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CARDIAC

Subclinical changes in MRI-determined right ventricular volumes and function in subjects with prediabetes and diabetes

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Abstract

Objectives The aim of this study was to assess subclinical changes in right ventricular volumes and function in subjects with prediabetes and diabetes and controls without a history of cardiovascular disease.

Methods Data from 400 participants in the KORA FF4 study without self-reported cardiovascular disease who underwent 3-T whole-body MRI were obtained. The right ventricle was evaluated using the short axis and a four-chamber view. Diabetes was defined according to WHO criteria. Associations between glucose tolerance and right ventricular parameters were assessed using multivariable adjusted linear regression models.

Results Data from 337 participants were available for analysis. Of these, 43 (13%) had diabetes, 87 (26%) had prediabetes, and 207 (61%) were normoglycaemic controls. There was a stepwise decrease in right ventricular volumes in men with prediabetes and diabetes in comparison with controls, including right ventricular end-diastolic volume ($\beta = -20.4$ and $\beta = -25.6$, respectively; $p \leq 0.005$), right ventricular end-systolic volume ($\beta = -12.3$ and $\beta = -12.7$, respectively; $p \leq 0.037$) and right ventricular stroke volume ($\beta = -8.1$ and $\beta = -13.1$, respectively, $p \leq 0.016$). We did not observe any association between prediabetes or diabetes and right ventricular volumes in women or between prediabetes or diabetes and right ventricular ejection fraction in men and women.

Conclusions This study points towards early subclinical changes in right ventricular volumes in men with diabetes and prediabetes.

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Key Points

- *MRI was used to detect subclinical changes in right ventricular parameters.*
- *Diabetes mellitus is associated with right ventricular dysfunction.*
- *Impairment of right ventricular volumes seems to occur predominantly in men.*

Keywords Prediabetic state · Heart ventricles · Diabetes mellitus · Magnetic resonance imaging · Ventricular dysfunction

Abbreviations

BMI	Body mass index
KORA	Cooperative Health Research in the Region of Augsburg *(Kooperative Gesundheitsforschung in der Region Augsburg)*
NGT	Normal glucose tolerance
RVD	Right ventricular dysfunction
RV-EDV	Right ventricular end-diastolic volume

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RV-EF Right ventricular ejection fraction
RV-ESV Right ventricular end-systolic volume
RV-SV Right ventricular stroke volume

Introduction

Diabetes is of increasing relevance in international health, not only in developed but also in developing countries [1]. In 2014 the worldwide prevalence of diabetes was about 9%, and in 2012 1.5 million deaths a year were considered to be directly caused by diabetes, most of them by type 2 diabetes [2]. Prediabetes, including impaired fasting glucose and impaired glucose tolerance, shows an even higher prevalence than diabetes [3, 4]. The prevalence of diabetes and prediabetes is expected to continue to increase strongly due to demographic changes, decreases in physical activity and increases in obesity and urbanization [5].

Diabetes is an independent risk factor for both the development of cardiovascular disease and associated negative outcomes such as renal disease, stroke and cardiomyopathy [6]. Early right and particularly left ventricular dysfunction occurs even in children with type 1 diabetes [7]. The direct impact of prediabetes on the development of cardiovascular disease is less clear, even though observational studies have shown an association between prediabetes and the development of, for example, kidney disease, neuropathy, retinopathy and macrovascular disease [8].

It is known that right ventricular function is an important predictive factor in patients with cardiovascular disease. Systolic right ventricular dysfunction (RVD), defined as reduced right ventricular ejection fraction (RV-EF), has a negative impact on overall and event-free survival in patients with, for example, heart failure, myocardial infarction, idiopathic dilated cardiomyopathy or myocarditis, and in patients prior to coronary artery bypass grafting [9–16]. Subjects without symptomatic cardiovascular disease might particularly benefit from early detection of the disease and adequate treatment to prevent cardiovascular complications which are often associated with substantial morbidity and mortality. However, data regarding early subclinical changes in right ventricular function and volumes in people without a history of cardiovascular disease are rare.

Therefore, in the present study we examined right ventricular function and volumes in patients with diabetes and prediabetes and in controls with normal glucose tolerance (NGT) without reported cardiovascular disease. We hypothesized that there would be a stepwise decline in right ventricular functional parameters, assessed by cardiac MRI, including RV-EF and stroke volume (RV-SV) as well as right ventricular volume parameters including end-diastolic volume (RV-EDV) and end-systolic volume (RV-ESV) in men and women with prediabetes and diabetes in comparison with normoglycaemic controls. It is known that gender has a great influence on right ventricular parameters [17]. Therefore, we hypothesized that differences in right ventricular parameters would vary according to gender and other cardiovascular risk factors such as body mass index (BMI).

