

# openheart Investigation of early signs of systolic and diastolic dysfunction among persons with type 1 diabetes

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## ABSTRACT

**Background** Persons with type 1 diabetes have a higher risk to develop heart failure than the general population, and the mechanism behind the increased risk is unclear. In epidemiological studies with hospitalisation for heart failure as endpoint HbA1c, body mass index and decreased kidney function are significant risk factors, but it is unclear how these risk factors influence the development of heart failure.

**Methods** In this study, we investigated early signs of systolic and diastolic dysfunction with transthoracic echocardiography. Statistical analysis on correlation of risk factors and early signs of diastolic and systolic dysfunction was made.

**Results** In this study population of 287 persons with type 1 diabetes, 160 were men and 127 were women with a mean age of 53.8 (SD 11.6) years and a mean diabetes duration of 36.2 (SD 13.5) years. There were 23 (8.2%) persons who fulfilled the definition of systolic dysfunction (ejection fraction <50% or regional wall motion abnormalities) and 24 persons (9%) the definition for diastolic dysfunction. When comparing the groups with either systolic or diastolic dysfunction to the rest of the population, the only significant risk factor was age in both groups and previous myocardial infarction in the systolic group.

**Conclusion** In our study population with type 1 diabetes, we found signs of diastolic dysfunction in 9% and systolic dysfunction in 8.2%. Compared with published data from the general population, this rate is somewhat higher in a younger population. Only age was a significant risk factor in the study.

## INTRODUCTION

Type 1 diabetes (T1D) is a common disease affecting more than 42000 individuals in Sweden,<sup>1</sup> with most diagnosed at early ages. Even with up-to date treatment, life expectancy is lower than of the general population,<sup>2,3</sup> and most excess mortality is due to cardiovascular disease (CVD).<sup>4,5</sup> Heart failure is a common manifestation of CVD among persons with T1D, and the risk for developing heart failure is more than fourfold compared with the general population.<sup>6</sup> Known risk factors for the development of heart failure are poor glycaemic control,<sup>7</sup> decreased renal function<sup>8</sup> and increased body mass index (BMI).<sup>9</sup> Recent studies have shown decreased cardiac function

## Key questions

### What is already known about this subject?

► Persons with type 1 diabetes has a higher risk for developing heart failure than the general population and they are usually younger. Studies with echocardiography have shown both increased risk for systolic and diastolic dysfunction.

### What does this study add?

► The results support previous results and provide additional evidence for the increased risk of systolic and diastolic heart dysfunction in type 1 diabetes in a representative group of persons with type 1 diabetes.

### How might this impact on clinical practice?

► An awareness for the increased risk of heart failure may lead to an earlier optimisation of treatment and possibly also prospective screening in high-risk groups.

related to the degree of albuminuria.<sup>10</sup> Some of these changes may already be detected among adolescents with T1D.<sup>11</sup> Even asymptomatic persons with T1D have a high risk of subclinical echocardiographic abnormalities that may progress to heart failure.<sup>12</sup> Early identification of persons with increased risk for developing heart failure may prevent progression into symptomatic heart failure leading to both high morbidity and mortality. The aim of this study was to investigate the prevalence of systolic and diastolic dysfunction among persons with T1D having at least one CVD risk factor to establish whether screening with echocardiography may be indicated in this population. A secondary aim was to identify variables associated with cardiac dysfunction.

## METHODS

### Study population and recruitment

We identified persons registered in the Swedish national diabetes registry (NDR) with a clinical diagnosis of T1D and age 40 or greater or age 30–40 with additional risk

factors (HbA1c >64 mmol/mol (8%), systolic blood pressure >145 mm Hg, current smoking, microalbuminuria or BMI >30 kg/m<sup>2</sup>) who were treated either within two NU-Hospital group sites (NÄL or Uddevalla) or at the diabetes clinic at Sahlgrenska University hospital/Östra. Potential participants with T1D and age-matched and sex-matched controls randomly identified from the national registry were invited by mail to take part in the study. All invited persons were then contacted by telephone. Those who decided to participate underwent echocardiography and completed a questionnaire. Blood was drawn to screen for laboratory markers and inclusion in a biobank. Initially, our plan was to compare T1D persons with controls, but due to low control participation it was decided the sample was not representative of the general population. In contrast, approximately 80% of persons with T1D who were invited choose to participate. Therefore, the primary evaluation was designed to be within the group of persons with T1D. The final population consisted of 287 individuals with T1D.

