


# BMJ Open Observational study investigating the prevalence of asymptomatic stage B heart failure in patients with type 2 diabetes who are not known to have coronary artery disease

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## ABSTRACT

**Objective** To identify the prevalence of stage B heart failure (SBHF) in patients with type 2 diabetes mellitus (T2DM) with no history of cardiovascular disease (CVD).

**Design** Observational study.

**Setting** A single-centre study in which eligible patients were recruited from T2DM clinic. Following consent, patients completed a questionnaire and underwent physical examinations. Patients had blood drawn for laboratory investigations and had a transthoracic echocardiography.

**Participants** A total of 305 patients who were not known to have CVD were recruited. Patients with deranged liver function tests and end stage renal failure were excluded.

**Main outcome measures** Echocardiographic parameters such as left ventricular ejection fraction, left ventricular mass index (LVMI), left ventricular hypertrophy, left atrial enlargement and diastolic function were examined.

**Results** A total of 305 patients predominantly females (65%), with mean body mass index of 27.5 kg/m<sup>2</sup> participated in this study. None of them had either a history or signs and symptoms of CVD. Seventy-seven percent of patients had a history of hypertension and 83% of this study population had T2DM for more than 10 years. Mean HbA1c of 8.3% was recorded. Almost all patients were taking metformin. Approximately, 40% of patients were on newer anti-T2DM agents such as sodium-glucose cotransporter-2 and dipeptidyl peptidase 4 inhibitors. Fifty-seven percent (n=174) of the study population had SBHF at the time of study: diastolic dysfunction, increased LVMI and increased left atrial volume index (LAVI) were noted in 51 patients (17%), 128 patients (42%) and 98 patients (32%), respectively. Thirty-seven patients (12%) had both increase LVMI and LAVI.

**Conclusion** Our study has revealed a high prevalence of SBHF in T2DM patients without overt cardiac disease in Malaysia that has one of the highest prevalence of TDM in the world.

## INTRODUCTION

A dramatic increase in prevalence of type 2 diabetes mellitus (T2DM) from 4.7% in 1980

## Strengths and limitations of this study

- First study reporting the prevalence of stage B heart failure in type 2 diabetes mellitus (T2DM) patients with no history of coronary artery disease from Malaysia that has one of the highest prevalence of T2DM in the world is of interest.
- Comprehensive 2-dimensional echocardiography was performed to identify structural and functional abnormalities of study population.
- A limitation is the absence of assessment of global longitudinal strain in our study.

to 8.5% in 2014 was reported globally.<sup>1</sup> In 2016, an estimated 1.6 million deaths were directly caused by T2DM.<sup>1</sup> In Malaysia, the prevalence of T2DM is one of the highest in the world with 3.6 million individuals affected (16.9% of the adult population) by it. Many of these patients with T2DM are expected to succumb to cardiovascular disease-related health problems. Among them, heart failure is of most concern as it is progressive in nature with unfavourable outcome.<sup>2-4</sup> Incidence of heart failure in T2DM is two to five-folds higher irrespective of concomitant risk factors such as hypertension, coronary artery disease and any other cardiac disease.<sup>5</sup> T2DM increases the relative risk of various vascular events by twofold in men and threefold in women. In the case of heart failure, the relative risk is eightfold higher in women.<sup>6</sup> Several pathophysiological mechanisms such as metabolic disturbances, myocardial fibrosis, microvascular dysfunction, cardiac autonomic neuropathy and insulin resistance have been proposed to contribute to structural and functional myocardial impairment

leading to a pathological condition known as diabetic cardiomyopathy.<sup>7,8</sup>

Recently, there has been much interest in subclinical stage B heart failure (SBHF) in patients with T2DM. Before the development of symptomatic heart failure, as much as 50% of patients with T2DM have asymptomatic left ventricular dysfunction (LVD).<sup>9,10</sup> Four stages of heart failure have been proposed as follows: stage A: high risk for development of heart failure with no structural heart disease, stage B: structural or functional cardiac dysfunction with no signs and symptoms of heart failure, stage C: clinical manifestations of heart failure and stage D: end stage or refractory heart failure.<sup>10</sup> Cardiac imaging plays a crucial role in diagnosis of SBHF. Definition of SBHF includes the presence of at least one of the following echocardiographic parameters: (1) left ventricular hypertrophy, (2) left atrial enlargement (LAE), (3) abnormal E/E' and impaired global longitudinal strain (GLS).<sup>11</sup> One year mortality of SBHF was reported as 5%–10% which increases to 15%–30% if the disease progress to stage C heart failure and to >50% in stage D heart failure. Early identification of preclinical stage of heart failure may propose early initiation of intensive therapies that will delay or prevent the disease progression to overt heart failure.