Materials and methods

Study sample

The study was approved by the local review board, and written informed consent was obtained from all participants [18]. This case-control study was nested in the population-based cohort study project *Kooperative Gesundheitsforschung in der Region Augsburg* (KORA; Cooperative

Health Research in the Region of Augsburg) in Southern Germany. A large sample of subjects between 25 and 74 years of age was recruited from among all residents in the area and four epidemiological cross-sectional surveys S1–S4 were formed to assess cardiovascular, pulmonary and other disease entities. Details of study design, sampling method and data collection are provided elsewhere [19]. Between 2013 and 2014 the FF4 follow-up-study, the second follow-up examination including 2,279 of the S4 participants from 1999/2001 was performed. A total of 1,851 participants were under 74 years of age. After further examinations at the KORA study centre including a questionnaire and an interview, 1,282 were eligible for the MRI substudy. Of these, 882 could not be included for various reasons, as shown in Fig. 1. Thus, a total of 400 participants were available to undergo MRI [18, 19].

Of the 400 participants, 57.8% were male. The participants' mean ± SD age was 56.3 ± 9 years. The assessment of further risk factors is described elsewhere [18]. We applied the WHO criteria to assign participants to the diabetes group, prediabetes group or control group with NGT. Subjects with 2-hour plasma glucose levels of ≥200 mg/dL after an oral glucose tolerance test (OGTT) or fasting glucose levels of ≥126 mg/dL were assigned to the diabetes group, whereas subjects with impaired glucose tolerance after an OGTT with plasma glucose levels of ≥140 and <200 mg/dL or impaired fasting glucose of ≥110 and <126 mg/dL were assigned to the prediabetes group [20]. Participants meeting none of the above criteria were classified as controls with NGT [18, 20]. The diabetes group consisted of 54 participants (13.5%) and the prediabetes group consisted of 103 participants (26.0%). The control group with NGT consisted of 243 participants (61%).

None of the participants showed a validated or self-reported history of cardiovascular diseases. Exclusion criteria were age >72 years, reported history of stroke, myocardial infarction or revascularization, or the presence of an implantable cardiac pacemaker or defibrillator, clipped cerebral

