MATERIAL
SUPPLEMENTAL METHODS

Echocardiography

Echocardiograms were obtained by research technicians according to a standardized protocol consisting of 2D, M-mode, color flow Doppler, pulsed and continuous wave Doppler, and Tissue Doppler recordings with use of echo equipment (Vivid E9 with 2.5-3.5 MHz and 4V transducer, GE Vingmed). All recordings were digitally stored and analyzed off-line (EchoPAC PC, version 112) by four researchers blinded to glucose metabolism status and other data.

Measures of left ventricular diastolic function

According to 2016 guidelines average E/e’-ratio and maximum tricuspid regurgitation flow were used as functional measures of left ventricular (LV) diastolic function, and left atrial volume index (LAVI) and left ventricular mass index (LVMI) were used as structural measures of left ventricular diastolic function. In addition, left ventricular diastolic function was classified according to 2016 guidelines into normal, indeterminate or abnormal diastolic function.

Mitral inflow velocities were obtained with pulsed-wave Doppler in the apical four-chamber view with placement of the sample volume at the tips of the mitral leaflets. The peak flow velocity of the passive filling wave (E-wave) and active filling wave (A-wave) were measured. Pulsed Doppler tissue echocardiography was performed in the apical four-chamber view, with placement of the sample volume at the LV lateral and septal segment of the mitral annulus. At each site the peak myocardial systolic (S’), early (e’) and late diastolic (a’) longitudinal velocities were measured. The mitral E/e’ ratio’s (septal, lateral and average) were calculated.

Continuous wave Doppler recordings of the tricuspid flow were obtained in an apical four-chamber view. Maximal tricuspid valve regurgitation velocity was measured and the maximal gradient was calculated with use of the Bernoulli equation.

End-systolic left atrial volume was estimated in the four- and two-chamber view with use of the modified Simpson’s method. Left atrial volume from biplane measurements was indexed to body surface area (BSA) calculated according to Mosteller.

End-diastolic and end-systolic interventricular septum (IVSD, IVSS), posterior wall thickness (PWTD, PWTS), and LV diameters (LVEDD, LVESD) were determined in the parasternal long axis view, between the tip of the mitral leaflets and the chordae level perpendicular to the LV long axis. LV mass (LVM) was then calculated as 0.8*1.04* ((LVEDD+IVSD+PWDT)³−(LVEDD³)+0.6). LVM was indexed (LVMI) by height².4².4³

In addition, left ventricular diastolic function was classified according to current guidelines (i.e. average E/e’>14, septal e’<7 or lateral e’<10, tricuspid regurgitation>2.8,
LAVI>34) into normal, indeterminate or abnormal diastolic function. If ≥2 criteria were missing, diastolic function was classified as not specified.

**Other echocardiography variables**

End-diastolic and end-systolic LV volumes (LVEDV, LVESV) were determined in the apical four- and two-chamber view with use of the modified Simpson’s method. Systolic function was defined with the use of Simpson’s LV ejection fraction calculated from biplane LVEDV and LVESV measurements. The presence of wall motion abnormalities was evaluated by a trained researcher and checked by a senior cardiologist.

Valve function was investigated in a qualitative and semi-quantitative way. The global severity of valve stenosis and regurgitation was based on valve morphology, color Doppler images, transvalvular (mean) gradient and jet velocity with the criteria specified in current guidelines. Significant valvular dysfunction was defined as any moderate or severe valve stenosis or regurgitation of the aortic, mitral, tricuspid or pulmonary valve or the presence of a valve prosthesis.

From the E-wave and A-wave the E/A ratio was calculated. Furthermore, the deceleration time (DT) of the E-wave was measured.

Pulmonary venous inflow velocities were obtained with pulsed-wave Doppler in the apical four-chamber view with placement of the sample volume into the right upper pulmonary vein. Peak systolic (S) and anterograde diastolic (D) velocities were measured.

Pulsed waved Doppler was obtained in the apical five-chamber view at the level of the LV outflow tract and the mitral inflow for assessment of closure to opening time (CTOT), isovolumetric contraction time (IVCT), ejection time (ET) and isovolumetric relaxation time (IVR).

Reproducibility of the analysis was assessed in 12 individuals (50% women; 57.8±11.5 years; four T2DM, four pre-diabetes) who were analysed by four observers. Intraclass correlation coefficients of observed agreement are described as below.
Sub-maximal cycle ergometer test: cardiorespiratory fitness

The sub-maximal cycle ergometer test to determine cardiorespiratory fitness (CRF) in $W_{\text{max}}$ was performed as described previously. The ergometer test and echocardiography were performed at the same clinical visit. As an objective measure of CRF estimated maximum power output adjusted for body mass ($W_{\text{max}}/\text{kg}$) was used. $W_{\text{max}}$ was estimated from a graded sub-maximal exercise protocol performed on a cycle ergometer system (CASETM version 6.6 in combination with e-bike, GE Healthcare, Milwaukee, WI, USA). Exclusion criteria for the sub-maximal cycle ergometer test were: having suffered from cardiovascular disease three months prior to the ergometer test, having an resting ECG with previously unknown abnormalities, having severe hypertension (SBP $\geq$180 and/or DBP $\geq$110), or being in the possession of an ICD/pacemaker. Participants eligible for the test were fitted with a blood pressure cuff on the upper left arm (Suntech Tango+TM, SunTech Medical, Inc. Morisville, NC, USA) and electrodes on the thorax to provide continuously a 12-leads ECG. In addition, (percentage of) predicted $W_{\text{max}}$ was calculated by the formula of Jones et al.

As described previously, the protocol consisted of a short warm-up period and at most 7 stages with increasing work load. Participants were instructed to cycle at a cadence of 60-70 rotation per minute (rpm) during a short familiarization period without any external workload. For the first exercise stage, external workload was set at 25 W. Every consecutive 2 minutes external workload was increased with 25 W. At the end of each stage, heart rate (HR) and blood pressure were measured. Further, the participant was asked to provide a rating of perceived exertion (RPE) on the 15-point Borg-scale; an interval scale ranging from 6 („no exertion at all”) up to 20 („maximal exertion”). The exercise protocol was considered as „completed” when HR reached $\geq$ 85% of the estimated maximum HR (220-age) or when a RPE $\geq$ 17 was scored by the participant. If HR $<$ 85% or RPE $<$ 17 by the end of stage 7 (work

| Variable                  | ICC (95% CI)         | Variable                  | ICC (95% CI)         | Variable                  | ICC (95% CI)         |
|---------------------------|----------------------|---------------------------|----------------------|---------------------------|----------------------|
| LVEDD                     | 0.88 (0.75-0.96)     | E peak mitral            | 0.95 (0.86-0.98)     | S' LV septal             | 0.87 (0.48-0.97)     |
| LVESD                     | 0.94 (0.85-0.98)     | A peak mitral            | 0.83 (0.53-0.95)     | e' LV septal             | 0.96 (0.81-0.99)     |
| IVSD                      | 0.61 (0.29-0.85)     | Dec. time E peak         | 0.86 (0.71-0.95)     | a' LV septal             | 0.87 (0.56-0.96)     |
| PWTD                      | 0.71 (0.45-0.89)     | A peak duration          | 0.92 (0.82-0.98)     | S' LV lateral            | 0.86 (0.48-0.96)     |
| LVEDV                     | 0.59 (0.16-0.85)     | S peak                   | 0.86 (0.53-0.96)     | e' LV lateral            | 0.93 (0.66-0.98)     |
| LVESV                     | 0.66 (0.23-0.88)     | D peak                   | 0.88 (0.62-0.96)     | a' LV lateral            | 0.61 (0.14-0.87)     |
| Left atrial volume        | 0.83 (0.59-0.94)     | Tricuspid                | 0.70 (0.44-0.88)     |                          |                      |

The data are given in intraclass correlation coefficients (ICC) with their 95% confidence interval (95% CI). For clarification of other abbreviations see previous text.
load of 175 W), the test was also stopped. The test could also be prematurely terminated on medical grounds or when the participant was unwilling to continue.

As described previously, submaximal values of HR and RPE with workload from each stage were extrapolated to 100% of maximum HR or an RPE of 20 and corresponding workload (=W\text{max}) using individual linear regression models. Using RPE to predict W\text{max} overcomes the issue that certain medical conditions, such as autonomous neuropathy and medication use (e.g. beta blockers) may affect the linear association of HR with power output. Consequently, this protocol is suitable for participants who otherwise would have been excluded from exercise testing. A previous substudy of The Maastricht Study demonstrated that estimated W\text{max} using HR (W\text{max} when HR reached 85%) was comparable to W\text{max} based on RPE (W\text{max} when a RPE ≥ 17 was scored).

As described previously, W\text{max} was calculated from HR values if the test was completed based on HR, i.e. HR ≥ 85% of estimated HR\text{max}. W\text{max} was calculated from RPE values if the test was completed based on RPE, i.e. RPE ≥ 17. In addition to completed tests, W\text{max} from uncompleted tests was calculated from HR if ≥ 75% of HR\text{max} was achieved and W\text{max} was calculated from RPE values if an RPE ≥ 15 was scored. A previous sub study of The Maastricht Study demonstrated that estimations of W\text{max} from these lower ranges of HR and RPE were found to be similar to completed tests. Tests where both 75% of HR\text{max} and RPE15 were not achieved were considered as invalid.

Covariates
We assessed fasting glucose, glycated hemoglobin (HbA1c), glucose metabolism status, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) cholesterol, total-to-HDL cholesterol ratio, triglycerides, body mass index (BMI), office blood pressure, 24-hour ambulatory blood pressure, medication use (glucose-lowering, antihypertensive and lipid-modifying), smoking status (never, former, current), alcohol consumption (non, low, high), medical cardiovascular history, serum creatinine, serum cystatin C, 24-hour urinary albumin excretion, educational level (low, intermediate, high) and (self-reported) physical activity as described previously. Glucose metabolism status was classified as described previously. For the present study impaired fasting glucose and impaired glucose tolerance were combined into prediabetes. Hypertension was defined as an office systolic pressure ≥ 140 mmHg, an office diastolic pressure ≥ 90 mmHg and(or) the use of antihypertensive medication. Alcohol consumption was classified as non-, low- (≤7 glasses per week for women; ≤14 glasses per week for men), or high-consumers (≥7 glasses per week for women and ≥14 glasses per week for men). Prior cardiovascular disease was defined as a self-reported history of myocardial infarction, cerebrovascular infarction or hemorrhage, and(or) vascular surgery (including percutaneous angioplasty) of the coronary, abdominal, peripheral
or carotid arteries. Prior coronary heart disease was defined as either 12-lead resting ECG signs of prior myocardial infarction (Minnesota code 1-1-1 to 1-2-8\textsuperscript{54}) and/or self-reported history of myocardial infarction. Presence of current atrial fibrillation or atrial flutter was classified on the 12-lead resting electrocardiogram by The Minnesota Code Classification System for electrocardiographic findings (code 8-3-1 or 8-3-2\textsuperscript{54}). Estimated glomerular filtration rate was calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation based on both serum creatinine and serum cystatin C.\textsuperscript{55} Presence of micro- or macro-albuminuria (an urinary albumin excretion of 30-300mg or an urinary albumin excretion of >300mg per 24 hours,\textsuperscript{56} respectively) was dichotomized. Level of education was assessed during the cognitive assessment and was classified into eight categories commonly used in the Netherlands:\textsuperscript{57} 1) no formal education; 2) primary education; 3) lower vocational education; 4) intermediate general secondary education; 5) intermediate vocational education; 6) higher general secondary education; 7) higher vocational education; and 8) university level of education. For the present study, education level was further classified into low (level 1 to 3), intermediate (level 4 to 6) and high (level 7 to 8).\textsuperscript{58} Moderate-to-vigorous physical activity in hours per week was assessed with a modified version of the Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire.\textsuperscript{59}
Table S1. Overview of population-based studies of the associations between measures of LV diastolic function and cardiorespiratory fitness.