The aim of our study was to identify the prevalence of preclinical stage of LVD (SBHF) in patients with T2DM with no history of coronary artery disease or heart failure. Previous studies exploring asymptomatic LVD in T2DM have mainly been reported in the Western world and Caucasian populations.

## METHODS

### Study design

This is a single-centre observational (cross-sectional) study in which clinical and echocardiographic characteristics of T2DM patients were examined. A total of 305 patients were recruited. Patients with history of heart failure, coronary artery disease, valvular heart disease, cardiac arrhythmia, congenital heart disease, cardiomyopathy, deranged liver function test and end stage renal failure were excluded. Eligibility of patients was assessed by questionnaire and physical examination. New York Heart Association (NYHA) classification and Canadian Cardiovascular Society (CCS) grading of angina pectoris (CCS Angina Grading Scale or CCS Functional Classification of Angina) were used to assess functional and angina status. Laboratory investigations and 2-dimensional echocardiography were performed on patients after informed consent.

Echocardiographic parameters such as left ventricular ejection function (LVEF), left ventricular mass index (LVMI), left atrial volume index (LAVI), left ventricular wall thickness, E/A ratio of trans mitral flow, deceleration time (DT) and diastolic function were recorded. LVEF was determined by using biplane modified Simpson's measurements. The mitral flow was assessed in the apical

four-chamber view by pulsed wave Doppler. Diastolic dysfunction was identified according to updated 2016 American Society of Echocardiography guideline. Left ventricular mass was calculated by using Devereux and Reichek 'cube' formula: LV mass (g)=0.8{1.04{([LVEDD +IVSd +PWd]<sup>3</sup> –LVEDD<sup>3</sup>)}+0.6. LVMI was indexed according to individual body surface area and categorised into normal and increased LVMI by taking account of gender as follows; normal range in female 43–95 g/m<sup>2</sup>, male 49–115 g/m<sup>2</sup>. Calculation of relative wall thickness (RWT) with the formula (2x posterior wall thickness)/(LV internal diameter at end diastole) permitted further categorisation of increase LVMI as either concentric (RWT >0.42) or eccentric (RWT <0.42) hypertrophy. Patients whose LVMI within normal range were identified as having concentric remodelling and normal geometry accordingly, based on RWT results. LAVI was measured from standard apical two chamber and four chamber views. Volume was calculated by using area-length approximation: 8/3π (A1xA2/L) and indexed to body surface area (BSA). LAE was defined as LAVI ≥34 mL/m<sup>2</sup>.<sup>12</sup>

Blood tests were taken for HbA1c and B-type natriuretic peptide (BNP). The evaluation of BNP levels was done by analysing plasma using Siemens Advia Centaur assay which is an automated two site sandwich chemiluminescent immunoassay.

### Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

### Data variables

Demographic characteristics, coexisting medical conditions, current medications, established macrovascular (peripheral and cerebrovascular diseases) and microvascular (retinopathy, neuropathy and nephropathy) complications, echocardiographic parameters and laboratory investigations results were recorded.

### Statistical analysis

Descriptive statistics were used for analysis of demographic characteristics. Continuous variables were expressed as mean±SD. The differences between normally distributed numeric variables were evaluated by t-test or one-way analysis of variance, while non-normally distributed variables were analysed by Mann-Whitney U test or Kruskal-Wallis variance analysis, as appropriate. X<sup>2</sup> test was employed for the comparison of categorical variables and testing the null hypothesis. Multivariable logistic regression analysis was done to identify the association of independent variables to LVD. Correlations of LVMI with baseline characteristics and echocardiographic parameters were checked by multivariable linear regression analysis. All data were analysed by SPSS.