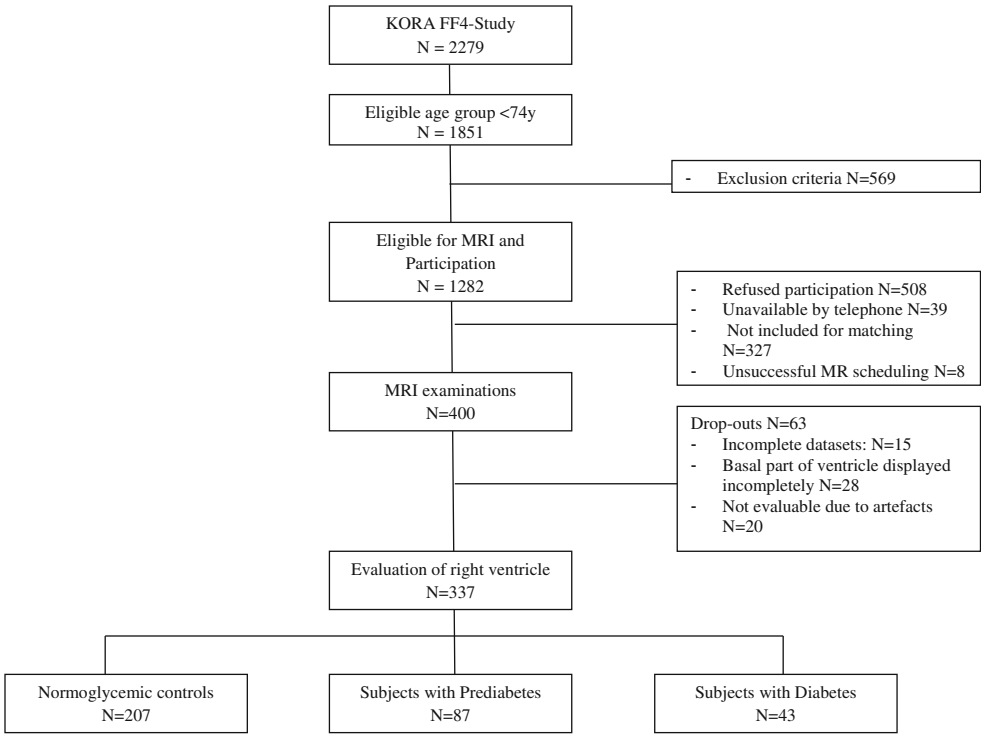

Fig. 1 Flow chart of the participant selection process

aneurysm, neural stimulator, any type of ear implant, ocular foreign body or any other implanted device. Pregnant or breast-feeding women, claustrophobic patients and patients with a known allergy to gadolinium compounds or a serum creatinine level of >1.3 mg/dL were also excluded [18].

MR imaging protocols

All images were obtained with the same 3-T MR system (Magnetom Skyra; Siemens Healthcare, Erlangen, Germany). An 18-channel body surface coil and a table-mounted spine matrix coil were used. The study protocol included imaging of the brain, carotid arteries, heart, fat compartments and ectopic fat (see Appendix Table A1). For the evaluation of right ventricular parameters, an unenhanced stack of short-axis cine steady-state free precession sequences and a four-chamber view with the following parameters were used: slice thickness 8 mm, voxel size 1.5 × 1.5 mm, field of view 297 × 360 mm, matrix 240 × 160, repetition time 29.97 ms, echo time 1.46 ms and flip angle 62°.

Evaluation of right ventricular MRI parameters

Right ventricular parameters were evaluated with cvi^{42} software (version 4.1.5(190); Circle Cardiovascular Imaging Inc., Calgary, Canada) by one blinded reader with more than five years experience in cardiac MRI. In the end-diastolic and end-systolic phases the contours of the right ventricular lumen were manually delineated. Slices from the apex up to the pulmonary valve were included in the right ventricular volume (Fig. 2) [17, 21, 22]. Parameters including RV-EF, RV-SV and right ventricular cardiac output were calculated from RV-EDV and RV-ESV measurements. Systolic RVD was defined as RV-EF <50% [23].

Covariate measurements

Several risk factors were measured in the KORA FF4 study by standardized interview, basic health examinations, laboratory analyses and medication records. BMI was calculated as weight (in kilograms) divided by height (in metres) squared. Smoking status categories included never-smoker, ex-smoker and current smoker. Systolic and diastolic blood pressure (BP) was measured three times in the right arm with the patient seated after a 5-minute rest period. The mean of the second and third BP measurements was used in the present analyses. Hypertension was defined as systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg or administration of antihypertensive medication for known hypertension. Laboratory measurements including glucose and HbA1c as well as total cholesterol, high-density and low-density lipoprotein cholesterol and triglycerides are reported elsewhere [24].

Statistical analysis

Participants with NGT, prediabetes and diabetes were separately characterized in terms of mean ± standard deviation for