| Reference | Study design | Study population, N | Population characteristics | Echocardiographic measures of diastolic function reported | Measure of cardiorespiratory fitness reported | Adjustments reported | Main results: association of measures of diastolic function with cardiorespiratory fitness |
|-----------|--------------|---------------------|---------------------------|--------------------------------------------------------|---------------------------------------------|---------------------|----------------------------------------------------------------------------------|
| Leite et al. (2017)¹¹ | Asymptomatic volunteers from community-based population aged ≥ 18 years without moderate-to-severe valvular disease, pulmonary hypertension, and history of cardiac disease. | 20 | Mean age 51 years; 13 men / 7 women; 0 with diabetes. | Left atrium function by 2D speckle tracking (LA conduit strain rate); LVEDD, LVMi, LAVI, E/A-ratio, deceleration time, E/e'-ratio, S/D-ratio. | Peak oxygen uptake (VO2) via cardiopulmonary exercise testing by treadmill. | Unadjusted correlation (r); multivariable linear regression (beta) with adjustment for E/e’-ratio and age (only reported for significant associations). | After adjustment only LA conduit strain rate was associated with peak VO2. E/e’-peak VO2: r=-0.72; p<0.01. LA function: LA conduit strain rate – peak VO2: r=-0.82, p<0.01; beta=-0.69, p=0.02. Other measures (unadjusted significantly associated): LVEDD – peak VO2: r=0.47, p=0.04. After adjustment other measures were not associated with peak VO2. |
| Pellet et al. (2013)¹² | Community-based Louisiana healthy ageing study in individuals aged ≥60 years who underwent echocardiography and performed the CS-PFP-10 test without active atrial fibrillation and a calculated mitral valve area of less than 1.5 cm². | 36 | Age range 62-101 years; 15 men / 21 women; 6 with diabetes. | LAVI, pulmonary venous atrial reversal velocity, E/A-ratio, mitral a-wave duration, deceleration time, atrial reverse wave duration, E/e’-ratio and LVMi. | 10-item continuous scale physical performance test (CS-PFP-10) with domains balance and coordination, endurance, lower body strength, upper body strength, upper body flexibility. 6 minute walking distance (6MWD) | Correlation (r) adjusted for age and sex and after correction for multiple comparisons (p<0.001). | After adjustment only LAVI was associated with total CS-PFP-10 and the endurance domain. LAVI – total CS-PFP-10: r=-0.59, p=0.0005. LAVI – endurance domain: r=-0.63, p=0.0002. After adjustment other measures were not associated with the CS-PFP-10 score (after correction for multiple comparisons). |
| Perry et al. (2011)¹³ | Community-dwelling older adults aged ≥65 years without heart failure, valvular disease and atrial fibrillation. | 89 | Mean age 74 years (range 65-93); 41 men / 48 women; 6 with diabetes. | Normal diastolic function (E/A-ratio 0.75-1.5 and E/e’-ratio <10); grade I (E/A-ratio <0.75, regardless of E/e’-ratio), II (E/A-ratio 0.75-1.5 and E/e’-ratio >10) and III (E/A-ratio >1.5 and E/e’-ratio >10) dichotomized into LV diastolic dysfunction no/yes (grade I-III). | Normal diastolic function: LA conduit strain rate, LVEDV, LVMi, LAVI, E/A-ratio, deceleration time, E/e’-ratio, S/D-ratio. | Unadjusted correlation (r); multivariable linear regression adjusted for age, cardiovascular morbidity, sex, race, BMI, systolic blood pressure. | After adjustment LV diastolic dysfunction was not associated with 6MWD. LV diastolic dysfunction – 6MWD: 1013 versus 1128 feet; unadjusted r=-0.25 p=0.017; adjusted r=-0.44, p=0.365. |
| Okura et al. (2000)¹⁰ | Healthy individuals who received medical checkup in Kobe Rehabilitation Hospital without atrial fibrillation, long-term use of medication, hypertension, diabetes mellitus, cardiovascular disease, exercise-limiting musculoskeletal, hematologic or pulmonary | 160 | Mean age 55 years; 101 men / 59 women; 0 with diabetes (excluded). | E-peak, A-peak, E/A-ratio, deceleration time, LVEDV, LV mass. No TDI measurements. | Metabolic equivalent (METs) via exercise testing by treadmill. | Unadjusted correlation (r); multivariable regression (beta (95% CI)) with E/A-ratio, vital capacity, BMI, age, hemoglobin (only reported for significant associations). | After adjustment only E/A ratio was associated with METs. E/A-ratio – METs: r=0.58, p<0.0001; beta=1.385 (0.796:1.975), p<0.001. Other measures (unadjusted significantly associated): E-peak – METs: r=0.24, p=0.0024. A-peak – METs: r=0.51, p=0.0001. Deceleration time – METs: r=0.30, p=0.0002. LVEDV – METs: r=0.19, p=0.0172. |
diseases, and who had no positive results for ischemic heart disease by treadmill exercise test. Individuals from Framingham Offspring (Heart) study without coronary artery disease, congestive heart failure, valvular heart disease, atrial fibrillation, bundle branch block, pre-excitation, use of digoxin and beta-blockers.

Lauer et al. (1995)\textsuperscript{9}

Individuals from Framingham Offspring (Heart) study without coronary artery disease, congestive heart failure, valvular heart disease, atrial fibrillation, bundle branch block, pre-excitation, use of digoxin and beta-blockers.

Mean age men 43 years, women 43 years; 1,408 men / 1,618 women; 32 men with diabetes and 14 women with diabetes.

LV mass indexed by height. No TDI measurements.

Metabolic equivalent (METs) via exercise testing by treadmill.

Multivariable linear regression analyses adjusted for age, BMI, cigarette smoking, beta-blocker therapy, hypertension treatment, number of awake sedentary hours spent per day.

Sex-stratified analyses showed that the association between LV mass index and exercise capacity in METs remained significant after adjustment (p=0.0001 for both sexes; numbers not given). Presence of LV hypertrophy was associated with reduced exercise capacity.

Studies in patients without cardiac ischemia referred for exercise testing

Genovesi-Ebert et al. (1994)\textsuperscript{8}

Volunteers from medical and paramedical staff university Pisa and airport staff and borderline to severe essential hypertensive patients.

Mean age 45.8 years; 43 men / 8 women; diabetes status unknown. 20 volunteers and 34 patients.

A-peak, A/E-ratio, early filling fraction (ratio between velocity-time integral under the E-peak and that of the whole diastolic flow).

Exercise time via exercise testing by cycle ergometer.

Multivariable linear regression analyses with diastolic blood pressure, LV mass index, age and either A-peak, E/A-ratio or early filling fraction (only reported for significant associations).

After adjustment only A-peak and early filling fraction were associated with exercise time. A-peak – exercise time: r=0.54, p<0.0001; beta=0.077, p<0.05. Early filling fraction: r=0.51, p<0.001; beta=11.807, p<0.05. Other measures (unadjusted significantly associated): A/E-ratio – exercise time: r=0.46, p<0.001. LV mass – exercise time: r=0.31, p<0.025. LV mass index – exercise time: -0.38, p<0.01. After adjustment the other measures were not associated with exercise time. After adjustment only A/E-ratio and LVESV were associated with VO2. E/A-ratio – VO2: r=0.87; LVESV index – VO2: r=0.51; Other measures (unadjusted significantly associated): E/A-ratio – VO2: r=0.78, p<0.001; A-peak – VO2: r=0.73, p<0.001. LVESV index – VO2: r=0.61, p<0.001. E/A-ratio – VO2: r=0.51, p<0.001. LV mass – VO2: r=0.42, p<0.001. After adjustment the other measures were not associated with VO2.

Vanoverschelde et al. (1985)\textsuperscript{7}

Normal sedentary volunteers and endurance athletes.

Mean age 36 (range 20-76) years, 9 endurance athletes: mean age 37 (range 26-51) years; 40 men / 26 women; diabetes status unknown.

E/A-ratio, E-peak, A-peak, LVESV index, IVRT, LV mass.

Peak oxygen uptake (VO2) via exercise testing by cycle ergometer.

Stepwise multivariable regression analyses with E/A-ratio, E-peak, A-peak, LVESV index, IVRT, systolic blood pressure at maximum exercise, age, LVESV index, heart rate at maximum exercise, LV mass, sex, resting heart rate, resting stroke index, LV ejection fraction, end-systolic wall stress, radius/thickness-ratio and mean velocity of fiber shortening.

After adjustment the other measures were not associated with METs.
| Reference          | Study design                                                                 | Study population, N | Population characteristics                                                                 | Echocardiographic measures of diastolic function reported | Measure of cardiorespiratory fitness reported | Adjustments reported | Main results: association of measures of diastolic function with cardiorespiratory fitness |
|--------------------|------------------------------------------------------------------------------|---------------------|---------------------------------------------------------------------------------------------|----------------------------------------------------------|---------------------------------------------|---------------------------------------------|------------------------------------------------------------------------------------------|
| Otto et al. (2011) | Patients who underwent exercise testing and echocardiography within 30 days with retrospectively low risk for coronary artery disease. | 640                 | Mean age 49 years; 384 men / 256 women; 50 with diabetes.                                     | LV mass index, LVEDD, E-peak, A-peak, E/A-ratio, deceleration time, e'-peak, E/e'-ratio. E/e'-ratio > 10. Presence of diastolic dysfunction: normal (E/A-ratio<0.8, e'<8cm/s, normal LA vol, E/e'-ratio not considered); Abnormal relaxation (E/A-ratio<0.8, e'<8 cm/s, variable LA vol, variable E/e'-ratio'); pseudonormal diastolic dysfunction (E/A-ratio>0.8, e'<8 cm/s, LA volume usually increased, and E/e'-ratio>15), and restrictive diastolic dysfunction (E/A-ratio>1.8, e'/ < 8cm/s, LA volume usually increased, and E/e'-ratio/ >15). Diastolic function categorized in normal, mild (impaired relaxation; E/A-ratio <0.75), moderate (pseudonormal; 0.75≤E/A-ratio<1.5 and LAVI ≥28 mL/m² and E/e'-ratio ≥10), or severe (restrictive; E/A-ratio >1.5 and LAVI ≥28 mL/m² and E/e'-ratio ≥10) dysfunction. Resting E/e'-ratio ≥15. Postexercise E/e'-ratio ≥15. LVEDD, deceleration time, LA volume index. | Metabolic equivalent (METs) < and ≥ 7 via exercise testing by treadmill. | Unadjusted comparisons of group METs < and ≥ 7; multivariable logistic regression (odds ratio (OR)) with adjustment from significant univariate analyses: age, sex, diabetes mellitus, hypertension, obesity, LV mass index, A-peak, E/A-ratio, e'-peak, S-peak, E/e'-ratio. | After adjustment only A-peak was associated with METs <7. A-peak unadjusted difference METs < and ≥ 7; p<0.001; OR 1.03, p<0.004. Other measures unadjusted significantly associated: LV mass index (p=0.011), A-peak (p<0.001), E/A-ratio (p<0.001), e'-peak (p<0.001), E/e'-ratio (p<0.001). After adjustment the other measures were not associated with METs <7. (unadjusted) E/e'-ratio > 10 was significantly higher in the MET <7 group vs MET ≥7 group (41.7% vs 9.4%, p=0.001), as was the presence of any degree of diastolic dysfunction (76.6% vs 34.1%, p=0.001). |
| Grewal et al. (2009) | Patients who underwent exercise echocardiography according to the Bruce protocol without atrial fibrillation, moderate or severe valvular heart disease, ejection fraction <50% evidence of myocardial ischemia on the test, or had poor image quality. | 2,867               | Mean age normal diastolic function 53 years, mild dysfunction 67 years, moderate or severe dysfunction 66 years (N=1,784/785/298); 1,569 men / 1,298 women; 290 with diabetes. | Stepwise multivariable regression beta (95% CI) with normal/mild/moderate and severe diastolic function or E/e'-ratio >15, age, sex, pulse pressure, heart rate, BMI, coronary artery disease, diabetes mellitus, hypertension, previous or current smoker; and considered but not significant: ejection fraction, wall motion score index, LVEDD, deceleration time, LA volume index, hyperlipidemia, systolic blood pressure, beta-blocker use, calcium channel blocker use, angiotensin converting enzyme | Metabolic equivalents (METs) via exercise testing by treadmill. | After adjustment mild and moderate diastolic dysfunction and resting and postexercise E/e' ≥15 were associated with lower METs. Mild dysfunction vs normal – METS: beta -0.70 (-0.88;-0.46), p<0.001. Moderate or severe dysfunction vs normal – METS: beta -1.30 (-1.52;-0.99), p<0.001. Resting E/e'-ratio ≥15 – METS: -0.41(-0.70;-0.11), p=0.007. Postexercise E/e'-ratio ≥15 – METS: -0.41 (-0.70;0.11), p=0.007. Other measures unadjusted significantly associated: LVEDD – METS: beta 0.08 (0.06;0.11), p<0.001. Deceleration time per 40 milliseconds – METS: beta -0.34 (-0.44;-0.26), p<0.001. LAVI >30 mL/m² – METS: beta -0.45 (-0.69;-0.26), p<0.001. After adjustment the other measures were not significantly associated with METs. |
Skaluba et al. (2004)\textsuperscript{15}

Patients who underwent exercise echocardiography aged >18 years without pacemaker, severe native valvular disease or prosthetic heart valves and evidence of cardiac ischemia on the test.