**Table 1** Demographic characteristics, concomitant risk factors, current medication and laboratory investigations of T2DM patients with asymptomatic stage B heart failure and normal left ventricular function

Variables	Total study population (305 patients)	Stage B heart failure (174 patients, 57%)	Normal LV function (131 patients, 43%)	P value
Age (years)	62±10	64±10	60±10	0.001
Age more than 60 years	200 (65.6%)	123 (70.7%)	77 (58.8%)	0.030
Male	108 (35.4%)	46 (26.4%)	62 (47.3%)	0.000
Female	197 (64.6%)	128 (73.6%)	69 (52.7%)	0.000
BMI (kg/m <sup>2</sup> )	27.5±4.9	27.7±4.7	27.2±5.1	0.383
Ethnic groups				0.011
Malay	88 (28.9%)	54 (31.0%)	34 (26.0%)	
Chinese	87 (28.5%)	59 (33.9%)	28 (21.4%)	
India	124 (40.7%)	57 (32.8%)	67 (51.1%)	
Active smokers	25 (8.3%)	14 (8.09%)	11 (8.4%)	0.879
Alcohol	31 (10.3%)	12 (7.0%)	19 (14.7%)	0.088
Duration of diabetes				0.187
Less than 5 years	21 (6.9%)	8 (4.6%)	13 (9.9%)	
5–10 years	30 (9.8%)	17 (9.8%)	13 (9.9%)	
More than 10 years	254 (83.3%)	149 (85.6%)	105 (80.2%)	
Hypertension	234 (76.7%)	144 (82.8%)	90 (68.7%)	0.004
Systolic blood pressure (mm Hg)	137±17	139±17	134±16	0.006
Diastolic blood pressure (mm Hg)	74±11	74±11	74±11	0.706
Heart rate (beats/min)	85±14	84±13	85±16	0.581
Dyslipidaemia	278 (91.1%)	161 (92.5%)	117 (89.3%)	0.328
T2DM-related complications				
Cerebrovascular accidents	16 (5.2%)	11 (6.3%)	5 (3.8%)	0.331
Peripheral vascular disease	6 (2.0%)	4 (2.3%)	2 (1.5%)	0.631
Retinopathy	67 (22.0%)	39 (22.4%)	28 (21.4%)	0.828
Neuropathy	56 (18.4%)	33 (19%)	23 (17.6%)	0.753
Albuminuria	86 (28.2%)	52 (29.9%)	34 (26.0%)	0.450
Laboratory				
HbA1c (%) (mmol/mol)	8.3±1.8	8.3±1.8	8.3±1.8	0.797
eGFR (mL/min/1.73m <sup>2</sup> )	78±17	75±18	82±14	0.001
BNP (pg/mL)	18 (7, 33)	24 (11, 41)	11 (5, 22)	
Current medications				
Metformin	279 (91.5%)	158 (90.8%)	121 (92.4%)	0.629
Sulphonylurea	93 (30.5%)	54 (31.0%)	39 (29.8%)	0.812
DPP4i	122 (40.0%)	71 (40.8%)	51 (38.9%)	0.741
SGLT2i	127 (41.6%)	66 (37.9%)	61 (46.6%)	0.130
GLP-1RA	26 (8.5%)	11 (6.3%)	15 (11.5%)	0.112
Insulin	186 (61.0%)	106 (60.9%)	80 (61.1%)	0.979
ACEI	227 (74.4%)	130 (74.7%)	97(74.0%)	0.895
CCB	139 (45.6%)	93 (53.4%)	46 (35.1%)	0.001
Diuretics	55 (18.0%)	37 (21.3%)	18 (13.7%)	0.091
Beta blockers	42 (13.8%)	28 (16.1%)	14 (10.7%)	0.175
Statin	275 (90.2%)	156 (89.7%)	119 (90.8%)	0.731
Aspirin	205 (67.2%)	116 (66.7%)	89 (67.9%)	0.815
Clopidogrel	9 (3.0%)	4 (2.3%)	5 (3.8%)	0.438

ACEI, angiotensin converting enzyme inhibitors; BMI, body mass index; BNP, B-type natriuretic peptide; CCB, calcium channel blockers; DPP4i, dipeptidyl peptidase 4 (DPP-4) inhibitors; eGFR, glomerular filtration rate; GLP-1RA, glucagon-like peptide-1 receptor agonist; LV, left ventricular; SGLT2i, sodium-glucose transport protein 2 inhibitors; T2DM, type 2 diabetes mellitus.