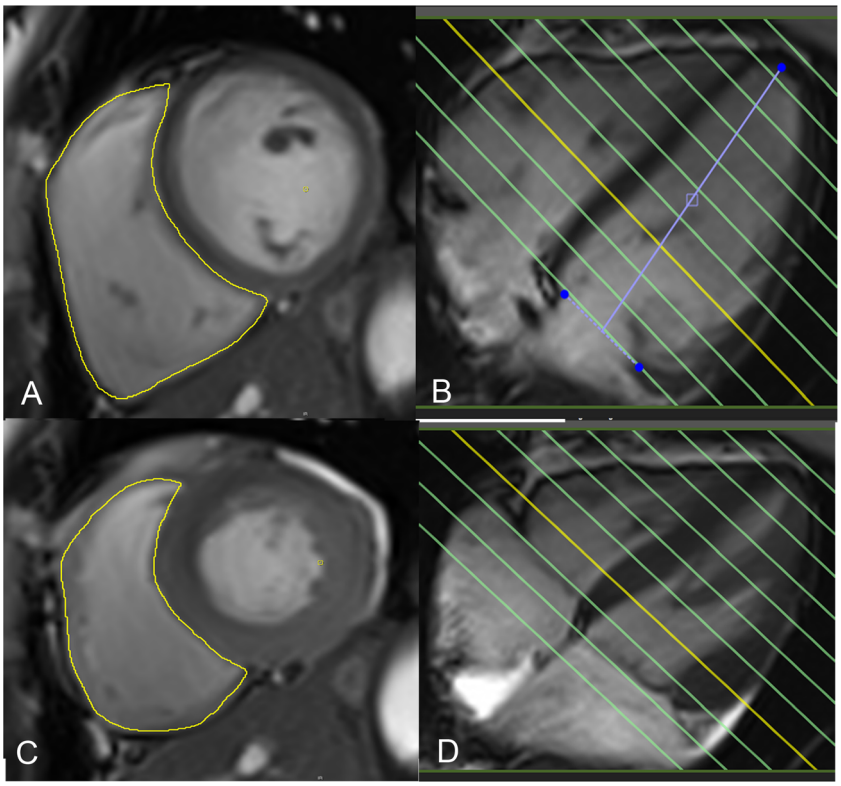

Fig. 2 Evaluation of right ventricular volume. The right ventricular volume is manually delineated (yellow line), including papillary muscles, in end-diastole (a) and end-systole (c). The four-chamber view shows the corresponding layers for evaluation of enddiastole (b) and end-systole (d)

continuous variables and absolute numbers and percentages for categorical variables. Differences among the diabetes subgroups were evaluated by one-way ANOVA (continuous data) or the chi-squared test (categorical data).

The associations between diabetes status and right ventricular parameters were assessed by linear regression models providing β coefficients with 95% confidence intervals. Parameter distributions were visually compared with the normal distribution. Adjusting variables included age, gender, BMI, systolic BP, smoking status, and high-density lipoprotein and triglyceride levels as common risk factors for diabetes mellitus and heart dysfunction. The distribution of regression model residuals was checked visually for normality. Unadjusted differences in right ventricular parameters between the diabetes status groups are graphically displayed as violin plots.

The association between diabetes status and reduced RV-EF (<50%) was assessed using a logistic regression model providing odds ratios with 95% confidence intervals. Effect modifications by different variables including gender were tested, and stratified results are presented.

All analyses were additionally adjusted for sampling weights considering differences in age, gender and diabetes status between the study sample (n = 400) and the entire KORA cohort (n = 2,279, median age 60 years, 48% men, 15% with diabetes) but yielded no substantial changes in the findings. A p value of <0.05 was considered statistically significant. Statistical analyses were performed using Stata 14.1 (Stata Corporation, College Station, TX, USA).

Results

Study population

Data from 63 (16%) of the 400 participants who underwent MRI could not be fully evaluated. In 15 (4%) of participants the MRI scan was not completed due to technical problems or was aborted by the study participant. Artefacts prevented reliable analysis in 20 participants (5%). In 28 (7%) of participants the basal part of the right ventricle was not completely acquired. Thus a total of 337 participants (84%) could be fully evaluated, and of these 207 (61%), 87 (26%) and 43 (13%) formed the control, prediabetes and diabetes groups, respectively. The dropouts did not alter the proportions of participants in the three groups (Fig. 1).

Table 1 shows the characteristics of the study population. The proportions of men increased from 52% to 63% to 74% in the control, prediabetes and diabetes groups, respectively. The participants' median age and BMI, and the prevalence of hypertension, increased from the healthy control group, to the prediabetes group to the diabetes group (all p < 0.001). Participants with diabetes and prediabetes had slightly lower levels of high-density lipoprotein and slightly higher levels of triglycerides than the normoglycaemic controls (both p < 0.001). In the NGT control group the proportion of ex-smokers was lower than in the prediabetes and diabetes groups.

Table 1 Study population

	Controls ($n = 207$)	Prediabetes ($n = 87$)	Diabetes ($n = 43$)	p valuea
Age (years)	54.3 ± 8.5	58.3 ± 8.9	61.2 ± 8.2	<0.001
Male	107 (52%)	55 (63%)	32 (74%)	0.011
Body mass index (kg/m^2)	26.6 ± 4.3	30.4 ± 4.7	30 ± 5.1	<0.001
Height (cm)	171.5 ± 10.4	172.1 ± 9.4	171.6 ± 7.3	0.863
Weight (kg)	78.4 ± 15.6	89.8 ± 14.4	88.6 ± 18	<0.001
Hypertension	42 (20%)	40 (46%)	30 (70%)	<0.001
Systolic blood pressure (mmHg)	116 ± 15	124 ± 16	131 ± 22	<0.001
Diastolic blood pressure (mmHg)	74 ± 9	78 ± 10	78 ± 13	0.001
Smoking status				
Never-smoker	79 (38%)	28 (32%)	14 (33%)	0.477
Ex-smoker	84 (41%)	42 (48%)	23 (53%)	
Current smoker	44 (21%)	17 (20%)	6 (14%)	
Total cholesterol (mg/dl)	215 ± 36	224 ± 32	215 ± 48	0.177
HDL (mg/dl)	66 ± 18	58 ± 14	53 ± 17	<0.001
LDL (mg/dl)	138 ± 32	145 ± 30	135 ± 43	0.142
Triglycerides (mg/dl)	105 ± 62	150 ± 82	207 ± 120	<0.001
Right ventricle paramters				
RV-EF (%)	53 ± 7)	53 ± 7	51 ± 7	0.192
Reduced RV-EF (<50%)	64 (31%)	25 (29%)	21 (49%)	0.049
RV-SV (ml)	89 ± 20	85 ± 17	78 ± 18	0.003
RV-EDV (ml)	169 ± 43	162 ± 32	154 ± 36	0.042
RV-ESV (ml)	81 ± 28	77 ± 22	76 ± 24	0.333

