Defining Subclinical Myocardial Dysfunction and Implications for Patients With Diabetes Mellitus and Preserved Ejection Fraction

Arnold C.T. Ng, MBBS, PhD[a,b,c], Matteo Bertini, MD, PhD[a], See Hooi Ewe, MBBS, PhD[a], Enno T. van der Velde, PhD[a], Dominic Y. Leung, MBBS, PhD[c], Victoria Delgado, MD, PhD[a,*], and Jeroen J. Bax, MD, PhD[a]

Left ventricular (LV) global longitudinal strain (GLS) can detect subclinical myocardial systolic dysfunction in individuals with diabetes. The present study investigates the clinical usefulness and incremental net benefit of identifying subclinical myocardial systolic dysfunction in individuals with diabetes. A cohort of 397 type 2 diabetic individuals was followed up for the occurrence of all-cause mortality. Clinical and echocardiographic data of diabetic patients were assessed retrospectively. LV GLS was evaluated on transthoracic echocardiography using speckle tracking imaging. Subclinical LV systolic dysfunction was defined as LV GLS > −17.0% from 104 healthy volunteers recruited from the community. A total of 178 (44.8%) diabetic individuals had evidence of subclinical LV systolic dysfunction and 46 (11.6%) died during follow-up. The presence of subclinical LV systolic dysfunction was independently associated with all-cause mortality on follow-up (hazard ratio [HR] 2.83, 95% confidence interval [CI] 1.40 to 5.71, p = 0.004). Diabetic individuals without subclinical LV systolic dysfunction had similar survival as the general population (standardized mortality ratio 0.94, 95% CI 0.52 to 1.58). Decision curve analysis showed identification of subclinical LV systolic dysfunction and quantification of LV GLS provided an incremental net clinical benefit at risk stratifying patients for risk of death at 5 years. In conclusion, subclinical LV systolic dysfunction is independently associated with all-cause mortality in diabetic patients. Decision curve analyses suggest use of LV GLS and identification of subclinical LV systolic dysfunction is clinically useful, and provided incremental net clinical benefit for diabetic individuals. **(Am J Cardiol 2019;124:892−898)**

Diabetes mellitus is the most common endocrinological disease in the world and its presence portends an increased risk for the subsequent development of cardiovascular disease, heart failure, and death.[1,2] Echocardiographic techniques such as 2-dimensional (2D) speckle tracking global longitudinal strain analysis permits early identification of subclinical left ventricular (LV) systolic dysfunction despite preserved LV ejection fraction (EF) in asymptomatic type 2 diabetic individuals.[3] However, limited data exist on the prevalence and prognostic implications of subclinical LV systolic dysfunction with preserved LVEF in diabetic population. Thus, we conducted a multicenter study aimed to:

1. Evaluate the prevalence of subclinical LV systolic dysfunction with preserved LVEF in type 2 diabetic individuals by using 2D speckle tracking global longitudinal strain cut-off value derived from normal healthy volunteers; and
2. Determine the prognostic implications of subclinical LV systolic dysfunction in type 2 diabetic patients and compare it with the general population; and
3. Determine the clinical usefulness and incremental net benefit of identifying subclinical LV systolic dysfunction on echocardiography.

Methods

A total of 104 healthy volunteers were prospectively recruited from the community (Liverpool Hospital, Australia; and Princess Alexandra Hospital, Australia) to derive a cut-off value for normal global longitudinal strain and define subclinical LV systolic dysfunction. All the healthy volunteers had normal physical examinations, in normal sinus rhythm and had normal echocardiograms. Exclusion criteria for the healthy volunteers included history of diabetes, hypertension, smoking, use of cardiac medications, known underlying significant coronary artery disease, previous myocardial infarction, and cardiomyopathy. As the LV global longitudinal strain from this normal population demonstrated a unimodal Gaussian distribution, the lower limit of normal was defined as 2 standard deviations from the mean. Thus, subclinical LV

[a]Department of Cardiology, Leiden University Medical Center, Leiden, The Netherlands; [b]Department of Cardiology, Princess Alexandra Hospital, Australia; and [c]The Faculty of Medicine, South Western Sydney Clinical School, The University of New South Wales, Australia. Manuscript received April 1, 2019; revised manuscript received and accepted June 12, 2019.

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*Corresponding author: Tel: +31 71 526 2020; fax: +31 71 526 6809.
E-mail address: v.delgado@lumc.nl (V. Delgado).

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systolic dysfunction was defined as an LV global longitudinal strain >2 standard deviations from the mean.

The definition of subclinical LV systolic dysfunction was subsequently applied to 397 type 2 diabetic patients (Leiden University Medical Center, The Netherlands) who were followed-up to evaluate the adverse risk of subclinical LV systolic dysfunction. These patients were identified from the departmental echocardiographic database, and all clinical data were originally prospectively entered in the departmental Cardiology Information System (EPD-Vision, Leiden University Medical Center).

Type 2 diabetes was diagnosed according to World Health Organization criteria.[4] All diabetic patients were in normal sinus rhythm and had normal LVEF defined as ≥50%. Exclusion criteria for all the diabetic patients included history of heart failure, known pre-existing underlying significant coronary artery disease, previous myocardial infarction, presence of segmental wall motion abnormalities on echocardiogram, or ≥ moderate valvular stenosis or regurgitation.