**Table 2** Echocardiographic parameters of study populations divided according to left ventricular function

Variables	Total study population (305 patients)	Stage B heart failure (174 patients, 57%)	Normal LV function (131 patients, 43%)	P value
Left ventricular ejection fraction (%)	68±4	68±4	67±4	0.062
E wave of transmitral flow (cm/s)	63.98±17.45	63.83±18.21	64.18±16.46	0.863
E/A ratio	108 (35.4%)	0.77±0.25	0.82±0.26	0.089
Deceleration time (msec)	197 (64.6%)	218.87±63.43	216.34±52.52	0.713
E/E' ratio	9.63±2.98	16.33±3.44	8.98±2.07	0.001
Diastolic function				0.0003
Normal	254 (83.3%)	123 (70.7%)	131 (100.0%)	
Indeterminate	43 (14.1%)	43 (24.7%)	0 (0.00%)	
Diastolic dysfunction	8 (2.6%)	8 (4.6%)	0 (0.00%)	
LV EDD (cm)	4.45±0.60	4.5±0.6	4.3±0.5	0.0002
Relative wall thickness (cm)	0.41±0.12	0.44±0.13	0.40±0.12	0.072
Left atrial volume (mL)	39.14±12.58	44.39±12.90	32.17±7.91	0.0001
Left atrial volume index (mL/m <sup>2</sup> )	22.77±7.10	34.86±7.11	18.36±4.02	0.0002
Reference range	207 (67.9%)	76 (43.7%)	131 (100.0%)	
Mild abnormal	56 (18.4%)	56 (32.2%)	0 (0.00%)	
Moderate abnormal	40 (13.1%)	40 (23.0%)	0 (0.00%)	
Severe abnormal	2 (0.7%)	2 (1.1%)	0 (0.00%)	
Left ventricular mass (g)	176.57±63.70	201.67±68.61	143.42±68.61	0.0002
Left ventricular mass index (g/m <sup>2</sup> )	101.08±32.29	115.98±33.40	81.40±16.37	0.0001
Reference range	177 (58.0%)	46 (26.4%)	131 (100.0%)	
Mild abnormal	45 (14.8%)	45 (25.9%)		
Moderate abnormal	33 (10.8%)	33 (19.0%)		
Severe abnormal	50 (16.4%)	50 (28.7%)		
Left ventricular hypertrophy				
Eccentric hypertrophy		52 (17.0%)		
Concentric hypertrophy		76 (24.9%)		
Concentric remodelling			71 (23.3%)	
Normal geometry			106 (34.8%)	

LV EDD, left ventricular end diastolic diameter.

## DATA AVAILABILITY

The data sets used and/or analysed are available from the corresponding author on reasonable request.

## RESULTS

A total of 305 patients (mean age of 62.78±10.58 years) participated in this study. Female predominance (65%) with mean BMI of 27.47±4.88 kg/m<sup>2</sup> were noted. Patients of Indian ethnicity constituted 41% of study population. Twenty-five patients (3.3%) were noted as active smoker and 31 patients (10.2%) were recorded as current alcohol consumers. Coexisting hypertension was present in 234 patients (77%) and dyslipidaemia in 278 patients (91%). Majority of study population (253 patients, 83%) were known to have diabetes for more than 10 years. Mean HbA1c of 8.3%±1.8% was recorded. Only 67 patients

(22%) had HbA1c<7% at the time of study. Almost all patients (92%) were on metformin and 61% were on insulin. Only 40% of study population were taking newer antidiabetic medications such as sodium-glucose cotransporter 2i and dipeptidyl peptidase 4i.

More than one-third of patients (114 patients, 37%) were diagnosed to have microvascular complications such as retinopathy in 67 patients (22%), neuropathy in 56 patients (18%) and albuminuria in 86 patients (28%). Macrovascular complications were noted in 21 patients (7%) as follows; peripheral vascular disease (PVD) in six patients (2%) and cerebrovascular accident (CVA) in 16 patients (5%). 99% of patients (302 patients) fell into NYHA class I. Two hundred and eighty-eight patients (98%) were totally free from angina symptoms and classified as CCS class 0. Clinical examinations revealed none of