The data are presented as number (%) or mean ± standard deviation

HDL high density lipoprotein, *LDL* low density lipoprotein, *RV-EF* right ventricular ejection fraction, *RV-SV* right ventricular stroke volume, *RV-EDV* right ventricular end-diastolic volume, *RV-ESV* right ventricular end-systolic volume

One-way ANOVA (continuous data) or chi-squared-test (categorical data)

Right ventricular function and volumes

Within the whole study population the mean values of RV-SV, RV-EDV and RV-ESV were 86.5 ± 19.5 ml, 165.5 ± 39.8 ml and 79.1 ± 25.9 ml, respectively, and the mean value of RV-EF was 53 ± 7.0%.

Only small changes in absolute non-adjusted median values were found among the study groups for the right ventricular volume and function parameters (Table 1; Figs. 3 and 4). Only the decrease in RV-SV among participants with diabetes was statistically significant ($p = 0.003$). There were significantly more participants with RVD in the diabetes group (49%) than in the prediabetes (29%) and control group (31%; $p = 0.049$; Table 1).

Association between diabetes status and right ventricular function and volume

Table 2 shows the associations between diabetes status and RV-EF, RV-EDV, RV-ESV and RV-SV adjusted for age, gender, BMI, systolic BP, smoking status, high-density lipoprotein, low-density lipoprotein and triglycerides. Compared with the control group, RV-EDV, RV-ESV and RV-SV were lower in the prediabetes group (RV-EDV $\beta = -11.87$, $p = 0.013$; RV-

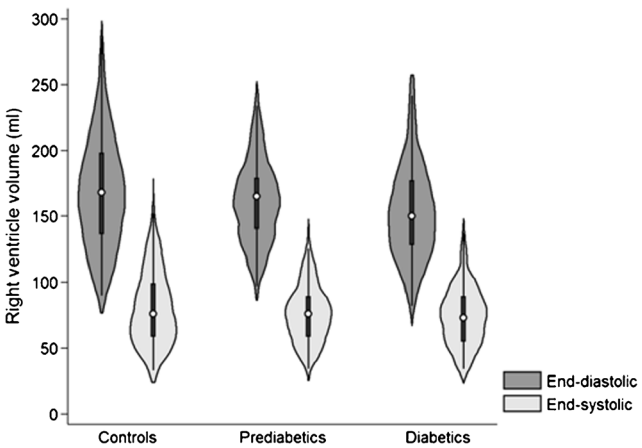

Fig. 3 Distributions of non-adjusted absolute right ventricular end-diastolic and end-systolic volumes in controls, prediabetics and diabetics. Circles indicate the medians, bars the interquartile ranges and spikes the upper and lower adjacent values. Only small changes in absolute non-adjusted median values occurred among the study groups

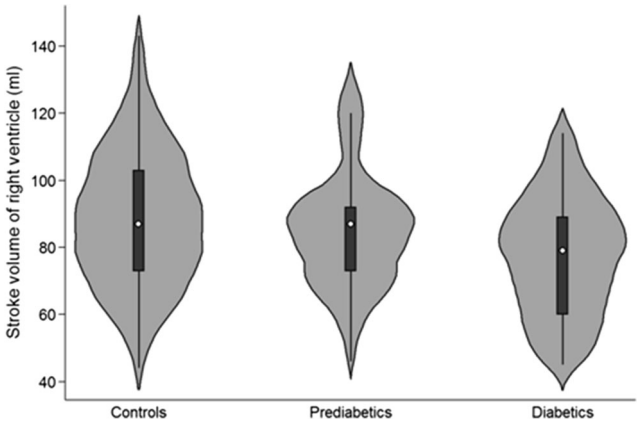

Fig. 4 Distributions of non-adjusted absolute right ventricular stroke volume in controls, participants with prediabetes and diabetes. Circles indicate the medians, bars the interquartile ranges and spike the upper and lower adjacent values. Only small changes in absolute non-adjusted median values occurred among the study groups.