Mean age 55 years; 59 men / 62 women; 16 with diabetes.

E-peak, A-peak, e’-peak, a’-peak, e’/a’-ratio, E/e’-ratio, LVEDD, LA area, deceleration time, isovolumetric relaxation time.

Metabolic equivalent (METs) ≤ and >7 via exercise testing by treadmill.

Unadjusted correlation; multivariable logistic and linear regression with adjustment for hypertension, age, coronary artery disease, diabetes, BMI, chronic renal insufficiency, LV hypertrophy, prevalence of outcome.

Of all the echo and clinical parameters assessed, E/Ea had the best correlation with exercise capacity ($r=0.684$, $p<0.001$) and was the strongest independent predictor of exercise capacity $\leq$ 7 METs by multivariate analysis (prevalence-corrected odds ratio=12.6, $p<0.001$).

E/e’-ratio – METs: $r=0.684$, $p<0.001$.

E/e’-ratio $\geq$10 – METs $\leq$7: unadjusted OR 18.2(4.8-24.9), $p<0.001$; adjusted OR 12.6(4.2-22.2), $p<0.001$.

E/e’-ratio – METs (continuous): beta -0.441, $p<0.001$.

Other measures unadjusted significantly associated:

A-peak – METs: $r=0.290$, $p=0.001$.

e’-peak – METs: $r=0.482$, $p<0.001$.

e'/a' -ratio – METs: $r=0.450$, $p<0.001$.

After adjustment the other measures were not significantly associated with METs.

Abbreviations: A-peak, mitral late filling velocity peak; BMI, body mass index; CI, confidence interval; E-peak, mitral early filling velocity peak; IVRT, isovolumetric relaxation time; LA, left atrial; LAVI, left atrial volume index; LV, left ventricular; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; S-peak, tissue Doppler imaging. e’-peak, a’-peak, S-peak, E/e’-ratio.
Table S2. General characteristics of the tissue Doppler imaging echocardiography study population according to tertiles of average E/e’-ratio

| Average E/e’ ratio | Low [2.8-6.9] (n=213) | Middle [6.9-8.6] (n=213) | High [8.6-17.1] (n=213) | P-value |
|-------------------|------------------------|--------------------------|------------------------|---------|
| Demographics      |                        |                          |                        |         |
| Men, %            | 56                     | 56                       | 48                     | 0.081   |
| Age, years        | 56±9                   | 60±8                     | 62±7                   | <0.001  |
| Educational level, low/middle/high, % | 12.7/32.5/54.7 | 16.4/44.1/39.4 | 17.8/46.5/35.7 | 0.001 |
| Glucose metabolism status, NGM/prediabetes/T2D, % | 71.8/14.1/14.1 | 58.2/17.8/23.9 | 41.8/20.2/38.0 | <0.001 |
| Prior cardiovascular disease, % | 8                     | 12                       | 18                     | 0.001   |
| Prior coronary heart disease,% | 2                     | 5                        | 8                      | 0.015   |
| Current atrial fibrillation or flutter, %a | 0.0                   | 1.0                      | 0.0                    | 0.984   |
| Blood pressure    |                        |                          |                        |         |
| Office systolic pressure, mmHg | 129±16                 | 134±16                   | 143±19                 | <0.001  |
| Office diastolic pressure, mmHg | 75±9                   | 76±10                    | 78±10                  | 0.001   |
| 24-hour systolic pressure, mmHgb | 116±11                 | 118±11                   | 121±12                 | <0.001  |
| Hypertension, %   | 32                     | 50                       | 72                     | <0.001  |
| Metabolic variables |                        |                          |                        |         |
| BMI, kg/m²        | 25.4±3.1               | 26.4±3.6                 | 27.9±3.8               | <0.001  |
| Waist, cm         | 92.1±10.7              | 94.7±11.5                | 97.7±12.2              | <0.001  |
| Total cholesterol, mmol/L | 5.38±1.04              | 5.26±1.06                | 5.23±1.18              | 0.173   |
| High-density lipoprotein, mmol/L | 1.49±0.48              | 1.40±0.45                | 1.37±0.42              | 0.006   |
| Low-density lipoprotein, mmol/L | 3.36±0.90              | 3.23±0.96                | 3.18±1.04              | 0.052   |
| Triglycerides, mmol/L | 1.03[0.75;1.47]        | 1.18[0.85;1.73]          | 1.38[0.96;1.91]        | <0.001  |
| Total-to-HDL-cholesterol ratio | 3.90±1.23              | 4.03±1.25                | 4.04±1.15              | 0.209   |
| HbA1C, in %c      | 5.7±0.84               | 5.9±0.7                  | 6.1±0.7                | <0.001  |
| Fasting plasma glucose, mmol/L | 5.7±1.5                | 5.9±1.0                  | 6.3±1.5                | <0.001  |
| Kidney function   |                        |                          |                        |         |
| eGFR, ml/min 1.73m² | 92.3±14.6              | 87.9±14.1                | 86.1±15.0              | <0.001  |
| Albuminuria, %    | 3.8                    | 5.2                      | 12.2                   | 0.001   |
| Lifestyle variables |                        |                          |                        |         |
| Smoking status: never/former/current, % | 35.7/48.8/15.5 | 35.2/49.8/15.0 | 31.9/55.4/12.7 | 0.885 |
| Alcohol use: no/low/high, % | 13.6/58.2/28.2 | 16.0/56.3/27.7 | 20.7/46.0/33.3 | 0.772 |
| Moderate to vigorous physical activity, hours/weekd | 4.8[3.0;8.0] | 5.0[3.0;8.3] | 4.5[2.5;7.5] | 0.439 |
| Medication        |                        |                          |                        |         |
| Anti-hypertensive medication, % | 21                    | 31                       | 51                     | <0.001  |
| RAS inhibitors, % | 16                     | 23                       | 38                     | <0.001  |
| Beta- blockers, % | 7                      | 16                       | 24                     | <0.001  |
| Diuretics, %      | 8                      | 8                        | 18                     | 0.001   |
| Calcium antagonists, % | 4                    | 4                        | 10                     | 0.005   |
| Oral antidiabetics and/or insulin use | 11                  | 19                       | 27                     | <0.001  |
| Lipid-modifying medication, % | 16                | 37                       | 46                     | <0.001  |
| Cardiorespiratory fitness (Wmax) | 178.7±46.5        | 166.9±46.1               | 152.9±44.7             | <0.001  |
Data are presented as mean ± SD, median [interquartile range] or frequencies (in %) as appropriate. Data present the tissue Doppler imaging echocardiography population for regression models 1-5. Linear trend was tested with ANOVA or chi-square test as appropriate. Abbreviations: eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin A1c; HDL, high-density lipoprotein; NGM, normal glucose metabolism; RAS, renin angiotensin system; T2D, type 2 diabetes.

| Data Point                                    | Total  | NGM | Prediabetes | T2D |
|-----------------------------------------------|--------|-----|-------------|-----|
| Cardiorespiratory fitness adjusted for body mass (W_max/kg) | 2.36±0.57 | 2.15±0.49 | 1.93±0.49 | <0.001 |
| Predicted cardiorespiratory fitness (predicted W_max) | 165.2±48.7 | 153.5±48.5 | 138.2±49.8 | <0.001 |
| Cardiorespiratory fitness (% of predicted W_max) | 113.9±30.8 | 114.8±30.8 | 119.4±38.7 | 0.188 |
| Mobility limitation, %* | 17 | 16 | 24 | 0.059 |

Numbers for specific variables (total, NGM/prediabetes/ T2D) are: 610, 200/203/207; b24-hour blood pressure measurements 590, 193/192/205; cHbA1c 638, 212/213/213; dmoderate to vigorous physical activity 554, 190/178/186; eMobility limitation 636, 212/213/211.
Data are presented as mean ± SD, median [interquartile range] or frequencies (in %) as appropriate. Data present the tissue Doppler imaging echocardiography population for regression models 1-5. Linear trend was tested with ANOVA or chi-square test as appropriate. Abbreviations: eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin A1c; HDL, high-density lipoprotein; NGM, normal glucose metabolism; RAS, renin angiotensin system; T2D, type 2 diabetes. Numbers for specific variables (total, NGM/prediabetes/T2D) are:

- Mitral inflow (m/s):
  - Total: 62.9±6.6, 63.0±6.6, 63.1±6.6
  - Men: 61.9±6.4, 62.0±6.5, 62.1±6.6
  - Women: 66.4±6.4, 66.5±6.5, 66.6±6.6

- LA volume index (ml/m^2):
  - Total: 29.8±6.6, 30.0±6.6, 30.4±6.5
  - Men: 29.9±6.7, 31.5±7.1, 30.8±6.5
  - Women: 29.7±6.1, 28.2±5.2, 30.1±6.4

- LV mass index (g/m^2):
  - Total: 28.9±6.4, 29.0±6.5, 31.6±7.0
  - Men: 30.9±7.1, 30.0±7.1, 32.2±7.4
  - Women: 27.4±4.9, 27.8±5.7, 31.1±6.5

- LV mass index (g/m^3):
  - Total: 66.4±13.7, 64.8±12.9, 67.7±15.2
  - Men: 70.3±14.7, 68.6±13.5, 71.4±16.6
  - Women: 61.3±10.2, 60.1±10.3, 64.4±12.9

- LV diastolic function according to 2016 guidelines (normal, indeterminate, abnormal), n (%):
  - Total: 114/86/12 (53.5/40.8/5.6)
  - Men: 78/103/32 (36.6/48.4/15.0)
  - Women: 36/71/4 (15.5/61.5/23.0)

Other measures LV diastolic function:

- Early peak velocity, m/s:
  - Total: 0.60±0.13, 0.67±0.12, 0.75±0.14
  - Men: 0.71±0.13, 0.63±0.12, 0.72±0.14
  - Women: 0.59±0.12, 0.64±0.13, 0.71±0.13
- Active peak velocity, m/s:
  - Total: 0.60±0.12, 0.67±0.13, 0.75±0.14
  - Men: 0.71±0.13, 0.63±0.12, 0.72±0.14
  - Women: 0.60±0.12, 0.67±0.13, 0.75±0.14

- E/A ratio:
  - Total: 0.99[0.82;1.25], 1.02[0.81;1.20], 0.92[0.79;1.13]
  - Men: 1.03[0.84;1.27], 1.00[0.83;1.16], 0.93[0.79;1.09]
  - Women: 0.96[0.80;1.15], 0.99[0.83;1.14], 0.91[0.77;1.07]

- Deceleration time E-peak, msec:
  - Total: 198±40, 190±32, 196±32
  - Men: 201±38, 190±32, 200±32
  - Women: 195±39, 191±31, 198±31
- Isovolumetric relaxation time, msec:
  - Total: 95±20, 96±22, 95±22
  - Men: 97±21, 96±22, 96±22
  - Women: 93±20, 94±21, 94±21
- S/D ratio:
  - Total: 1.39±0.33, 1.41±0.31, 1.44±0.32
  - Men: 1.41±0.31, 1.43±0.32, 1.45±0.33
  - Women: 1.37±0.31, 1.39±0.32, 1.40±0.33

Wall motion abnormalities, n yes (%):
- Total: 3 (1.4), 0 (0.0), 1 (0.5)
- Men: 2 (0.9), 0 (0.0), 1 (0.5)
- Women: 1 (0.5), 0 (0.0), 0 (0.0)

Valvular dysfunction (moderate or severe), n (%):
- Total: 22/13 (13.5), 18 (8.5)
- Men: 20/10 (11.4), 18 (8.5)
- Women: 2/3 (15.4), 0 (0.0)

Data for specific variables (total, NGM/prediabetes/T2D) are:
- Maximum tricuspid regurgitation flow:
  - Total: 1.90±0.42, 1.86±0.45, 1.96±0.52
  - Men: 1.90±0.42, 1.86±0.45, 1.96±0.52
  - Women: 1.90±0.42, 1.86±0.45, 1.96±0.52