### Echocardiography

Transthoracic echocardiography was performed by experienced sonographers or cardiologists following a standardised protocol and commercially available equipment (Vivid 7 or E9; General Electric, Milwaukee, WI). Measurements were made using software (EchoPac; GE) or in-line on the echo machine (Vivid 7 at Uddevalla) according to American Society of Echocardiography criteria.<sup>13,14</sup>

Left ventricular (LV) systolic dysfunction was defined as reduced global systolic function with ejection fraction (EF) <50% and/or presence of regional wall motion abnormalities,<sup>13,15</sup> as both measures confer an independent increased risk for adverse events.<sup>15,16</sup>

LV diastolic function was defined as reduced when both the left atrium was enlarged, and LV relaxation was slow. Left atrium was traced in apical four-chamber view and volume was calculated using the area length formula. Left atrial volume index (LAVI) >34 mL/m<sup>2</sup> was defined as enlarged.<sup>15</sup> LV relaxation was assessed with pulsed wave tissue Doppler of the mitral annulus and defined as reduced when  $e'$ sept was <8 cm/s.<sup>14</sup> In a subgroup of early participants (n=18), the quality of stored images was not high enough for a reliable measurement of left atrial volume. For this subgroup, an experienced cardiologist made a visual assessment of diastolic dysfunction.

Assessment of mitral and aortic valve function was also made to exclude valvular disease as the underlying cause of heart failure.

### Questionnaire

A questionnaire consisting of 89 multiple choice questions was administered covering personal factors (mode of living, relationship status), level of education and work, medical history (with a cardiac focus), medication, tobacco and alcohol habits, physical activity, sleep habits and respiratory problems.

### Laboratory tests

Blood was drawn from all participants for analysis of LDL, triglycerides, HDL, ApoA1, ApoB, Apo A/B, renal function (creatinine), glucose and HbA1c. Estimated glomerular filtration rate (eGFR) was calculated using CKD-EPI according to current guidelines.<sup>17</sup> Albumin creatinine index and blood pressure (systolic and diastolic) were retrieved from record data, as was HbA1c in instances where measurements were missing from blood samples.

### Endpoints

The primary predefined endpoint was the prevalence of systolic (EF <50%) and diastolic dysfunction. In this initial report, we also analysed whether systolic and diastolic function were related to age, sex, diabetes duration, albuminuria (normoalbuminuria, microalbuminuria or macroalbuminuria), eGFR (calculated by CKD-EPI formula),<sup>14</sup> HbA1c, systolic blood pressure, diastolic blood pressure, smoking, BMI or previous myocardial infarction (MI).

### Statistical analysis

For descriptive purposes, means with SDs are presented for continuous variables and numbers with percentages and the exact 95% CI where applicable are presented for categorical variables. Initially, we planned to include 400 persons with T1D, but due to recruiting problems and time constraints we limited the study to 300. The pre-determined level of statistical power was judged to be acceptable for estimating prevalence of systolic and diastolic function (primary effect variables) with 95% CI for proportion of 0.10 (95% CI 0.07 to 0.14) and 0.20 (95% CI 0.16 to 0.25).