**Table 3** Logistic regression analysis for predictors of stage B heart failure in T2DM patients

Variable	HR	95% CI	P value
Age	1.027	0.978 to 1.078	0.282
Age >60	1.197	0.453 to 3.166	0.717
Female gender*	3.305	1.811 to 6.031	0.000
Ethnic Chinese†	1.922	0.867 to 4.261	0.108
Ethnic Indian‡	0.445	0.229 to 0.864	0.017
BMI	1.137	1.059 to 1.221	0.000
Duration of diabetes			
5–10 years‡	1.356	0.264 to 6.952	0.715
More than 10 years‡	1.317	0.320 to 5.418	0.703
Hypertension	1.758	0.767 to 2.367	0.890
Duration of hypertension			
5–10 years§	3.791	0.400 to 35.898	0.245
More than 10 years§	5.040	0.591 to 42.992	0.139
Dyslipidaemia	6.233	1.478 to 26.295	0.013
PVD	1.208	0.135 to 10.763	0.866
CVA	1.364	0.350 to 5.314	0.654
Albuminuria	1.474	0.684 to 3.177	0.322
Neuropathy	1.004	0.397 to 2.539	0.993
Retinopathy	0.744	0.323 to 1.714	0.487
HbA1c	0.966	0.812 to 1.148	0.692
BNP	4.227	2.441 to 7.318	0.0003
eGFR	0.976	0.961 to 0.991	0.001
Metformin	1.039	0.369 to 2.922	0.943
Sulfonylurea	1.315	0.657 to 2.629	0.439
DPP4i	1.347	0.740 to 2.451	0.330
SGLT2i	0.632	0.346 to 1.154	0.135
GLP1-RA	0.397	0.137 to 1.148	0.088
Insulin	1.076	0.520 to 2.225	0.843
ACE/ARB	0.268	0.104 to 0.689	0.006
CCB	1.468	0.766 to 2.813	0.247
Beta blocker	0.575	0.235 to 1.405	0.224
Statin	0.227	0.054 to 0.947	0.042
AV calcifications	1.262	0.296 to 5.380	0.753
RWT	5.282	0.693 to 40.245	0.108
Left atrial volume	0.854	0.696 to 1.049	0.134
Left atrial volume index	1.732	1.201 to 2.500	0.003
Left ventricular mass	1.011	0.969 to 1.055	0.613
Left ventricular mass index	1.066	0.986 to 1.151	0.109

\*Male gender is the reference.

†Malay ethnic is the reference.

‡DM for less than 5 years is the reference.

§Hypertension for less than 5 years is the reference.

ACE, angiotensin-converting enzyme ; ARB, angiotensin II receptor blockers; AV, Aortic Valve; BMI, body mass index; BNP, B-type natriuretic peptide; CCB, calcium channel blockers; CVA, cerebrovascular accident; DPP4i, dipeptidyl peptidase 4 inhibitors; eGFR, glomerular filtration rate; GLP1-RA, glucagon-like peptide-1 receptor agonist; PVD, peripheral vascular disease; RWT, relative wall thickness; SGLT2i, sodium-glucose transport protein 2 inhibitors; T2DM, type 2 diabetes mellitus.

the recruited patients had signs of heart failure. Normal BNP result was recorded in 98% our study population.

Normal left ventricular systolic function with mean LVEF of 68%±4% was identified. One hundred and seventy-four patients (57%) had SBHF. Diastolic dysfunction, increased LVMI and increased LAVI were noted in 51 patients (17%), 128 patients (42%) and 98 patients (32%), respectively. Thirty-seven patients (12%) were having both increase LVMI and LAVI. Concentric hypertrophy (RWT >0.42) was identified in 76 patients (25%) and eccentric hypertrophy (RWT ≤0.42) was noted in 52 patients (17%) of patients with increased LVMI. Concentric remodelling in 71 patients (23%) and the rest 105 patients (34%) were diagnosed with normal geometry.

Demographic characteristics, concomitant risk factors, current medications and laboratory results among patients with asymptomatic LV dysfunction and normal LV function were shown in [table 1](#). Older age group, female predominance, higher mean BMI, lower mean glomerular filtration rate (eGFR) and higher BNP were noted in SBHF patient group. Pre-existing comorbid conditions such as hypertension and dyslipidaemia were more commonly seen in these patients. Microvascular and macrovascular manifestations were also more prevalent in patients with SBHF. Statistically significant differences in echocardiographic parameters among two groups of patients were identified. Higher mean E/E' ratio, left ventricular end diastolic diameter, LAVI and LVMI were noted in patients with SBHF ([table 2](#)).