- Mitral regurgitation flow:
  - Total: 636, 213/210/212
  - Men: 636, 213/210/212
  - Women: 636, 213/210/212

- LA volume index:
  - Total: 637, 212/212/213
  - Men: 637, 212/212/213
  - Women: 637, 212/212/213

- LV mass index:
  - Total: 634, 212/210/212
  - Men: 634, 212/210/212
  - Women: 634, 212/210/212

- LV diastolic function:
  - Total: 634, 212/211/211
  - Men: 634, 212/211/211
  - Women: 634, 212/211/211
Table S4. Clinical characteristics of the study population with tissue Doppler imaging echocardiography and individuals excluded from analyses due to missing values

| Demographics            | Normal glucose metabolism | Prediabetes | Type 2 Diabetes |
|-------------------------|---------------------------|-------------|-----------------|
|                         | Included (N=366)          | Excluded (N=192) | P   | Included (N=111) | Excluded (N=77) | P   | Included (N=162) | Excluded (N=169) | P   |
| Gender, %               | 43                        | 0            | 45              | 0.673 | 61                        | 0            | 57              | 0.571 | 70                        | 0            | 67              | 0.492 | 53                        | 0            | 56              | 0.448 |
| Age, years              | 60±8                      | 0            | 58±9            | 0.230 | 62±7                      | 0            | 61±8            | 0.403 | 62±7                      | 0            | 64±7            | 0.123 | 59±8                      | 0            | 61±9            | 0.004 |
| Educational level, %    | 10.7±39.2/17.1±41.3/25.9±42.3/1 | 1            | 9.9±39.8/20.8±40.3/3/ | 0.933 | 8.7                        | 0            | 39.0            | 0.783 | 0.9                        | 21.3         | 0.135 | 43.3                      | 1            | 37.7            | 0.094 |
| Glucose metabolism status, %* | -                          | -            | -              | -    | -                          | -            | -              | -    | -                          | -            | -    | -                          | -            | -    | -                          |
| Total cholesterol, mmol/L | 91.0±13.7                 | 12           | 90.7±14.0      | 0.845 | 85.1±14.6                 | 1            | 86.1±13.4       | 0.845 | 86.4±16.2                 | 7            | 82.1±18.6     | 0.028 | 88.8±14.7                 | 20           | 86.5±16.3     | 0.023 |
| High-density lipoprotein, mmol/L | 1.54±0.49               | 3            | 1.39±0.35      | <0.001 | 1.38±0.36                 | 0            | 1.34±0.43       | <0.001 | 1.19±0.32                 | 1            | 1.10±0.33     | 0.010 | 1.42±0.45                 | 4            | 1.27±0.38     | <0.001 |
| Low-density lipoprotein, mmol/L | 3.54±0.87                | 3            | 3.58±1.00      | 0.644 | 3.39±0.99                 | 0            | 3.42±1.10       | 0.644 | 2.53±0.78                 | 1            | 2.50±0.97     | 0.728 | 3.26±0.97                 | 4            | 3.13±1.12     | 0.056 |
| Triglycerides, mmol/L   | 1.01                      | 3            | 1.05±0.13      | 0.136 | 1.27                      | 0            | 1.47            | 0.082 | 1.63                      | 1            | 1.65          | 0.344 | 1.18                      | 4            | 1.35           | <0.001 |
| Total-to-HDL cholesterol ratio | 3.95±1.31               | 3            | 4.18±1.25      | 0.055 | 4.17±1.18                 | 0            | 4.38±1.35       | 0.055 | 3.93±0.94                 | 1            | 4.24±1.23     | 0.013 | 3.99±1.21                 | 4            | 4.24±1.26     | 0.001 |
| Gender, %               | 5.5±0.3                   | 3            | 5.6±0.3        | 0.005 | 5.8±0.4                   | 1            | 5.8±0.4         | 0.005 | 6.7±0.9                   | 0            | 7.1±1.1       | <0.001 | 5.9±0.7                   | 4            | 6.2±1.0       | <0.001 |
| Fasting plasma glucose, mmol/L | 5.2±0.4                  | 1            | 5.3±0.4        | 0.043 | 6.0±0.5                   | 0            | 5.9±0.6         | 0.043 | 7.6±1.7                   | 8            | 8.2±2.4       | 0.017 | 5.9±1.4                   | 2            | 6.5±2.1       | <0.001 |
| Kidney function         | 91.0±13.7                 | 12           | 90.7±14.0      | 0.845 | 85.1±14.6                 | 1            | 86.1±13.4       | 0.845 | 86.4±16.2                 | 7            | 82.1±18.6     | 0.028 | 88.8±14.7                 | 20           | 86.5±16.3     | 0.023 |
| Smoking status          | 38.9±45.5/21.4            | 5            | 30.5±48.1/14.4 | 0.085 | 29.7±54.1/16.2            | 3            | 28.6±41.3/18.2 | 0.401 | 27.8±57.4/14.8            | 15           | 19.5±64.3/14.4 | 0.222 | 34.3±51.3/14.4        | 23           | 26.3±55.2/14.4 | 0.014 |
| Alcohol use: no/low/high, % | 13.2±56.2/30.7           | 8           | 14.1±47.3/38.6 | 0.116 | 14.4±52.3/31.1            | 3            | 10.8±58.1/31.1 | 0.673 | 26.5±48.2/16.8            | 14           | 34.2±49.0/16.8 | 0.118 | 16.7±53.5/14.4        | 25           | 21.4±49.9/29.1 | 0.200 |
Moderate to vigorous physical activity, hours/week

|          | 5.5 | 69 | 5.3 | 0.425 | 4.5 | 25 | 3.0 | 0.040 | 3.6 | 74 | 3.0 | 0.021 | 4.8 | 168 | 4.5 | 0.001 |
|----------|-----|----|-----|-------|-----|----|-----|-------|-----|----|-----|-------|-----|-----|-----|-------|
| Medication | Anti-hypertensive |
| medication, % | 20 | 0 | 25 | 0.169 | 40 | 0 | 53 | 0.065 | 63 | 0 | 82 | <0.001 | 34 | 0 | 52 | <0.001 |
| RAS inhibitors, % | 13 | 0 | 17 | 0.228 | 30 | 0 | 34 | 0.558 | 51 | 0 | 68 | 0.001 | 26 | 0 | 40 | <0.001 |
| Beta-blockers, % | 6 | 0 | 12 | 0.046 | 19 | 0 | 27 | 0.176 | 33 | 0 | 37 | 0.448 | 15 | 0 | 24 | <0.001 |
| Diuretics, % | 6 | 0 | 9 | 0.211 | 16 | 0 | 21 | 0.424 | 19 | 0 | 36 | 0.001 | 11 | 0 | 21 | <0.001 |
| Calcium | 3 | 0 | 3 | 0.938 | 6 | 0 | 12 | 0.193 | 13 | 0 | 26 | 0.003 | 6 | 0 | 14 | <0.001 |
| Anticoagulants | - | - | - | - | - | - | - | - | 74 | 0 | 82 | 0.072 | 33 | 0 | 45 | <0.001 |
| Oral antidiabetics and/or insulin use | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Mobility limitation, % | 14 | 0 | 21 | 0.019 | 36 | 0 | 35 | 0.891 | 75 | 0 | 76 | 0.825 | 19 | 0 | 32 | <0.001 |
| Average E/e' ratio | 7.6±1.9 | 106 | 8.1±2.6 | 0.055 | 8.6±2.4 | 42 | 8.3±2.3 | 0.647 | 8.9±2.3 | 96 | 10.0±3.5 | 0.013 | 8.1±2.2 | 244 | 8.9±3.0 | 0.001 |
| Diastolic LV function | 162/161/42 | 27/51/11 | 25/67/19 | 10/21/6 | 38/92/32 | 16/41/18 | 225/321/93 | 53/113/35 |
| (normal, indeterminate, abnormal), n (%) | (44.4/44.1/103) | (30.5/37.3/103) | (22.5/60.4/40) | (27.0/56.8/856) | (23.5/56.8/94) | (21.3/54.7/748) | (35.2/55.2/237) | (26.4/56.2/0.064) |
| Cardiorespiratory fitness | 168.9±48.6 | 85 | 158.7±46.8 | 0.055 | 168.8±46.1 | 42 | 159.8±57.8 | 0.055 | 158.1±42.7 | 101 | 156.3±50.6 | 0.003 | 166.2±46.9 | 228 | 158.1±49.8 | 0.034 |
| Cardiorespiratory fitness adjusted for body mass | 2.28±0.55 | 85 | 2.13±0.57 | 0.012 | 2.08±0.48 | 42 | 2.00±0.72 | 0.605 | 1.89±0.49 | 101 | 1.73±0.54 | 0.034 | 2.15±0.55 | 228 | 1.98±0.61 | <0.001 |

Data are presented as mean ± SD, median [interquartile-range] or frequencies (in %) as appropriate. Data present the tissue Doppler imaging echocardiography study population for regression models 1-3. Significant difference between the tissue Doppler imaging echocardiography study population and excluded individuals with missing values in models 1 to 3 was tested by independent t-test or chi-square test as appropriate. Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin A1c; HDL, high-density lipoprotein; MINI, mini-international neuropsychiatric interview; NGM, normal glucose metabolism; PHQ, patient health questionnaire; T2D, type 2 diabetes. *The total number of missing in the study population is listed here. For the covariates included in regression models 1 to 3, the number of individuals available in the excluded group was 192/77/162/438 for respectively normal glucose metabolism, prediabetes, type 2 diabetes and the total study population, minus the number of missing in the study population. For the covariates not included in regression models 1 to 3, the number of individuals available in the study population and in regression models 1 to 3 are indicated with footnotes to it for respectively normal glucose metabolism, prediabetes, type 2 diabetes and the total study population. †=Educational level was available in 365/111/162/638 in the study population and 192/77/169/438 in the excluded group; ‡=Current atrial fibrillation or flutter was available in 350/103/157/610 in the study population and 184/74/161/419 in the excluded group; §=24-hour blood pressure measurements were available in 340/101/149/590 in the study population and 175/68/149/392 in the excluded group; ||=HbA1c was available in 365/110/162/637 in the study population and 190/77/169/436 in the excluded group; ||=Fasting plasma glucose was available in 366/111/162/639 in the study population and in 89/37/75/201 in the excluded group; |||=in the excluded group 107/35/68/210 were excluded due to missing on echocardiographic analyses or covariates.
### Table S5. Clinical characteristics of the study population with 2D echocardiography and individuals excluded from analyses due to missing values