For test between two groups with regards to dichotomous variables, Fisher's exact test was used, Mantel-Haenszel  $\chi^2$  test ordered categorical variables,  $\chi^2$  test for non-ordered categorical variables and Mann-Whitney U test for continuous variables. Logistic regression model with age, and age-adjusted models with sex, diabetes duration, smoking, HbA1c, systolic blood pressure, diastolic blood pressure, BMI, previous MI, albuminuria (normoalbuminuria, microalbuminuria and macroalbuminuria) and eGFR as independent variables and systolic cardiac function as dependent variable were performed. Using stepwise logistic regression including those variables being significantly related to systolic function in the age-adjusted analysis, the multivariable model was selected with independent predictors. The corresponding analyses were performed with diastolic function as dependent variable.

All tests were two-tailed and conducted at 0.05 significance level. All analyses are performed using SAS Software V.9.4 (SAS Institute, Cary, NC, USA).

### RESULTS

In total, there were 287 persons with T1D, including 160 (56%) men and 127 women (44%), with mean age of 53.8 (SD 11.6) years and mean diabetes duration of 36.2 (SD 13.5) years (table 1). Complete systolic echocardiographic

**Table 1** Baseline characteristics for persons with T1D

	T1D (n=287)
Age (years)	53.8 (11.6)
Sex	
Men	160 (55.7%)
Women	127 (44.3%)
Diabetes duration (years)	36.2 (13.5)
BMI (kg/m <sup>2</sup> )	26.3 (3.9)
HbA1c (mmol/mol)	61.8 (12.1)
Smoking	
Smoker	36 (12.7%)
Previous smoker	86 (30.3%)
Never smoked	162 (57.0%)
Missing	3
eGFR (CKD-EPI) (mL/min/1.73 m <sup>2</sup> )	91.9 (15.8)
Albuminuria	
Normal	230 (81.0%)
Microalbuminuria	46 (16.2%)
Macroalbuminuria	8 (2.8%)
Missing	3
Systolic blood pressure (mm Hg)	130.6 (14.6)
Systolic blood pressure (categorical)	
<140 mm Hg	215 (75.2%)
≥140 mm Hg	71 (24.8%)
Missing	1
Diastolic blood pressure (mm Hg)	72.4 (9.6)
Diastolic blood pressure (categorical)	
<90 mm Hg	271 (94.8%)
≥90 mm Hg	15 (5.2%)
Missing	1
Myocardial infarction	
Yes	12 (4.2%)
No	273 (95.5%)
Uncertain	1 (0.3%)
Missing	1
Therapeutic regimen	
Basal-bolus insulin	205 (74.54 %)
Mix insulin	2 (0.72 %)
Insulin pump	68 (24.73 %)

For categorical variables n (%) is presented.

For continuous variables mean (SD) is presented.

BMI, body mass index.

data were available in 282 (98%) persons with T1D and diastolic data in 266 (93%) with measurements of LAVI in 248 (86%). In the systolic group, 23 (8.2% (95% CI 5.2 to 12.0)) persons fulfilled the definition of systolic dysfunction (EF <50% or regional wall motion abnormalities) and

24 (9.0% (95% CI 5.9 to 13.1)) in the diastolic group met the definition of diastolic dysfunction. In the subgroup where visual assessment of diastolic function was made, 2 (11.1%) out of 18 had decreased diastolic function.

Among the 23 persons with systolic dysfunction, 2 had EF of 40% to <45%, and one had EF <40%. In the group with T1D and age 50 or older (n=165, 57.5% of the study group), there were 22/149 (14.8% (95% CI 9.5 to 21.5)) persons with diastolic dysfunction and 18/161 (11.2% (95% CI 6.8 to 17.1)) with systolic dysfunction.