ESV $\beta = -7.16$, $p = 0.023$; and RV-SV $\beta = -4.75$, $p = 0.057$) and in the diabetes group (RV-EDV $\beta = -20.71$, $p = 0.002$; RV-ESV $\beta = -9.55$, $p = 0.029$; and RV-SV $\beta = -11.36$, $p = 0.001$). Diabetes status showed no significant association with RV-EF.

Table 2 also shows the effects of the confounding variables age, male gender and BMI on RV parameters. Higher right ventricular volumes and RV-SV were observed in men: RV-EDV ($\beta = 42.06$, $p < 0.001$), RV-ESV ($\beta = 28.48$, $p < 0.001$) and RV-SV ($\beta = 13.52$, $p < 0.001$). Moreover, men had significantly lower RV-EF than women ($\beta = -5.25$; 9; $p < 0.001$) and a higher risk of RVD (OR 4.54, $p < 0.001$). Higher age was correlated slightly, but significantly. with lower RV-EDV ($\beta = -0.55$, $p = 0.016$) and lower RV-SV ($\beta = -0.37$, $p = 0.002$). BMI was correlated positively with RV-EDV ($\beta = 1.13$, $p = 0.012$) and RV-SV ($\beta = 0.69$, $p = 0.003$; Table 2). Of all tested confounding variables, only gender showed a significant effect on the association between diabetes status and RV parameters.

A gender-stratified variable regression analysis revealed that the stepwise decreases in right ventricular volumes and RV-SV in the prediabetes and diabetes groups were a result of decreases only in men ($p \leq 0.037$); there was no significant association in women ($p \geq 0.28$; Table 3). Compared with the control group, RV-EDV, RV-ESV and RV-SV in men were lower in the prediabetes group (RV-EDV $\beta = -20.44$, $p = 0.002$; RV-ESV $\beta = -12.31$, $p = 0.005$; and RV-SV $\beta = -8.14$, $p = 0.016$) and diabetes group (RV-EDV $\beta = -25.59$, $p = 0.005$; RV-ESV $\beta = -12.65$, $p = 0.037$; and RV-SV $\beta = -13.10$, $p = 0.006$).

Discussion

This study suggests an association between deterioration in glucose metabolism and subclinical changes in right ventricular function and volumes, observed as decreases in RV-SV,

Table 2 Associations between diabetes status and covariates and RV-EF, RV-EDV, RV-ESV and RV-SV

	RV-EF		Reduced RV-EF (<50%)		RV-EDV		RV-ESV		RV-SV	
	β (95% CI)	*p* value	Odds ratio (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value	β (95% CI)	*p* value
Diabetes status										
Controls	Reference	–	Reference	–	Reference	–	Reference	–	Reference	–
Prediabetes	0.69 (−1.12 to 2.50)	0.454	0.77 (0.41 to 1.45)	0.414	−11.87 (−21.27 to −2.47)	0.013	−7.16 (−13.32 to −1.00)	0.023	−4.75 (−9.65 to 0.15)	0.057
Diabetes	−0.40 (−2.91 to 2.12)	0.756	1.63 (0.70 to 3.79)	0.255	−20.71 (−33.79 to −7.63)	0.002	−9.55 (−18.12 to −0.98)	0.029	−11.36 (−18.17 to −4.54)	0.001
Age	−0.06 (−2.91 to 2.12)	0.150	1.02 (0.99 to 1.05)	0.283	−0.55 (−1.00 to −0.10)	0.016	−0.17 (−0.46 to 0.12)	0.249	−0.37 (−0.60 to −0.14)	0.002
Male gender	−5.25 (−6.9 to −3.59)	<0.001	4.54 (2.43 to 8.46)	<0.001	42.06 (33.47 to 50.65)	<0.001	28.48 (22.85 to 34.1)	<0.001	13.52 (9.04 to 18.00)	<0.001
Body mass index	0.07 (−0.10 to 0.24)	0.410	0.97 (0.91 to 1.03)	0.326	1.13 (0.25 to 2.02)	0.012	0.43 (−0.15 to 1.01)	0.146	0.69 (0.23 to 1.15)	0.003