Multivariate logistic regression analysis identified that female gender (HR: 3.305 (95% CI: 1.811 to 6.031), p=0.000098), higher BMI (HR: 1.137 (95% CI: 1.059 to 1.221), p=0.000425), hypercholesterolemia (HR: 6.233 (95% CI: 1.478 to 26.295), p=0.013) and LAVI (HR: 1.732 (95% CI: 1.201 to 2.500), p=0.003) were statistically significant predictors of SBHF. Higher eGFR, usage of ACE/ARB and statin were found out to have protective effect on the development of SBHF. Older age, coexisting hypertension, longer duration of diabetes, hypertension and the presence of microvascular and macrovascular manifestations were predictors of asymptomatic LV dysfunction but none of them reach statistically significant p value ([table 3](#)).

Subgroup analysis on echocardiographic parameters on the presence of hypertension was evaluated in T2DM patients with (n=234, 77%) and without hypertension (n=71, 23%). Normal left ventricular systolic function with similar mean LVEF was noted in both patient groups. Statistically significant higher average E/E', left atrial volume and LAVI were noted in T2DM patients with hypertension. SBHF was noted more commonly in patients with hypertension (61.5% vs 42.3%) ([table 4](#)).

## DISCUSSION

Our study cohort represents real-world asymptomatic T2DM patient group. It showed similar demographic characteristics (mean age of 63±11 years, female predominance)

**Table 4** Echocardiographic parameters among diabetic patients with or without hypertension

Parameter	T2DM with HTN (n=234)	T2DM without HTN (n=71)	P value
Ejection fraction (%)	68.28±4.53	68.24±4.32	0.950
Left ventricular mass (g)	176.96±65.29	175.29±58.60	0.847
LVMI (g/m <sup>2</sup> )	101.27±33.16	100.44±29.48	0.850
Reference range	132 (56.4%)	45 (63.4%)	0.404
Mild abnormal	34 (14.5%)	11 (15.5%)	
Moderate abnormal	25 (10.7%)	8 (11.3%)	
Severe abnormal	43 (18.4%)	7 (9.9%)	
E velocity (m/sec)	64.34±17.19	63.95±17.55	0.960
E/A	0.76±0.23	0.91±0.32	0.0004
DT (msec)	219.67±60.52	211.31±52.68	0.304
Average E/E'	9.94±3.12	8.64±2.21	0.001
Relative wall thickness	0.43±0.13	0.42±0.098	0.630
Left ventricular end diastolic diameter (cm)	4.44±0.62481	4.48±0.49	0.578
Diastolic function			0.103
Normal	189 (80.8%)	65 (91.5%)	
Indeterminate	38 (16.2%)	5 (7.0%)	
Abnormal	7 (3.0%)	1 (1.4%)	
Left atrial volume	40.32±12.65	35.27±11.60	0.003
Left atrial volume index (mL/m <sup>2</sup> )	23.47±7.18	20.46±6.31	0.001
Reference range	150 (64.1%)	57 (80.3%)	0.079
Mild abnormal	48(20.5%)	8 (11.3%)	
Moderate abnormal	34 (14.5%)	6 (8.5%)	
Severe abnormal	2 (0.9%)	0	
Stage B heart failure	144 (61.5%)	30 (42.3%)	0.004

DT, deceleration time; HTN, hypertension; LVMI, left ventricular mass index; T2DM, type 2 diabetes mellitus.

and prevalence of comorbidities (HTN in 77% and dyslipidaemia 91% of study population) as previous reports.<sup>13–15</sup> Mean BMI of 27.47±4.88kg/m<sup>2</sup> with higher percentage of patients (85%) were identified as overweight/obese in our study compared with previous study conducted in Malaysia that had reported similar prevalence (72%–75%) of patients who are overweight/obese.<sup>16 17</sup> In our study cohort, lower prevalence of macrovascular complications such as CVA and PVD (6.8% vs 32.2%),<sup>18</sup> microvascular complications such as nephropathy (albuminuria only, normal eGFR) (28.2% vs 30%–50%),<sup>19</sup> retinopathy (22.0% vs 30%)<sup>20</sup> and neuropathy (18.4% vs 30%–50%)<sup>21</sup> were noted comparing to previous reports. Seventy-eight percent of patients were noted to have poor glycaemic control (study population targeted HbA1c of 6.6%–7.0%)<sup>22</sup> out of which 56 patients (18%) were having HbA1c of >10%. Consistent findings on poor glycaemic control in Malaysian T2DM population were noted across various studies over few decades.<sup>16 23 24</sup>