Compared with the rest of the population, persons with systolic dysfunction were older (63.4 (SD 14.8) vs 52.8 (SD 10.8) years, p=0.0010) and had a longer diabetes duration (46.5 (SD 14.0) vs 35.3 (SD 13.1) p=0.001). There were also differences in eGFR levels (83.4 (SD 14.3) mL/min/1.73 m<sup>2</sup> vs 92.6 (SD 15.8) mL/min/1.73 m<sup>2</sup>, p=0.0010) and a smaller proportion of patients who never smoked in their past (7 (30.4%) vs 152 (59.4%), p=0.026; table 2) and MI rates (6 (26.1%) vs 6 (2.3%), p<0.0001) in the group with systolic dysfunction. After adjustment for age, only previous MI remained as a significant risk factor (OR 11.27 (95% CI 3.07 to 41.45), p=0.0003 for previous MI; OR 2.05 (95% CI 1.37 to 3.05), p=0.0004 for age by 10 years increase; table 3). Persons with diastolic dysfunction were older (65.5 (SD 11.8) vs 52.0 (SD 10.4) years, p<0.0001), had longer diabetes duration (43.3 (SD 13.5) vs 34.7 (SD 12.5) years, p=0.0069) and a lower eGFR level (83.1 (SD 12.7) vs 93.2 (SD 15.3) mL/min/1.73 m<sup>2</sup>, p<0.0001; table 4). There were no significant risk factors after adjustment for age (table 3).

The prevalence of systolic and diastolic dysfunction in those in the cohort without previous MI (n=273) was 6.3% (95% CI 3.7 to 10.0, n=17) and 8.7% (95% CI 5.5 to 12.9, n=22), respectively. In those age 50 or older, it was 7.9% (95% CI 4.2 to 13.5, n=12) and 14.3% (95% CI 9.0 to 21.2, n=20) compared with 4.3% (95% CI 1.4 to 9.7, n=5) and 1.8% (95% CI 0.2 to 6.3, n=2) in those younger than 50 years with no previous MI for systolic and diastolic dysfunction, respectively.

As a part of the questionnaire only one participant answered yes to the question of having been told by a physician that they had heart failure. When asked “Do you get breathless by walking up two stairs or equivalent at the same rate as your peers of the same age”, 38 (13.3%) answered yes. Of those, 3 (7.9%) had systolic dysfunction and 3 (7.9%) had diastolic dysfunction.

## DISCUSSION

In this study, which was performed to evaluate whether screening with echocardiography may be warranted in persons with T1D and at least one cardiovascular risk factor, the prevalences of systolic and diastolic dysfunction were 8.2% and 9.0%. There were 6 (26.1%) in the group with systolic dysfunction who had a previous MI compared with 6 (2.3%) in the group without systolic dysfunction. In the group without previous MI, 6.3% had systolic dysfunction and 8.7% had diastolic dysfunction. Most of those with either systolic or diastolic dysfunction

**Table 2** Characteristics per systolic dysfunction

	No systolic dysfunction (n=259)	Systolic dysfunction (n=23)	P value
Age (years)	52.8 (10.8)	63.4 (14.8)	0.0010
Age category			
<50 years	116 (44.8%)	5 (21.7%)	
≥50 years	143 (55.2%)	18 (78.3%)	0.033
Sex			
Men	147 (56.8%)	10 (43.5%)	
Women	112 (43.2%)	13 (56.5%)	0.31
Diabetes duration (years)	35.3 (13.1)	46.5 (14.0)	0.0010
BMI (kg/m <sup>2</sup> )	26.2 (3.9)	25.8 (3.0)	0.57
HbA1c	61.7 (12.3)	64.5 (10.6)	0.21
Smoking			
Smoker	31 (12.1%)	4 (17.4%)	
Previous smoker	73 (28.5%)	12 (52.2%)	
Never smoked	152 (59.4%)	7 (30.4%)	0.026
Missing	3	0	
eGFR (CKD-EPI) (mL/min/1.73 m <sup>2</sup> )	92.6 (15.8)	83.4 (14.3)	0.0010
Albuminuria			
Normal	210 (82.0%)	16 (69.6%)	
Microalbuminuria	39 (15.2%)	6 (26.1%)	
Macroalbuminuria	7 (2.7%)	1 (4.3%)	0.18
Missing	3	0	
LVEF category			
<40%	0 (0.0%)	1 (5.0%)	
40% to <45%	0 (0.0%)	2 (10.0%)	
45% to <50%	0 (0.0%)	7 (35.0%)	
≥50%	259 (100.0%)	10 (50.0%)	<0.0001
Missing	0	3	
Systolic blood pressure (mm Hg)	130.7 (14.6)	129.7 (15.8)	0.98
Diastolic blood pressure (mm Hg)	72.7 (9.4)	69.6 (11.6)	0.065
Myocardial infarction			
Yes	6 (2.3%)	6 (26.1%)	
No	251 (97.3%)	17 (73.9%)	
Uncertain	1 (0.4%)	0 (0.0%)	<0.0001
Missing	1	0	