| Demographics | Normal glucose metabolism | Prediabetes | Type 2 Diabetes | Total study population |
|--------------|---------------------------|-------------|-----------------|------------------------|
| Men, %       | Included (N=380) 24 0 48 | Included (N=115) 59 0 60 | Included (N=177) 68 0 70 | Included (N=672) 52 0 58 |
| Age, years   | Number of missings 0.232  | Number of missings 0.876  | Number of missings 0.813  | Number of missings 0.043  |
| Educational level, %** | Excluded (N=178) 58±9 0.526 | Excluded (N=73) 62±8 0.890  | Excluded (N=154) 63±7 0.081  | Excluded (N=405) 59±8 0.007  |
| Glucose metabolism status, N/CD/pre diabetes/T2D, % | - | - | - | - |
| Prior cardiovascular disease, % | Included (N=178) 10 16 13 | Included (N=73) 15 6 21 | Included (N=154) 20 23 41 | Included (N=405) 13 45 25 |
| Prior coronary heart disease, % | Included (N=178) 3 1 7 | Included (N=73) 6 0 7 | Included (N=154) 10 1 16 | Included (N=405) 6 2 10 |
| Current atrial fibrillation or flutter, %** | Included (N=178) 0 24 1.8 | Included (N=73) 0 11 2.9 | Included (N=154) 1.2 13 4.1 | Included (N=405) 0.3 48 2.8 |
| Blood pressure | | | | |
| Office systolic pressure, mmHg | Included (N=380) 130±16 0 | Included (N=115) 138±16 1 | Included (N=177) 144±17 0 | Included (N=672) 135±17 1 |
| Office diastolic pressure, mmHg | Included (N=380) 75±10 0 | Included (N=115) 79±10 1 | Included (N=177) 79±9 0 | Included (N=672) 76±10 1 |
| 24-hour systolic pressure, mmHg | Included (N=380) 116±11 43 | Included (N=115) 121±13 19 | Included (N=177) 122±11 33 | Included (N=672) 118±11 95 |
| 24-hour diastolic pressure, mmHg | Included (N=380) 73±8 43 | Included (N=115) 77±5 20 | Included (N=177) 73±7 33 | Included (N=672) 74±7 95 |
| Hypertension, % | Included (N=380) 37 0 46 | Included (N=115) 61 0 72 | Included (N=177) 80 0 94 | Included (N=672) 53 1 69 |
| Metabolic variables | | | | |
| BMI, kg/m² | Included (N=380) 25.6±3.7 0 | Included (N=115) 26.3±3.8 0 | Included (N=177) 28.1±4.5 0 | Included (N=672) 26.9±4.1 1 |
| Waist, cm | Included (N=380) 90.9±10.9 2 | Included (N=115) 98.8±11.6 0 | Included (N=177) 104.2±11.4 1 | Included (N=672) 95.7±12.6 3 |
| Total cholesterol, mmol/L | Included (N=380) 5.59±1.00 3 | Included (N=115) 5.47±1.11 0 | Included (N=177) 4.49±0.92 1 | Included (N=672) 5.28±1.11 4 |
| High-density lipoprotein, mmol/L | Included (N=380) 1.53±0.48 3 | Included (N=115) 1.39±0.37 0 | Included (N=177) 1.18±0.31 1 | Included (N=672) 1.41±0.45 4 |
| Low-density lipoprotein, mmol/L | Included (N=380) 3.54±0.88 3 | Included (N=115) 3.39±1.00 0 | Included (N=177) 2.54±0.79 1 | Included (N=672) 3.25±0.98 4 |
| Triglycerides, mmol/L | Included (N=380) 1.01 [0.76;1.41] 3 | Included (N=115) 1.32 [0.90;1.79] 0 | Included (N=177) 1.66 [1.17;2.09] 0 | Included (N=672) 1.19 [0.85;1.75] 4 |
| Total-to-HDL cholesterol ratio | Included (N=380) 3.96±1.30 3 | Included (N=115) 4.15±1.17 0 | Included (N=177) 3.95±0.95 1 | Included (N=672) 3.99±1.20 4 |
| Hba1C, in % | Included (N=380) 5.52±0.3 3 | Included (N=115) 5.90±0.4 1 | Included (N=177) 6.8±1.0 0 | Included (N=672) 5.9±0.8 4 |
| Fasting plasma glucose, mmol/L | Included (N=380) 5.2±0.4 1 | Included (N=115) 5.0±0.4 0 | Included (N=177) 7.8±2.0 1 | Included (N=672) 6.0±1.5 2 |
| Kidney function | Included (N=380) 91.0±13.9 12 | Included (N=115) 85.5±14.1 1 | Included (N=177) 86.3±16.3 7 | Included (N=672) 88.8±14.8 20 |
| eGFR, ml/min 1.73m² | Included (N=380) 3.2 5 | Included (N=115) 5.2 1 | Included (N=177) 16.9 7 | Included (N=672) 7.1 13 |
| Albuminuria, % | Included (N=380) 38.6/46.2/15.0 5 | Included (N=115) 26.8/31.0/4.5 3 | Included (N=177) 25.6/31.0/4.5 15 | Included (N=672) 25.7/31.0/4.5 15 |
| Smoking status: never/former/current, % | Included (N=380) 39.5/45.5/5.0 3 | Included (N=115) 28.7/31.0/4.5 3 | Included (N=177) 26.6/59.3/4.5 15 | Included (N=672) 34.1/57.8/4.5 23 |
| Alcohol use: no/low/high, % | Included (N=380) 31.8/62.0/6.2 8 | Included (N=115) 14.1/49.4/6.5 3 | Included (N=177) 32.9/50.7/6.4 14 | Included (N=672) 20.8/52.1/7.1 25 |
Cardiorespiratory fitness
Maximum tricuspid LV mass index, gr/m²

| Physical activity, hours/week² | 5.4  | 5.5  | 4.5  | 3.0  | 0.087 | 3.0  | 0.048 | 4.6  | 0.007 |
|-------------------------------|------|------|------|------|-------|------|-------|------|-------|
|                               | [3.0, 8.9] | [3.0, 8.6] | [2.3, 8.6] | [1.5, 7.0] | [2.3, 8.5] | [1.4, 5.8] | [3.0, 7.8] | [1.6, 7.5] |      |

Medication
Anti-hypertensive medication, %
RAS inhibitors, %
Beta-blockers, %
Diuretics, %
Calcium  antagonists, %
Oral antidiabetics and/or insulin use
Lipid-modifying medication, %

Mobility limitation, %¹
LA volume index, m²/m³
Total
Men
Women
LV mass index, gr/m²
Total
Men
Women
LV mass index, gr/m²
Total
Men
Women

Data are presented as mean ± SD, [interquartile-range] or frequencies (in %) as appropriate. Data present the two-dimensional echocardiography study population for regression models 1-3. Significant difference between the tissue Doppler imaging echocardiography study population and excluded individuals with missing values in models 1 to 3 was tested by independent t-test or chi-square test as appropriate. Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin A1c; HDL, high-density lipoprotein; MINI, mini-international neuropsychiatric interview; NGM, normal glucose metabolism; PHQ, patient health questionnaire; T2D, type 2 diabetes.

¹Mobility limitation was available in 378/114/176/668 in the study population and 167/68/130/365 in the excluded group; ²Moderate to vigorous physical activity was available in 336/96/151/583 in the study population and in 153/67/106/326 in the excluded group; ³Fasting plasma glucose was available in 380/115/177/672 in the study population and 177/73/153/403 in the excluded group; ⁴Moderate to vigorous physical activity was available in 336/96/151/583 in the study population and in 153/67/106/326 in the excluded group; ⁵=93/31/53/177 were excluded due to missing on echocardiographic analyses or covariate.
Table S6. Interaction effects between measures of LV diastolic function and glucose metabolism status (NGM as reference) in the associations with cardiorespiratory fitness

| Measure                                | Model | B       | 95% CI          | P    | B       | 95% CI          | P    |
|----------------------------------------|-------|---------|-----------------|------|---------|-----------------|------|
| Average E/e’-ratio                     | 2     | 0.022   | (-0.021;0.065)  | 0.310| 0.023   | (-0.017;0.062)  | 0.258|
| e’ average, cm/s                       | 2     | 0.008   | (-0.039;0.055)  | 0.731| -0.027  | (-0.073;0.018)  | 0.239|
| Maximum tricuspid regurgitation flow, m/s | 2     | -0.152  | (-0.341;0.037)  | 0.115| -0.070  | (-0.245;0.105)  | 0.432|
| LA volume index, ml/m²                 | 2     | -0.017  | (-0.031;-0.003) | 0.016| -0.011  | (-0.023;0.001)  | 0.069|
| LV mass index, gr/m²²                  | 2     | -0.010  | (-0.024;0.004)  | 0.179| -0.012  | (-0.024;-0.012) | 0.065|
| LV mass index, gr/m²²                  | 2     | -0.005  | (-0.011;0.002)  | 0.179| -0.020  | (-0.012;-0.001) | 0.021|
| Diastolic function 2016 guidelines     |       |         |                 |      |         |                 |      |
| Indeterminate                          | 2     | -0.163  | (-0.337;0.012)  | 0.131| -0.122  | (-0.321;0.077)  | 0.230|
| Abnormal                               | 2     | -0.183  | (-0.493;0.126)  | 0.246| -0.146  | (-0.409;0.117)  | 0.277|

N=672 or 639 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the interaction effect between one unit higher level of measure of diastolic function (or for diastolic function according to 2016 guidelines versus normal diastolic function) and (pre)diabetes as compared to normal glucose metabolism, in the association with cardiorespiratory fitness in Wmax/kg. Model 2: adjusted for age, sex, height, prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic pressure, use of antihypertensive medication, albuminuria and interaction term between measure of diastolic function and glucose metabolism status.

Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.
Table S7. Associations between measures of LV diastolic function and cardiorespiratory fitness (Wmax/kg) in the total study population

| Model | B     | 95% CI     | P       |
|-------|-------|------------|---------|
| Average E/e’-ratio | | | |
| 1     | -0.048 | (-0.066;-0.030) | <0.001 |
| 2     | -0.037 | (-0.055;-0.018) | <0.001 |
| 3     | -0.025 | (-0.043;-0.008) | 0.005   |
| e’ average, cm/s | | | |
| 1     | 0.033  | (-0.013;-0.054) | 0.002   |
| 2     | 0.013  | (-0.008;0.035)  | 0.222   |
| 3     | 0.007  | (-0.013;0.027)  | 0.501   |
| Maximum tricuspid regurgitation flow, m/s | | | |
| 1     | 0.103  | (0.023;0.183)   | 0.011   |
| 2     | 0.070  | (-0.008;0.147)  | 0.080   |
| 3     | 0.047  | (-0.024;0.118)  | 0.194   |
| LA volume index, ml/m² | | | |
| 1     | 0.010  | (0.005;0.016)   | <0.001  |
| 2     | 0.008  | (0.003;0.014)   | 0.003   |
| 3     | 0.007  | (0.002;0.011)   | 0.009   |
| LV mass index, gr/m²² | | | |
| 1     | 0.000  | (-0.006;0.005)  | 0.894   |
| 2     | 0.003  | (-0.003;0.009)  | 0.291   |
| 3     | 0.010  | (0.004;0.015)   | <0.001  |
| Diastolic function 2016 guidelines | | | |
| Indeterminate | | | |
| 1     | -0.056 | (-0.142;0.030)  | 0.202   |
| 2     | -0.018 | (-0.102;0.066)  | 0.676   |
| 3     | 0.035  | (-0.043;0.113)  | 0.378   |
| Abnormal | | | |
| 1     | 0.022  | (-0.099;0.144)  | 0.720   |
| 2     | 0.073  | (-0.046;0.192)  | 0.231   |
| 3     | 0.093  | (-0.018;0.203)  | 0.099   |

N=672 or 639 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the difference in cardiorespiratory fitness in Wmax/kg per one unit higher level of measure of diastolic dysfunction, and for diastolic function according to 2016 guidelines versus normal diastolic function. Model 1: age, sex, height; Model 2: model 1 + prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic pressure, use of antihypertensive medication, albuminuria; model 3: model 2 + waist. Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.
Table S8. Associations between measures of LV diastolic function and cardiorespiratory fitness (Wmax/kg) – additional analyses with unindexed or other indexed measures of diastolic function

| Model | Normal glucose metabolism (N=380) | Prediabetes (N=115) | Type 2 diabetes (N=177) |
|-------|-----------------------------------|---------------------|-------------------------|
|       | B 95% CI  P                       | B 95% CI  P         | B 95% CI  P            |
| LA volume index, ml/m² | | | |
| 1 | 0.017 (0.010;0.025) <0.001 | -0.003 (-0.015;0.010) 0.674 | 0.003 (-0.008;0.014) 0.516 |
| 2 | 0.015 (0.008;0.022) <0.001 | -0.007 (-0.021;0.008) 0.357* | 0.001 (-0.009;0.012) 0.804* |
| 3 | 0.014 (0.007;0.021) <0.001 | -0.006 (-0.018;0.007) 0.358 | -0.002 (-0.011;0.007) 0.618 |
| LA volume, ml | | | |
| 1 | 0.003 (-0.001;0.007) 0.088 | -0.006 (-0.011;0.000) 0.057 | -0.004 (-0.009;0.001) 0.158 |
| 2 | 0.004 (0.000;0.008) 0.063 | -0.007 (-0.014;-0.001) 0.026* | -0.004 (-0.009;0.001) 0.145* |
| 3 | 0.007 (0.010;0.010) <0.001 | -0.003 (-0.009;0.002) 0.247 | -0.002 (-0.006;0.003) 0.412 |
| LV mass index, gr/m² | | | |
| 1 | 0.005 (-0.003;0.013) 0.224 | -0.002 (-0.015;0.011) 0.722 | -0.009 (-0.020;0.002) 0.097 |
| 2 | 0.009 (0.001;0.017) 0.035 | 0.001 (-0.013;0.015) 0.857 | -0.006 (-0.017;0.005) 0.259* |
| 3 | 0.015 (0.008;0.023) <0.001 | 0.009 (-0.004;0.022) 0.166 | 0.001 (-0.009;0.010) 0.859 |
| LV mass index, gr/m² | | | |
| 1 | 0.008 (0.005;0.012) <0.001 | 0.004 (-0.002;0.011) 0.171 | 0.001 (-0.004;0.007) 0.567 |
| 2 | 0.009 (0.005;0.012) <0.001 | 0.006 (-0.001;0.013) 0.904 | 0.002 (-0.003;0.007) 0.416* |
| 3 | 0.008 (0.005;0.011) <0.001 | 0.005 (-0.001;0.011) 0.128 | 0.001 (-0.003;0.006) 0.587 |
| LV mass, gr | | | |
| 1 | 0.001 (0.000;0.003) 0.125 | -0.001 (-0.004;0.002) 0.641 | -0.002 (-0.004;0.000) 0.885 |
| 2 | 0.002 (0.000;0.004) 0.016 | 0.000 (-0.003;0.004) 0.939* | -0.001 (-0.004;0.001) 0.236* |
| 3 | 0.004 (0.002;0.005) <0.001 | 0.002 (-0.001;0.005) 0.222 | 0.000 (-0.002;0.002) 0.897 |

N=672 or 639 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the difference in cardiorespiratory fitness in Wmax/kg per one unit higher level of measure of diastolic function. Model 1: age, sex, height; Model 2: model 1 + prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic pressure, use of antihypertensive medication, albuminuria; model 3: model 2 + waist.

Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.

*Pinteraction<0.10, represents the P-value of the interaction effect between measures of diastolic function and (pre)diabetes as compared to normal glucose metabolism in the association with cardiorespiratory fitness.
Table S9. Associations between measures of LV diastolic function and cardiorespiratory fitness as % of predicted value Wmax

|                         | Normal glucose metabolism (N=380/366) | Prediabetes (N=115/111) | Type 2 diabetes (N=177/162) |
|-------------------------|---------------------------------------|--------------------------|-------------------------------|
|                         | B         | 95% CI       | P          | B         | 95% CI        | P          | B         | 95% CI       | P          |
| **Average E/e′-ratio**  |                        |                          |            |                        |                          |            |                        |                          |            |
| 1                       | -1.058    | (-2.388;0.271) | 0.118      | -0.850    | (-3.536;1.835) | 0.532      | -0.497    | (-2.397;1.404) | 0.607      |
| 2                       | -1.337    | (-2.743;0.069) | 0.062      | 0.065    | (-3.025;3.155) | 0.967      | -1.044    | (-3.028;0.940) | 0.300      |
| 3                       | -1.513    | (-2.923;-0.103) | 0.035      | -0.248    | (-3.392;2.897) | 0.876      | -0.887    | (-2.858;1.085) | 0.375      |
| **e′ average, cm/s**    |                        |                          |            |                        |                          |            |                        |                          |            |
| 1                       | -0.428    | (-1.751;0.895) | 0.525      | 0.432    | (-2.945;3.809) | 0.800      | -0.520    | (-2.942;1.901) | 0.672      |
| 2                       | -0.137    | (-1.600;1.327) | 0.854      | -0.564    | (-4.620;3.492) | 0.783      | -0.485    | (-3.085;2.116) | 0.713      |
| 3                       | -0.089    | (-1.549;1.371) | 0.905      | -0.337    | (-4.416;3.742) | 0.870      | -0.556    | (-3.129;2.017) | 0.670      |
| **Maximum tricuspid regurgitation flow, m/s** |                        |                          |            |                        |                          |            |                        |                          |            |
| 1                       | 4.710     | (-1.014;10.434) | 0.107      | -5.746    | (-16.742;5.251) | 0.303      | -0.964    | (-9.213;7.286) | 0.818      |
| 2                       | 5.576     | (-0.276;11.427) | 0.062      | -7.754    | (-19.869;4.361) | 0.207      | -2.736    | (-11.161;5.688) | 0.522      |
| 3                       | 6.003     | (0.183;11.823) | 0.043      | -7.679    | (-19.878;4.521) | 0.215      | -2.732    | (-11.116;5.652) | 0.521      |
| **LA volume index, ml/m²** |                        |                          |            |                        |                          |            |                        |                          |            |
| 1                       | 0.556     | (0.190;0.923) | 0.003      | -0.307    | (-1.187;0.573) | 0.491      | -0.091    | (-0.664;0.481) | 0.753      |
| 2                       | 0.609     | (0.230;0.989) | 0.002      | -0.465    | (-1.454;0.524) | 0.353*     | -0.173    | (-0.753;0.407) | 0.556      |
| 3                       | 0.629     | (0.253;1.006) | 0.001      | -0.468    | (-1.462;0.526) | 0.352      | -0.224    | (-0.803;0.356) | 0.447      |
| **LV mass index, gr/m²** |                        |                          |            |                        |                          |            |                        |                          |            |
| 1                       | 0.907     | (0.525;1.288) | <0.001     | 0.526     | (-0.369;1.420) | 0.247      | -0.017    | (-0.585;0.551) | 0.952      |
| 2                       | 0.993     | (0.599;1.386) | <0.001     | 1.012     | (0.038;1.986) | 0.042*     | 0.026     | (-0.576;0.627) | 0.933*     |
| 3                       | 0.932     | (0.529;1.334) | <0.001     | 1.031     | (0.027;2.034) | 0.044      | 0.125     | (-0.485;0.735) | 0.686      |

Diastolic function 2016 guidelines

|                        | Model 1 | Model 2 | Model 3 |
|------------------------|---------|---------|---------|
| **Indeterminate**      |         |         |         |
| 1                      | 5.555   | (0.164;10.947) | 0.043      | 2.853    | (-12.072;17.779) | 0.705      | -3.819    | (-13.840;6.203) | 0.453      |
| 2                      | 5.056   | (-0.469;10.582) | 0.073      | -1.388   | (-17.184;14.408) | 0.862      | -3.372    | (-13.738;6.994) | 0.521      |
| **Abnormal**           |         |         |         |
| 1                      | 4.480   | (-1.074;10.033) | 0.114      | -2.827   | (-18.814;13.161) | 0.726      | -2.430    | (-12.725;7.865) | 0.641      |
| 2                      | 10.191  | (1.879;18.504) | 0.016      | 3.278    | (-16.501;23.057) | 0.743      | -7.991    | (-20.689;4.706) | 0.216      |
| 3                      | 10.763  | (2.292;19.234) | 0.013      | 5.380    | (-15.103;25.864) | 0.603      | -7.676    | (-20.698;5.345) | 0.246*     |
| 4                      | 10.604  | (2.152;19.056) | 0.014      | 4.706    | (-15.790;25.203) | 0.649      | -7.504    | (-20.387;5.378) | 0.251      |

N=672 or 639 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the difference in cardiorespiratory fitness in Wmax/kg per one unit higher level of measure of diastolic function, and for diastolic function according to 2016 guidelines versus normal diastolic function. Model 1: age, sex, height; Model 2: model 1 + prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic pressure, use of antihypertensive medication, albuminuria; model 3: model 2 + waist. Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.

*Pinteraction<0.04, represents the P-value of the interaction effect between measures of diastolic function and (pre)diabetes as compared to normal glucose metabolism in the association with cardiorespiratory fitness.
| Model | Normal glucose metabolism (N=380/366) | Prediabetes (N=115/111) | Type 2 diabetes (N=177/162) |
|-------|--------------------------------------|--------------------------|-----------------------------|
|       | B         | 95% CI       | P         | B         | 95% CI       | P         | B         | 95% CI       | P         |
| Average E/e'-ratio |
| 2     | -0.044    | (-0.071;-0.016) | 0.002    | -0.030    | (-0.072;0.012) | 0.156    | -0.037    | (-0.072;-0.001) | 0.043    |
| 2a    | -0.039    | (-0.067;-0.010) | 0.008    | -0.025    | (-0.070;0.020) | 0.280    | -0.032    | (-0.071;0.006) | 0.101    |
| 2b    | -0.045    | (-0.075;-0.016) | 0.003    | -0.033    | (-0.076;0.010) | 0.135    | -0.048    | (-0.087;-0.009) | 0.015    |
| 2c    | -0.042    | (-0.070;-0.014) | 0.003    | -0.028    | (-0.070;0.014) | 0.185    | -0.038    | (-0.074;-0.001) | 0.041    |
| 2d    | -0.044    | (-0.072;-0.016) | 0.002    | -0.033    | (-0.074;0.009) | 0.120    | -0.035    | (-0.072;0.002) | 0.063    |
| 2e    | -0.037    | (-0.066;-0.008) | 0.012    | -0.026    | (-0.070;0.018) | 0.242    | -0.034    | (-0.069;0.001) | 0.059    |
| 2f    | -0.046    | (-0.076;-0.017) | 0.002    | -0.036    | (-0.099;0.026) | 0.251    | -0.023    | (-0.062;0.016) | 0.246    |
| 2g    | -0.044    | (-0.071;-0.016) | 0.002    | -0.036    | (-0.077;0.005) | 0.086    | -0.035    | (-0.070;0.000) | 0.047    |
| 2h    | -0.049    | (-0.079;-0.023) | 0.001    | -0.038    | (-0.078;0.003) | 0.066    | -0.036    | (-0.071;-0.001) | 0.041    |
| 2i    | -0.051    | (-0.080;-0.025) | <0.001   | -0.029    | (-0.075;0.017) | 0.218    | -0.034    | (-0.071;0.004) | 0.077    |
| 2j    | -0.049    | (-0.077;-0.021) | <0.001   | -0.028    | (-0.073;0.018) | 0.230    | -0.032    | (-0.069;0.005) | 0.088    |
| 2k    | -0.044    | (-0.071;-0.017) | 0.002    | -0.031    | (-0.073;0.011) | 0.148    | -0.037    | (-0.073;0.001) | 0.042    |
| 2l    | -0.044    | (-0.072;-0.016) | 0.002    | -0.028    | (-0.070;0.015) | 0.202    | -0.037    | (-0.073;-0.002) | 0.041    |

| 3     | -0.033    | (-0.060;-0.007) | 0.014    | -0.015    | (-0.055;0.025) | 0.450    | -0.028    | (-0.059;0.003) | 0.077    |
| 3a    | -0.029    | (-0.055;-0.002) | 0.033    | -0.016    | (-0.056;0.023) | 0.409    | -0.023    | (-0.054;0.009) | 0.156    |
| 3b    | -0.029    | (-0.055;-0.002) | 0.035    | -0.017    | (-0.056;0.022) | 0.394    | -0.020    | (-0.052;0.011) | 0.207    |

| E' average cm/s |
|-----------------|
| 2               | 0.013    | (-0.016;0.042) | 0.388    | 0.040    | (-0.016;0.095) | 0.158    | -0.010    | (-0.057;0.037) | 0.662    |
| 2a              | 0.014    | (-0.016;0.044) | 0.347    | 0.038    | (-0.026;0.101) | 0.240    | -0.020    | (-0.068;0.027) | 0.403    |
| 2b              | 0.014    | (-0.016;0.044) | 0.357    | 0.036    | (-0.021;0.092) | 0.217    | -0.003    | (-0.055;0.049) | 0.914    |
| 2c              | 0.010    | (-0.019;0.040) | 0.492    | 0.021    | (-0.038;0.080) | 0.483    | -0.004    | (-0.053;0.045) | 0.878    |
| 2d              | 0.013    | (-0.016;0.042) | 0.385    | 0.034    | (-0.021;0.089) | 0.227    | -0.014    | (-0.062;0.033) | 0.551    |
| 2e              | 0.009    | (-0.021;0.039) | 0.546    | 0.039    | (-0.017;0.096) | 0.172    | -0.010    | (-0.058;0.037) | 0.664    |
| 2f              | 0.019    | (-0.012;0.050) | 0.233    | 0.071    | (-0.006;0.137) | 0.033    | -0.023    | (-0.077;0.032) | 0.413    |
| 2g              | 0.012    | (-0.018;0.041) | 0.430    | 0.039    | (-0.017;0.095) | 0.168    | -0.013    | (-0.060;0.034) | 0.585    |
| 2h              | 0.018    | (-0.011;0.047) | 0.217    | 0.049    | (-0.005;0.102) | 0.073    | -0.009    | (-0.055;0.038) | 0.714    |
| 2i              | 0.027    | (-0.002;0.057) | 0.066    | 0.030    | (-0.025;0.085) | 0.286    | -0.008    | (-0.057;0.041) | 0.748    |
| 2j              | 0.025    | (-0.005;0.054) | 0.098    | 0.030    | (-0.025;0.086) | 0.282    | -0.009    | (-0.058;0.040) | 0.717    |
|   | 2k | 2l | 3 | 3a | 3b |
|---|----|----|---|----|----|
|   | 0.013 | (-0.016;0.042) | 0.381 | 0.041 | (-0.014;0.096) | 0.146 | -0.009 | (-0.057;0.038) | 0.697 |
|   | 0.015 | (-0.014;0.024) | 0.318 | 0.040 | (-0.015;0.096) | 0.149 | -0.010 | (-0.057;0.038) | 0.688 |
|   | **0.009** | (-0.018;0.037) | **0.501** | **0.028** | (-0.023;0.079) | **0.280** | **-0.014** | (-0.055;0.026) | **0.487** |
|   | 0.007 | (-0.021;0.034) | 0.622 | 0.035 | (-0.016;0.086) | 0.174 | -0.014 | (-0.055;0.027) | 0.508 |
|   | 0.007 | (-0.020;0.034) | 0.622 | 0.033 | (-0.017;0.084) | 0.196 | -0.015 | (-0.056;0.025) | 0.453 |