The data presented are the results of linear or logistic regression analysis additionally adjusted for systolic blood pressure, smoking status, high-density lipoprotein, low-density lipoprotein and triglycerides
RV-EF right ventricular ejection fraction, *RV-EDV* right ventricular end-diastolic volume, *RV-ESV* right ventricular end-systolic volume, *RV-SV* right ventricular stroke volume

Table 3 Impact of prediabetes and diabetes on right ventricular function and volumes in men and women

	Men		Women	
	β (95% CI)	p value	β (95% CI)	p value
RV-EF				
Prediabetes	1.04 (−1.34 to 3.42)	0.389	0.27 (−2.66 to 3.2)	0.854
Diabetes	−0.07 (−3.38 to 3.24)	0.967	−0.47 (−4.62 to 3.68)	0.823
RV-EDV				
Prediabetes	−20.44 (−33.25 to −7.62)	0.002	2.6 (−11.57 to 16.76)	0.717
Diabetes	−25.59 (−43.44 to −7.75)	0.005	−9.2 (−29.31 to 10.88)	0.366
RV-ESV				
Prediabetes	−12.31 (−20.83 to −3.79)	0.005	1.15 (−7.88 to 10.19)	0.801
Diabetes	−12.65 (−24.51 to −0.79)	0.037	−3.66 (−16.48 to 9.16)	0.573
RV-SV				
Prediabetes	−8.14 (−14.77 to −1.51)	0.016	1.33 (−6.15 to 8.82)	0.725
Diabetes	−13.10 (−22.33 to −3.86)	0.006	−5.78 (−16.40 to 4.84)	0.284

The data presented are the results of linear regression analysis adjusted for age, body mass index, systolic blood pressure, smoking status, high-density lipoproteins, low-density lipoproteins and triglycerides

RV-EF right ventricular ejection fraction, *RV-EDV* right ventricular end-diastolic volume, *RV-ESV* right ventricular end-systolic volume, *RV-SV* right ventricular stroke volume

RV-EDV and RV-ESV, in subjects without a history of cardiovascular disease. A gender-specific analysis revealed that this association was clear in men, but no significant relationship was found in women.

Previous studies have generally concentrated on reduced RV-EF as a parameter in the assessment of the right ventricle in patients with confirmed cardiovascular disease, without taking into account other right ventricular parameters such as RV-SV, RV-EDV and RV-ESV [9–15, 23]. In contrast participants with apparent cardiovascular disease were excluded from the present study. In this population without known cardiovascular disease, RV-EF actually seemed to be unaffected by glycaemic status. However, we found lower values of RV-EDV, RV-ESV and RV-SV in the prediabetes and diabetes groups than in the control group. Therefore, it seems possible that reduced right ventricular volumes and RV-SV represent an early form of RVD before symptom onset.

We evaluated the gender-specific effects of altered glucose metabolism on right ventricular parameters. We found that decreases in RV-EDV, RV-ESV and RV-SV in the prediabetes and diabetes groups in relation to the control group were a result of decreases only in men.

It is unclear why impairment of right ventricular function and volumes is more common in men than in women. Differences in sex hormone metabolism could be an explanation. Ventetuolo et al. showed that higher levels of androgen in both sexes as well as higher levels of oestradiol in women undergoing hormone therapy are correlated with higher right ventricular volumes and mass, higher RV-EF and lower RV-ESV, respectively [25].

Roifman et al. not only identified RVD as a risk factor for negative outcomes in patients with ST elevation myocardial infarction, but also found that the development of RVD is strongly associated with concomitant diabetes mellitus. Yet only 12 (11%) of the 106 patients were women and the patients were not divided according to gender [23].

The present study fills a gap by providing data on subclinical changes in right ventricular volumes and function in patients with diabetes, prediabetes and NGT without a prior history of cardiovascular disease. As it is likely that prediabetes and diabetes affect all left and right ventricular parameters a long time before symptoms occur or cardiovascular disease can be assessed, it may be of great importance to detect these changes early. In the prospective MESA-right ventricle study it was found that men without confirmed cardiovascular disease with impaired RV-SV, RV-EDV, RV-ESV and reduced right ventricular mass were more likely to develop self-reported dyspnoea over a follow-up period of 60 months [26]. Furthermore, correlations were detected between right ventricular volumes, mainly elevated RV-EDV, and right ventricular mass and obesity, varying intensity of physical activity and elevated levels of pentraxin-3 that is known to be a marker in left heart disease [27–29].