For categorical variables n (%) is presented.

For continuous variables mean (SD) is presented.

For comparison between groups, Fisher's exact test (lowest 1-sided p value multiplied by 2) was used for dichotomous variables, Mantel-Haenszel  $\chi^2$  test was used for ordered categorical variables,  $\chi^2$  test was used for non-ordered categorical variables and Mann-Whitney U test was used for continuous variables.

BMI, body mass index; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction.

were over age 50, where we found 18 (11.2%) with systolic dysfunction and 22 (14.8%) with diastolic dysfunction.

T1D carries a considerable excess risk for cardiovascular disease<sup>5</sup>; therefore, early recognition of those with higher risk for developing heart failure and preventive efforts focusing on modifiable risk factors may be ways to decrease the cardiovascular burden.

Many registry studies investigating heart failure use clinical heart failure as an endpoint (admission to hospital due to heart failure) due to lack of echocardiographic data. By using admission for heart failure, it is possible to retrospectively study a large population over time based on existing registry data.<sup>6</sup> In recent years, a couple of cross-sectional studies with cardiac ultrasound

**Table 3** Analyses of risk factors for systolic and diastolic dysfunction

	Adjusted for age (years) (Systolic)	Adjusted for age (years) (Diastolic)
	OR (95% CI) p value	OR (95% CI) p value
Age (OR per 10 years)	2.15 (1.47 to 3.14) <0.0001	2.95 (1.90 to 4.57) <0.0001
Sex (women vs men)	1.75 (0.71 to 4.28) 0.22	1.44 (0.58 to 3.60) 0.43
Diabetes duration (OR per 10 years)	1.37 (0.91 to 2.05) 0.13	1.03 (0.71 to 1.50) 0.89
BMI (OR per 5 kg/m <sup>2</sup> )	1.08 (0.58 to 1.99) 0.81	0.91 (0.47 to 1.73) 0.75
HbA1c (OR 10 mmol/mol)	1.30 (0.90 to 1.87) 0.16	0.71 (0.46 to 1.09) 0.12
Smoking (current vs never)	3.33 (0.88 to 12.5) 0.075	0.86 (0.17 to 4.35) 0.85
eGFR (CKD-EPI) (OR for decrease of 10 mL/min/1.73 m <sup>2</sup> )	1.06 (0.79 to 1.45) 0.68	1.01 (0.71 to 1.43) 0.97
Microalbuminuria (yes vs no)	1.72 (0.60 to 4.92) 0.31	0.41 (0.08 to 1.97) 0.26
Macroalbuminuria (yes vs no)	2.18 (0.27 to 29.23) 0.39	2.06 (0.16 to 26.79) 0.58
Systolic blood pressure (OR per 5 mm Hg)	0.89 (0.76 to 1.05) 0.18	0.99 (0.86 to 1.15) 0.94
Diastolic blood pressure (OR per 5 mm Hg)	0.96 (0.77 to 1.20) 0.71	0.95 (0.77 to 1.18) 0.64
Myocardial infarction (yes vs no)	11.27 (3.07 to 41.45) 0.0003	1.39 (0.25 to 7.71) 0.70

in asymptomatic persons with T1D<sup>12 18</sup> have shown a relatively high prevalence of systolic and diastolic dysfunction.