Left ventricular diastolic dysfunction with normal systolic function in diabetic patients has been an area of interest over decades. Prevalence of diastolic dysfunction in T2DM patients with preexisting comorbidities ranged from 48% to 81% among various studies.<sup>25–27</sup> Lower prevalence of

diastolic dysfunction (16.7%) was noted in our study population. Female gender, ageing, high BMI, HbA1c level, diabetic microangiopathies and duration of diabetes have been reported as predictors of incidence of LV diastolic dysfunction.<sup>27–29</sup> Among them, hypertension has been a debatable coexisting medical condition for the development of LV diastolic dysfunction.<sup>25 28</sup> In terms of treatment strategies, the The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) updated clinical practice guidelines recommend the use of disease modifying medications in an attempt to prevent or delay progression to overt heart failure in patients with high risk factors (stage A heart failure) and asymptomatic structural heart disease (SBHF) to initiate.<sup>30</sup>

There have been previous studies that had reported on the prevalence of SBHF in T2DM patients. In a study conducted in Australia, Wang *et al* reported a similar prevalence—58% of non-ischaemic SBHF in asymptomatic T2DM patients aged ≥65 years with preserved LVEF. Similar echocardiographic parameters were used as our study apart from GLS that was abnormal in 23% of that study population.<sup>31</sup> In an earlier study conducted in Italy, the SHORTWAVE investigators reported that 68% of asymptomatic T2DM patients

had abnormal circumferential and longitudinal LV systolic functions as well as diastolic dysfunction.<sup>9</sup> In another Australian study involving patients with at least one cardiovascular risk factors that included T2DM, Yang *et al* reported that 62% of Caucasian patients had SBHF.<sup>11</sup> To put into context, the prevalence of SBHF in the community is approximately 35% in the Olmsted County community study.<sup>32</sup> Taking all this into consideration, the prevalence of stage B cardiomyopathy in our study cohort in Malaysia, the prevalence of stage B cardiomyopathy of 57% is similar to that reported in the Western developed world. This might suggest that the pathophysiology of stage B cardiomyopathy in Malaysia may be similar to that reported in these other populations. In our study, we were not designed to explore the underlying pathophysiology of SBHF. However, there may be a role of coexisting hypertension as a subanalysis of our study showed statistically significant higher prevalence of SBHF in T2DM patients with hypertension compared with those with no history of hypertension (61.5% vs 42.3%, *p* value=0.004). Clearly, more studies are needed to better understand the pathophysiology of stage B cardiomyopathy in T2DM.

## LIMITATIONS

There are several limitations in our study. First of all, the concomitant presence of coronary artery disease was not investigated with coronary angiography or coronary CT. We did however rule out coronary artery disease patients as assessed by questionnaire and CCS scoring system. Second, GLS data were not available in our study which is one of the criteria to diagnose SBHF. Lack of data on strain could possibly lead us to underestimate the overall prevalence of SBHF. Third, in terms of an evaluation of T2DM glycaemic control, only a single reading of HbA1c level was available for this assessment. It would have been useful to have determined a mean HbA1c over a period in our analysis. Finally, we do not have follow-up data although plans are underway for follow-up of development of heart failure with repeated echocardiography.

## CONCLUSION

Our study had shown a high prevalence (57%) of SBHF in asymptomatic T2DM patients without overt cardiac disease in Malaysia. This high prevalence has similarly been reported in study populations in Western developed countries.

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examination and investigations; data entry, processing, cleaning up the data and analysing the data; writing up the paper and submitting to the journal; editing the paper. KLT: design and idea of the research work; data entry, processing, cleaning up the data and analysing the data; writing up the paper and submitting to the journal. ATBT, SRV and RJA/LR: design and idea of the research work; planning and recruiting the patients from T2DM clinic; data entry, processing and cleaning up the data; interpreting the analysed data and idea to write up the paper; editing the paper.

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