**Maximum tricuspid regurgitation flow, m/s**

|   | 2  | 2a | 2b | 2c | 2d | 2e | 2f | 2g | 2h | 2i | 2j | 2k | 2l | 3  | 3a | 3b |
|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
|   | **0.137** | (0.023;0.252) | **0.019** | **-0.054** | (-0.213;0.134) | **0.653** | **-0.021** | (-0.175;0.133) | **0.785** |
|   | 0.141 | (0.023;0.259) | 0.020 | 0.044 | (-0.146;0.235) | 0.645 | -0.139 | (-0.305;0.027) | 0.101 |
|   | 0.132 | (0.016;0.249) | 0.026 | -0.059 | (-0.238;0.119) | 0.513 | -0.026 | (-0.189;0.138) | 0.758 |
|   | 0.134 | (0.019;0.249) | 0.022 | -0.077 | (-0.252;0.097) | 0.382 | -0.023 | (-0.184;0.138) | 0.779 |
|   | 0.138 | (0.023;0.253) | 0.019 | -0.060 | (-0.235;0.115) | 0.499 | -0.023 | (-0.180;0.134) | 0.772 |
|   | 0.146 | (0.028;0.265) | 0.016 | -0.017 | (-0.192;0.158) | 0.847 | 0.019 | (-0.139;0.177) | 0.809 |
|   | 0.209 | (0.084;0.335) | 0.001 | -0.069 | (-0.298;0.161) | 0.552 | -0.016 | (-0.200;0.168) | 0.865 |
|   | 0.142 | (0.027;0.256) | 0.016 | -0.028 | (-0.198;0.143) | 0.749 | -0.025 | (-0.179;0.129) | 0.746 |
|   | 0.129 | (0.015;0.243) | 0.027 | -0.023 | (-0.198;0.151) | 0.791 | -0.022 | (-0.175;0.131) | 0.776 |
|   | 0.142 | (0.021;0.262) | 0.022 | -0.042 | (-0.233;0.149) | 0.664 | -0.027 | (-0.189;0.134) | 0.738 |
|   | 0.142 | (0.021;0.262) | 0.021 | -0.040 | (-0.229;0.149) | 0.677 | -0.023 | (-0.184;0.137) | 0.774 |
|   | 0.141 | (0.027;0.255) | 0.016 | -0.062 | (-0.235;0.110) | 0.475 | -0.024 | (-0.181;0.132) | 0.761 |
|   | 0.137 | (0.022;0.252) | 0.019 | -0.040 | (-0.216;0.135) | 0.648 | -0.022 | (-0.176;0.133) | 0.784 |
|   | **0.114** | (0.007;0.222) | **0.037** | **-0.064** | (-0.218;0.090) | **0.411** | **-0.021** | (-0.153;0.111) | **0.754** |
|   | 0.108 | (0.001;0.216) | 0.048 | -0.044 | (-0.198;0.111) | 0.578 | -0.021 | (-0.154;0.112) | 0.758 |
|   | 0.107 | (0.000;0.214) | 0.051 | -0.048 | (-0.202;0.107) | 0.542 | -0.024 | (-0.156;0.107) | 0.718 |

N=672, 380/115/177 or 639, 366/111/162 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the difference in cardiorespiratory fitness in Wmax/kg per one unit higher level of measure of diastolic function, and for diastolic function according to 2016 guidelines versus normal diastolic function. Model 1: age, sex, height; Model 2: model 1 + prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic blood pressure, use of antihypertensive medication, albuminuria; Model 2a: additional adjustment for moderate to vigorous physical activity (N=336/96/151 or N=322/94/138); Model 2b: exclusion of individuals with prior coronary heart disease (N=368/96/151 or N=355/104/148); Model 2c: exclusion of individuals with atrial fibrillation (N=364/107/169 or N=350/103/155); Model 2d: exclusion of individuals with wall abnormalities (N=377/114/173 or N=365/110/159); Model 2e: exclusion of individuals with valvular dysfunction (N=356/108/168 or N=343/104/154); Model 2f: exclusion of individuals with mobility limitations (N=332/83/122 or N=320/82/114); Model 2g: replacement of office systolic pressure with office diastolic pressure; Model 2h: replacement of office systolic pressure and antihypertensive medication with presence of hypertension; Model 2i: replacement of office systolic pressure with 24-hour diastolic pressure (N=351/103/163 or N=340/101/149); Model 2j: replacement of office systolic pressure with 24-hour diastolic pressure (N=351/103/163 or N=340/101/149); Model 2k: additional adjustment for renin-angiotensin-system-inhibitors; Model 3: model 2 + waist; Model 3a: replacement of waist with body mass index; Model 3b replacement of waist with weight.

Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.
### Table S11. Additional analyses in the associations between measures of LV diastolic function and cardiorespiratory fitness

|                  | Normal glucose metabolism (N=380/366) | Prediabetes (N=115/111) | Type 2 diabetes (N=177/162) |
|------------------|---------------------------------------|--------------------------|----------------------------|
|                  | Model                                 | B           | 95% CI            | P              | B           | 95% CI            | P              | B           | 95% CI            | P              |
| LA volume index, ml/m² | 2                                     | 0.015       | (0.008;0.022)    | <0.001         | -0.007       | (-0.021;0.008) | 0.357          | 0.001       | (-0.009;0.012)    | 0.804          |
|                  | 2a                                    | 0.014       | (0.006;0.022)    | <0.001         | 0.008        | (-0.010;0.025) | 0.327          | -0.002      | (-0.014;0.009)    | 0.662          |
|                  | 2b                                    | 0.015       | (0.008;0.023)    | <0.001         | -0.004       | (-0.019;0.010) | 0.580          | 0.000       | (-0.011;0.012)    | 0.935          |
|                  | 2c                                    | 0.014       | (0.007;0.022)    | <0.001         | -0.006       | (-0.021;0.008) | 0.384          | 0.005       | (-0.007;0.017)    | 0.432          |
|                  | 2d                                    | 0.015       | (0.007;0.022)    | <0.001         | -0.006       | (-0.020;0.009) | 0.434          | 0.003       | (-0.008;0.014)    | 0.580          |
|                  | 2e                                    | 0.016       | (0.008;0.024)    | <0.001         | 0.000        | (-0.016;0.016) | 0.982          | 0.005       | (-0.007;0.018)    | 0.398          |
|                  | 2f                                    | 0.016       | (0.008;0.023)    | <0.001         | -0.011       | (-0.027;0.006) | 0.206          | -0.002      | (-0.014;0.010)    | 0.726          |
|                  | 2g                                    | 0.014       | (0.006;0.021)    | <0.001         | -0.009       | (-0.023;0.005) | 0.220          | 0.001       | (-0.010;0.011)    | 0.881          |
|                  | 2h                                    | 0.014       | (0.007;0.022)    | <0.001         | -0.005       | (-0.019;0.009) | 0.467          | 0.002       | (-0.009;0.012)    | 0.757          |
|                  | 2i                                    | 0.015       | (0.007;0.022)    | <0.001         | -0.001       | (-0.015;0.014) | 0.901          | 0.000       | (-0.011;0.011)    | 0.968          |
|                  | 2j                                    | 0.015       | (0.007;0.023)    | <0.001         | -0.001       | (-0.016;0.013) | 0.896          | 0.000       | (-0.011;0.011)    | 0.988          |
|                  | 2k                                    | 0.014       | (0.007;0.022)    | <0.001         | -0.008       | (-0.022;0.006) | 0.273          | 0.001       | (-0.010;0.012)    | 0.822          |
|                  | 2l                                    | 0.015       | (0.007;0.022)    | <0.001         | -0.007       | (-0.021;0.008) | 0.361          | 0.001       | (-0.009;0.012)    | 0.808          |
|                  | 3                                     | 0.014       | (0.007;0.021)    | <0.001         | -0.006       | (-0.018;0.007) | 0.358          | -0.002      | (-0.011;0.007)    | 0.618          |
|                  | 3a                                    | 0.014       | (0.007;0.021)    | <0.001         | -0.004       | (-0.017;0.008) | 0.485          | 0.001       | (-0.008;0.010)    | 0.818          |
|                  | 3b                                    | 0.014       | (0.007;0.021)    | <0.001         | -0.005       | (-0.017;0.008) | 0.476          | 0.001       | (-0.008;0.010)    | 0.890          |
| LV mass index, gr/m² | 2                                     | 0.009       | (0.001;0.017)    | 0.035          | 0.001       | (-0.013;0.015) | 0.857          | -0.006      | (-0.017;0.005)    | 0.259          |
|                  | 2a                                    | 0.009       | (0.001;0.017)    | 0.035          | 0.010       | (-0.005;0.024) | 0.201          | -0.005      | (-0.018;0.008)    | 0.463          |
|                  | 2b                                    | 0.009       | (0.001;0.017)    | 0.032          | 0.003       | (-0.012;0.017) | 0.728          | -0.008      | (-0.019;0.004)    | 0.184          |
|                  | 2c                                    | 0.008       | (0.000;0.017)    | 0.042          | 0.006       | (-0.009;0.020) | 0.439          | -0.007      | (-0.019;0.004)    | 0.210          |
|                  | 2d                                    | 0.009       | (0.001;0.017)    | 0.033          | 0.003       | (-0.012;0.017) | 0.724          | -0.007      | (-0.019;0.004)    | 0.210          |
|                  | 2e                                    | 0.009       | (0.001;0.018)    | 0.025          | 0.004       | (-0.012;0.019) | 0.652          | -0.008      | (-0.019;0.004)    | 0.187          |
|                  | 2f                                    | 0.010       | (0.002;0.019)    | 0.021          | 0.001       | (-0.016;0.018) | 0.904          | -0.004      | (-0.016;0.008)    | 0.469          |
|                  | 2g                                    | 0.008       | (0.000;0.016)    | 0.038          | 0.001       | (-0.013;0.015) | 0.905          | -0.006      | (-0.017;0.004)    | 0.246          |
|                  | 2h                                    | 0.007       | (-0.001;0.015)   | 0.079          | -0.001      | (-0.015;0.014) | 0.939          | -0.007      | (-0.018;0.004)    | 0.197          |
|                  | 2i                                    | 0.006       | (-0.002;0.014)   | 0.141          | 0.005       | (-0.010;0.020) | 0.490          | -0.006      | (-0.019;0.006)    | 0.286          |
|                  | 2j                                    | 0.006       | (-0.002;0.014)   | 0.125          | 0.005       | (-0.010;0.019) | 0.532          | -0.007      | (-0.018;0.005)    | 0.256          |
|   | B       | CI            | p   | B       | CI            | p    | B       | CI            | p    |
|---|---------|---------------|-----|---------|---------------|------|---------|---------------|------|
| 2k| 0.008   | (0.000;0.016) | 0.052 | 0.001   | (-0.013;0.015) | 0.872 | -0.006  | (-0.017;0.005) | 0.265 |
| 2l| 0.009   | (0.001;0.016) | 0.035 | 0.001   | (-0.013;0.016) | 0.850 | -0.006  | (-0.017;0.005) | 0.262 |
| 3 | 0.015   | (0.008;0.023) | <0.001 | 0.009   | (-0.004;0.022) | 0.166 | 0.001   | (-0.009;0.010) | 0.859 |
| 3a| 0.018   | (0.010;0.025) | <0.001 | 0.011   | (-0.002;0.024) | 0.095 | 0.003   | (-0.007;0.013) | 0.520 |
| 3b| 0.018   | (0.011;0.026) | <0.001 | 0.011   | (-0.002;0.024) | 0.095 | 0.003   | (-0.006;0.013) | 0.498 |

N=672, 380/115/177 or 639, 366/111/162 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the difference in cardiorespiratory fitness in Wmax/kg per one unit higher level of measure of diastolic function, and for diastolic function according to 2016 guidelines versus normal diastolic function. Model 1: age, sex, height; Model 2: model 1 + prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic blood pressure, use of antihypertensive medication, albuminuria; Model 2a: additional adjustment for moderate to vigorous physical activity (N=336/96/151 or N=322/94/138); Model 2b: exclusion of individuals with prior coronary heart disease (N=368/96/151 or N=355/104/148); Model 2c: exclusion of individuals with atrial fibrillation (N=364/107/169 or N=350/103/155); Model 2d: exclusion of individuals with wall abnormalities (N=377/114/173 or N=365/110/159); Model 2e: exclusion of individuals with valvular dysfunction (N=356/108/168 or N=343/104/154); Model 2f: exclusion of individuals with mobility limitations (N=332/83/122 or N=320/82/114); Model 2g: replacement of office systolic pressure with office diastolic pressure; Model 2h: replacement of office systolic pressure and antihypertensive medication with presence of hypertension; Model 2i: replacement of office systolic pressure with 24-hour systolic pressure (N=351/103/163 or N=340/101/149); Model 2j: replacement of office systolic pressure with 24-hour diastolic pressure (N=351/103/163 or N=340/101/149); Model 2k: additional adjustment for renin-angiotensin-system-inhibitors; Model 2l: additional adjustment for beta-blockers; Model 3: model 2 + waist; Model 3a: replacement of waist with body mass index; Model 3b replacement of waist with weight.

Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.
| Model  | Diastolic function 2016 guidelines | Normal glucose metabolism (N=380/366) |  | Prediabetes (N=115/111) |  | Type 2 diabetes (N=177/162) |  |
|--------|----------------------------------|---------------------------------------|---|-------------------------|---|--------------------------|---|
|        | Indeterminate                     | B: 0.050 (0.061;0.160) P: 0.374 |  | B: -0.208 (0.422;0.005) P: 0.055 |  | B: -0.115 (0.302;0.073) P: 0.229 |  |
| 2a     | Normal glucose metabolism         | 0.068 (0.047;0.183) P: 0.244 |  | -0.208 (0.430;0.014) P: 0.066 |  | -0.073 (0.262;0.117) P: 0.450 |  |
| 2b     | Normal glucose metabolism         | 0.062 (0.0511;0.175) P: 0.282 |  | -0.223 (0.443;0.004) P: 0.046 |  | -0.089 (0.290;0.111) P: 0.381 |  |
| 2c     | Normal glucose metabolism         | 0.055 (0.058;0.168) P: 0.340 |  | -0.141 (0.357;0.075) P: 0.199 |  | -0.105 (0.297;0.086) P: 0.279 |  |
| 2d     | Normal glucose metabolism         | 0.050 (0.061;0.160) P: 0.378 |  | -0.203 (0.412;0.007) P: 0.058 |  | -0.076 (0.267;0.115) P: 0.433 |  |
| 2e     | Normal glucose metabolism         | 0.056 (0.055;0.168) P: 0.319 |  | -0.238 (0.457;0.019) P: 0.034 |  | -0.183 (0.386;0.020) P: 0.077 |  |
| 2f     | Normal glucose metabolism         | 0.047 (0.070;0.165) P: 0.429 |  | -0.451 (0.712;0.189) P: 0.001 |  | -0.059 (0.273;0.155) P: 0.586 |  |
| 2g     | Normal glucose metabolism         | 0.044 (0.065;0.154) P: 0.429 |  | -0.213 (0.426;0.000) P: 0.050 |  | -0.109 (0.297;0.079) P: 0.252 |  |
| 2h     | Normal glucose metabolism         | 0.033 (0.077;0.143) P: 0.550 |  | -0.192 (0.407;0.022) P: 0.078 |  | -0.119 (0.305;0.067) P: 0.208 |  |
| 2i     | Normal glucose metabolism         | 0.021 (0.093;0.135) P: 0.718 |  | -0.240 (0.466;0.014) P: 0.038 |  | -0.119 (0.309;0.072) P: 0.219 |  |
| 2j     | Normal glucose metabolism         | 0.028 (0.085;0.142) P: 0.624 |  | -0.239 (0.466;0.013) P: 0.039 |  | -0.120 (0.309;0.069) P: 0.211 |  |
| 2k     | Normal glucose metabolism         | 0.043 (0.068;0.153) P: 0.447 |  | -0.210 (0.422;0.003) P: 0.054 |  | -0.118 (0.307;0.071) P: 0.218 |  |
| 2l     | Normal glucose metabolism         | 0.048 (0.062;0.159) P: 0.390 |  | -0.219 (0.433;0.005) P: 0.045 |  | -0.113 (0.302;0.075) P: 0.237 |  |
| 3      | Normal glucose metabolism         | 0.095 (0.009;0.199) P: 0.074 |  | -0.144 (0.345;0.057) P: 0.157 |  | -0.064 (0.227;0.100) P: 0.441 |  |
| 3a     | Normal glucose metabolism         | 0.093 (0.011;0.197) P: 0.080 |  | -0.155 (0.353;0.043) P: 0.123 |  | -0.075 (0.240;0.090) P: 0.369 |  |
| 3b     | Normal glucose metabolism         | 0.093 (0.0111;0.196) P: 0.080 |  | -0.144 (0.342;0.054) P: 0.151 |  | -0.071 (0.234;0.093) P: 0.393 |  |
|        | Abnormal                          | 0.165 (0.004;0.335) P: 0.055 |  | 0.053 (0.329;0.224) P: 0.706 |  | 0.065 (0.301;0.170) P: 0.229 |  |
| 2a     | Abnormal                          | 0.188 (0.009;0.368) P: 0.040 |  | 0.088 (0.214;0.389) P: 0.563 |  | -0.041 (0.307;0.225) P: 0.763 |  |
| 2b     | Abnormal                          | 0.169 (0.004;0.343) P: 0.056 |  | 0.015 (0.265;0.296) P: 0.914 |  | -0.027 (0.280;0.226) P: 0.835 |  |
| 2c     | Abnormal                          | 0.167 (0.005;0.340) P: 0.057 |  | 0.044 (0.238;0.327) P: 0.756 |  | -0.044 (0.284;0.197) P: 0.722 |  |
| 2d     | Abnormal                          | 0.166 (0.004;0.335) P: 0.056 |  | 0.008 (0.283;0.267) P: 0.953 |  | -0.028 (0.267;0.211) P: 0.815 |  |
| 2e     | Abnormal                          | 0.207 (0.025;0.390) P: 0.026 |  | -0.026 (0.307;0.251) P: 0.843 |  | -0.004 (0.260;0.252) P: 0.974 |  |
| 2f     | Abnormal                          | 0.184 (0.006;0.362) P: 0.042 |  | -0.262 (0.608;0.084) P: 0.135 |  | 0.052 (0.206;0.309) P: 0.692 |  |
| 2g     | Abnormal                          | 0.160 (0.009;0.328) P: 0.063 |  | -0.062 (0.340;0.215) P: 0.657 |  | -0.070 (0.305;0.164) P: 0.554 |  |
| 2h     | Abnormal                          | 0.145 (0.025;0.316) P: 0.095 |  | -0.060 (0.338;0.219) P: 0.672 |  | -0.064 (0.298;0.171) P: 0.592 |  |
| 2i     | Abnormal                          | 0.086 (0.092;0.135) P: 0.718 |  | 0.018 (0.264;0.300) P: 0.985 |  | -0.102 (0.343;0.140) P: 0.406 |  |
| 2j | 0.102 | (-0.074;0.279) | 0.255 | -0.018 | (-0.266;0.301) | 0.902 | -0.104 | (-0.346;0.138) | 0.398 |
| 2k | 0.144 | (-0.026;0.314) | 0.097 | -0.067 | (-0.344;0.210) | 0.633 | -0.064 | (-0.301;0.172) | 0.591 |
| 2l | 0.163 | (-0.007;0.332) | 0.060 | -0.076 | (-0.355;0.203) | 0.588 | -0.066 | (-0.302;0.171) | 0.583 |
| 3  | 0.178 | (0.019;0.337) | 0.028 | -0.022 | (-0.280;0.235) | 0.862 | -0.056 | (-0.260;0.149) | 0.590 |
| 3a | 0.189 | (-0.031;0.348) | 0.020 | -0.007 | (-0.262;0.248) | 0.956 | -0.040 | (-0.246;0.167) | 0.703 |
| 3b | 0.189 | (0.031;0.347) | 0.019 | -0.001 | (-0.255;0.254) | 0.996 | -0.045 | (-0.249;0.160) | 0.393 |

N=672, 380/115/177 or 639, 366/111/162 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the difference in cardiorespiratory fitness in Wmax/kg per one unit higher level of measure of diastolic function, and for diastolic function according to 2016 guidelines versus normal diastolic function. Model 1: age, sex, height; Model 2: model 1 + prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic blood pressure, use of antihypertensive medication, albuminuria; Model 2a: additional adjustment for moderate to vigorous physical activity (N=336/96/151 or N=322/94/138); Model 2b: exclusion of individuals with prior coronary heart disease (N=368/96/151 or N=355/104/148); Model 2c: exclusion of individuals with atrial fibrillation (N=364/107/169 or N=350/103/155); Model 2d: exclusion of individuals with wall abnormalities (N=377/114/173 or N=365/110/159); Model 2e: exclusion of individuals with valvular dysfunction (N=356/108/168 or N=343/104/154); Model 2f: exclusion of individuals with mobility limitations (N=332/83/122 or N=320/82/114); Model 2g: replacement of office systolic pressure with office diastolic pressure; Model 2h: replacement of office systolic pressure and antihypertensive medication with presence of hypertension; Model 2i: replacement of office systolic pressure with 24-hour systolic pressure (N=351/103/163 or N=340/101/149); Model 2j: replacement of office systolic pressure with 24-hour diastolic pressure (N=351/103/163 or N=340/101/149); Model 2k: additional adjustment for renin-angiotensin-system-inhibitors; Model 2l: additional adjustment for beta-blockers; Model 3: model 2 + waist; Model 3a: replacement of waist with body mass index; Model 3b replacement of waist with weight.

Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.
Table S13. Interaction effects between measures of diastolic function and sex in the associations with cardiorespiratory fitness

| Measure                                           | Model | B     | 95% CI            | P     |
|---------------------------------------------------|-------|-------|-------------------|-------|
| Average E/e’-ratio                                | 2     | 0.021 | (-0.013;0.055)    | 0.219 |
| e’ average, cm/s                                   | 2     | -0.020| (-0.055;0.014)    | 0.250 |
| Maximum tricuspid regurgitation flow, m/s          | 2     | -0.046| (-0.202;0.109)    | 0.558 |
| LA volume index, ml/m²                             | 2     | 0.002 | (-0.009;0.013)    | 0.715 |
| LV mass index, gr/m²                               | 2     | -0.008| (-0.019;0.003)    | 0.175 |

N=672 or 639 for the two-dimensional or tissue Doppler imaging echocardiography study population, respectively. The unstandardized regression coefficients (B) represent the interaction effect between one unit higher level of measure of diastolic function (or for diastolic function according to 2016 guidelines versus normal diastolic function) and (pre)diabetes as compared to normal glucose metabolism, in the association with cardiorespiratory fitness in Wmax/kg. Model 2: adjusted for age, sex, height, prior cardiovascular disease, smoking status, alcohol use, total-to-HDL-cholesterol ratio, triglycerides, use of lipid-modifying medication, estimated glomerular filtration rate, health status, office systolic pressure, use of antihypertensive medication, albuminuria, interaction term between measure of diastolic function and glucose metabolism status, and interaction term between measure of diastolic function and sex.

Abbreviations: CI, confidence interval; LA, left atrial; LV, left ventricular.
Figure S1. Two-dimensional and tissue Doppler imaging echocardiography study population selection.

Categories of missing data were not mutually exclusive. No data was missing for the covariates sex, age and glucose metabolism status. After selection of the population with echocardiography performed and complete data on the sub-maximal cycle ergometer test no additional data was missing for the covariates height, lipid-modifying medication, office systolic blood pressure, and antihypertensive medication.