Wai *et al*<sup>12</sup> found a prevalence of echocardiographic changes of 29% (39 of 136) with a majority (27 individuals, 20%) having diastolic dysfunction. Jensen *et al*<sup>18</sup> found 157 (13%) of 1093 persons to have diastolic dysfunction and 17 (1.7%) with systolic dysfunction. The main risk factor in both studies was age. Jensen *et al*<sup>18</sup> also found albuminuria and female sex to be important risk factors in a multivariate analysis, while Wai *et al*<sup>12</sup> found BMI to be a significant risk factor.

There are some studies on systolic and diastolic dysfunction in the general population, among those are the Copenhagen City Heart Study,<sup>19</sup> which reported a prevalence of LVEF <50% in 1036 individuals with a mean age of 59.8 years to be 1.1%. Redfield *et al*<sup>20</sup> found in a cohort of 2042 persons with a mean age of 62.8 years a 6.0% prevalence of EF <50% and diastolic dysfunction of any grade in 27% (with 71% of cases of diastolic dysfunction among those over age 65 years).

Direct comparison between different studies is complicated as both the definition of systolic and diastolic dysfunction differs between studies, and results, especially for diastolic dysfunction, differ between investigators.<sup>21</sup>

Our prevalence data for diastolic dysfunction are nearly equal with Jensen *et al*s,<sup>18</sup> while we had a higher rate of systolic dysfunction. This may partly be explained by different definitions of systolic dysfunction (EF <45% vs <50% and regional wall motion abnormalities). Using EF <45%, the prevalence of systolic dysfunction was 1.1% in our study. Compared with studies in the general population, our rate of systolic dysfunction is higher (with nearly the same definition) but in a population 7–10 years younger. Excluding those with previous MI (n=12 in the group with systolic data), the prevalence in our study was 6.3%.

The mechanism causing changes in cardiac function has been proposed to be part of diabetic cardiomyopathy where the myocardium becomes stiffer and there are changes in the dynamics of left ventricular filling and increased importance of the support of the left atrium in the inflow phase.<sup>22</sup> In our earlier epidemiological studies, HbA1c and albuminuria were significant risk factors for hospitalisation for heart failure in multivariate analysis.<sup>6</sup> In univariate comparison in this study, there was no significant difference in HbA1c between diabetes groups with and without diastolic dysfunction. This may either be a function of the small population or that HbA1c is a late risk factor and other factors are more important for the early development of heart failure. Another reason may be that we only had one HbA1c measurement, while glycaemic control over time may be the main risk factor.

As changes in cardiac haemodynamics occur with increasing age, for example *e'* decreases with 1 cm/s, and decade,<sup>23</sup> there may be a reason to use age-adjusted criteria for decreased cardiac function.<sup>24</sup>

The current findings combined with earlier studies demonstrate that a discussion on whether screening with echocardiography should be performed in certain persons with T1D is essential. From our results, we believe general screening should not be indicated in persons younger than age 50, where cardiac dysfunction was not very common. However, in older patients with T1D, where the prevalence was higher, detecting cardiac dysfunction may be more worthwhile and lead to better prevention of more severe heart failure (eg, by increasing physical activity or optimising antihypertensive treatment) and in certain cases optimising treatment (eg, with renin aldosterone angiotensin system