Further investigations are necessary to assess whether the early changes in right ventricular volumes and function found in this study can really be attributed to altered glucose metabolism. Further research is also necessary to determine whether these early changes are followed by apparent cardiovascular disease.

Limitations

The prediabetes and diabetes groups were smaller than the control group (26% and 13% of all participants, respectively). Furthermore, the proportion of women decreased from the control to the prediabetes to the diabetes group (48%, 37%, 26%, respectively). Therefore, further studies with greater numbers of female participants with prediabetes and diabetes should be undertaken to confirm the results obtained in this study.

All patients with reported cardiovascular disease were excluded from the study. Therefore, the impact of our findings on patients with confirmed cardiovascular disease is unclear. To address the potential impact of common cardiovascular risk factors on right ventricular structure and function we adjusted for these risk factors using multiple linear regression analysis. However, there might be other important risk factors which were not addressed by our analysis. Advanced pulmonary disease (e.g. sarcoidosis, pulmonary hypertension, fibrosis), obstructive sleep apnoea, amyloidosis, mitral regurgitation and right bundle branch block can also result in right ventricular changes. In a post-hoc analysis including review of clinical and imaging data, we did not identify subjects with these conditions in our study cohort. Furthermore, left ventricular impairment might also affect right ventricular function; however, this effect is generally absent in subjects with normal or mildly impaired function, as in our study cohort [18, 30].

This was a cross-sectional-study. Hence, it is not yet possible to definitely attribute the changes in right ventricular parameters to changes in glucose metabolism. Follow-up examinations are necessary to confirm this association.

If these early changes in right ventricular volumes and function represent an early form of RVD, detecting them before symptom onset in patients at risk might facilitate diagnosis and treatment of developing RVD. Negative clinical outcomes might be prevented or at least postponed. However, the impact of reduced right ventricular volumes on long-term outcomes in asymptomatic patients is not known and needs to be further investigated.

Conclusions

A stepwise impairment of right ventricular volumes and function was found in men from those with NGT to those with prediabetes to those with diabetes. Further investigations are necessary to assess whether these early changes in right ventricular volumes lead to altered clinical development. These findings might form the rationale for prevention and intervention trials with regard to RVD in subjects with prediabetes and diabetes without known cardiovascular disease.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Holger Hetterich.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors has significant statistical expertise.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohort overlap Some study subjects or cohorts have been previously reported in papers on the KORA MRI substudy. Those previously published papers included data from all subjects of the present work. However, so far no data on right ventricular parameters has been published, which are the main focus of the present paper.

- Association between MRI-derived hepatic fat fraction and BP in participants without history of cardiovascular disease. Lorbeer R, Bayerl C, Auweter S, Rospleszcz S, Lieb W, Meisinger C, Heier M, Peters A, Bamberg F, Hetterich H.
- Subclinical disease burden as assessed by whole-body MRI in subjects with prediabetes, subjects with diabetes, and normal control subjects from the general population: the KORA-MRI study. Bamberg F, Hetterich H, Rospleszcz S, Lorbeer R, Auweter SD, Schlett CL, Schafnitzel A, Bayerl C, Schindler A, Saam T, Müller-Peltzer K, Sommer W, Zitzelsberger T, Machann J, Ingrisch M, Selder S, Rathmann W, Heier M, Linkohr B, Meisinger C, Weber C, Ertl-Wagner B, Massberg S, Reiser MF, Peters A.
- Feasibility of a three-step magnetic resonance imaging approach for the assessment of hepatic steatosis in an asymptomatic study population. Holger Hetterich, Christian Bayerl, Annette Peters, Margit Heier, Birgit Linkohr, Christa Meisinger, Sigrid Auweter, Stephan A.R.Kannengießer, Harald Kramer, Birgit Ertl-Wagner, Fabian Bamberg
- Pancreatic fat content by magnetic resonance imaging in subjects with prediabetes, diabetes, and controls from a general population without cardiovascular disease. Sophia D. Heber, Holger Hetterich, Roberto Lorbeer, Christian Bayerl, Jürgen Machann, Sigrid Auweter, Corinna Storz, Christopher L. Schlett, Konstantin Nikolaou, Maximilian Reiser, Annette Peters, Fabian Bamberg

Methodology
- retrospective
- cross sectional study
- performed at one institution

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