**Table 4** Characteristics per diastolic dysfunction

	No diastolic dysfunction (n=242)	Diastolic dysfunction (n=24)	P value
Age (years)	52.0 (10.4)	65.5 (11.8)	<0.0001
Age category			
<50 years	115 (47.5%)	2 (8.3%)	
≥50 years	127 (52.5%)	22 (91.7%)	0.0002
Sex			
Men	137 (56.6%)	11 (45.8%)	
Women	105 (43.4%)	13 (54.2%)	0.42
Diabetes duration (years)	34.7 (12.5)	43.3 (13.5)	0.0069
BMI (kg/m <sup>2</sup> )	26.4 (3.9)	25.6 (3.1)	0.40
HbA1c	62.2 (12.2)	58.1 (11.9)	0.072
Smoking			
Smoker	33 (13.8%)	2 (8.3%)	
Previous smoker	65 (27.1%)	12 (50.0%)	
Never smoked	142 (59.2%)	10 (41.7%)	0.43
Missing	2	0	
eGFR (CKD-EPI) (mL/min/1.73 m <sup>2</sup> )	93.2 (15.3)	83.1 (12.7)	<0.0001
Albuminuria			
Normal	195 (81.6%)	21 (87.5%)	
Microalbuminuria	37 (15.5%)	2 (8.3%)	
Macroalbuminuria	7 (2.9%)	1 (4.2%)	0.65
Missing	3	0	
LVEF category			
<40%	1 (0.4%)	0 (0.0%)	
40% to <45%	2 (0.8%)	0 (0.0%)	
45% to <50%	3 (1.3%)	4 (16.7%)	
≥50%	232 (97.5%)	20 (83.3%)	0.051
Missing	4	0	
Systolic blood pressure (mm Hg)	129.8 (14.0)	133.5 (18.7)	0.16
Diastolic blood pressure (mm Hg)	72.9 (9.2)	68.8 (13.6)	0.099
Myocardial infarction			
Yes	9 (3.7%)	2 (8.3%)	
No	231 (95.9%)	22 (91.7%)	
Uncertain	1 (0.4%)	0 (0.0%)	0.53
Missing	1	0	

For categorical variables n (%) is presented.

For continuous variables mean (SD) is presented.

For comparison between groups, Fisher's exact test (lowest 1-sided p value multiplied by 2) was used for dichotomous variables, Mantel-Haenszel  $\chi^2$  test was used for ordered categorical variables,  $\chi^2$  test was used for non-ordered categorical variables and Mann-Whitney U test was used for continuous variables.

BMI, body mass index; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction.

inhibitors and beta-blockers). In a randomised study, imaging-guided cardioprotective treatment has actually been shown to improve prognosis in a general population of asymptomatic high-risk patients who adhered to treatment.<sup>25</sup> But inadequate adherence and up-titration of medication was low and there was no effect

using intention-to-treat analysis. In order to implement screening, further randomised studies with improved methodology is required.

A strength of this study is that the population is likely to be a representative sample of persons older than age 40 with T1D followed at adult diabetes clinics since

approximately 80% of individuals chose to participate. Another strength is that examinations were masked for as long as possible since healthy individuals were also intermittently examined. However, it should be noted that staff performing echocardiography may have been capable of identifying certain persons with T1D (eg, by noticing lipohypertrophy from insulin injections) although not technically informed about T1D diagnosis. Another strength is the use of LAVI for defining diastolic dysfunction with the possibility of using reference values and which is recommended in recent guidelines.<sup>13</sup> The low number of participants with either systolic or diastolic dysfunction in the study is another limitation making it more problematic to find associations between cardiac dysfunction and risk factors. Another limitation is that only one measurement was available when examining possible risk factors for cardiac dysfunction. However, in future studies, it may be possible to link the current cohort to the NDR in order to maintain long-term information on risk factors. Finally, some variables (eg, blood pressure) were obtained from clinical records where the measurement closest to the echocardiography was used, and which may not be fully representative of blood pressure levels at the time of echocardiography.

## CONCLUSION

In conclusion, our findings support earlier studies of a higher rate of both systolic and diastolic dysfunction among persons with T1D compared with the general population according to earlier published data.<sup>18</sup> The main risk factor in our study was older age, while BMI was not statistically different between the groups. Among persons with T1D and age 50 or older, the high prevalence of systolic dysfunction (9.9%) and diastolic dysfunction (14.8%) indicates that it may be warranted to screen persons with T1D over age 50 for early signs of cardiac dysfunction.

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**Competing interests** None declared.

**Patient consent for publication** Obtained.

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**Data availability statement** Data are available on reasonable request.

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