Baseline clinical variables that were recorded include cardiac risk factors, hemoglobin level, glycated hemoglobin (HbA1c), and glomerular filtration rates (GFR) calculated by the Modification of Diet in Renal Disease formula as recommended by the National Kidney Foundation, Kidney Disease Outcomes Quality Initiative Guidelines.[5] Heart rate and blood pressures were recorded at the time of echocardiographic examination. Baseline echocardiographic variables recorded included LV volumes, LVEF, and LV global longitudinal strain.

All diabetic individuals were followed up after the baseline echocardiographic examination for the occurrence of death. The prognostic significance of subclinical LV systolic dysfunction was determined. Furthermore, to validate the cut-off value for the definition of subclinical LV dysfunction in the diabetic population, their survival was compared with the general Dutch population matched by age, gender, and time period using life-tables provided by the Dutch Central Bureau of Statistics. The clinical usefulness of identifying subclinical LV systolic dysfunction was also analyzed using decision curve analysis.

All the institutional review boards approved the study. All healthy volunteers prospectively recruited from the community provided written informed consent (Liverpool Hospital and Princess Alexandra Hospital, Australia). For the diabetic population, the Leiden University Medical Center institutional review board waived the need for patient written informed consent as all clinically acquired data were retrospectively analyzed and anonymously handled.

Transthoracic echocardiography was performed in all subjects at rest using commercially available ultrasound systems (Vivid 7 and E9, GE-Vingmed, Horten, Norway). All images were digitally stored on hard disks. All offline analyses were performed using a single software system (EchoPAC version 108.1.5, GE-Vingmed, Horten, Norway) at the Leiden University Medical Center echocardiography core laboratory by 2 operators (ACTN and MB). A complete 2D, color, pulsed and continuous-wave Doppler echocardiogram was performed. LV end-diastolic volume index (EDVI) and end-systolic volume index (ESVI) were calculated using Simpson's biplane method of discs and corrected for body surface area. LVEF was calculated and expressed as a percentage. LV mass index was calculated from the formula as recommended by the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[6]

Quantification of LV global longitudinal strain was performed using 2D speckle tracking echocardiography in the 3 apical (2-, 3- and 4-chamber) views. During image analysis, the LV endocardial border was manually traced at end-systole and the region of interest width adjusted to include the entire myocardium. The 2D speckle tracking software then automatically tracks the motion of LV myocardial segments throughout the entire cardiac cycle. From the 3 individual apical views, peak LV global longitudinal strain was calculated. Previous work has reported that the intra- and interobserver variabilities (expressed as mean absolute difference ± 1 standard deviation and intraclass correlation coefficient) for LV global longitudinal strain were 1.2 ± 0.5% and 0.939 and 0.9 ± 1.0% and 0.942, respectively.[3]

All continuous variables were tested for Gaussian distribution using the Kolmogorov-Smirnov test for normality. Continuous variables are presented as mean ± 1 standard deviation and categorical variables are presented as frequencies and percentages. The unpaired Student's *t* test was used to compare 2 independent groups of continuous variables and the Chi-square test was used to compare categorical variables. Cumulative event rates were calculated using the Kaplan-Meier method and between groups comparisons were made using the log-rank tests with respect to the primary outcome of all-cause mortality.[7]

Comparison of the diabetic cohort against the mortality of the total Dutch population matched by age, gender, and time period was performed using standardized mortality ratios (SMR). The SMR is the ratio of the observed number of deaths in the study cohort relative to the expected number of deaths in the general population. Multivariate Cox proportional-hazards models were then constructed to determine the independent prognostic value of subclinical LV systolic dysfunction and LV global longitudinal strain, adjusted for baseline clinical, biochemical, and echocardiographic characteristics (age, hemoglobin, GFR, and LV mass index).[8] These variables were selected as they were significant determinants of all-cause mortality on univariable analysis. The first model included LV global longitudinal strain as a categorical variable defined as the presence or absence of subclinical LV systolic dysfunction. The second model included LV global longitudinal strain as a continuous variable in increments of per unit (1%) worsening. The Cox proportional-hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for all independent predictors of all-cause mortality. A Pearson's correlation coefficient of >0.7 was used to identify high colinearity between the univariable predictors and avoid concurrent inclusion in the multivariable Cox regression model. Validity of the Cox regression assumption of proportionality was confirmed for all continuous covariates by scaled Schoenfeld residuals. For categorical variables, the assumption of proportionality was confirmed by log minus log plots.

To determine the incremental prognostic value of identifying subclinical LV systolic dysfunction using LV global longitudinal strain, the integrated discrimination improvement (IDI) and the continuous net reclassification improvement

(NRI) were initially used.[9,10] Next, a formal cost-benefit analysis using decision curve analysis was undertaken to determine the clinical usefulness of identifying subclinical LV systolic dysfunction using LV global longitudinal strain to predict all-cause mortality at 5 years.[11] It compares the clinical usefulness and net benefits of the model 1 (i.e., "traditional" risk factors that included age, GFR, hemoglobin and LV mass index) versus model 2 (model 1 + subclinical LV dysfunction/ LV global longitudinal strain), against 2 default clinical strategies: (1) assume all diabetic patients have subclinical LV systolic dysfunction and therefore perform an echocardiographic quantification of LV global longitudinal strain in everyone, or (2) assume all diabetic individuals are well and do not have subclinical LV dysfunction and therefore quantify LV global longitudinal strain in no one.[11]

A 2-tailed p value of <0.05 was considered significant. All statistical analyses were performed using SPSS for Windows (SPSS Inc, Chicago) version 16, STATA version 10 (StatCorp, Texas) and R version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

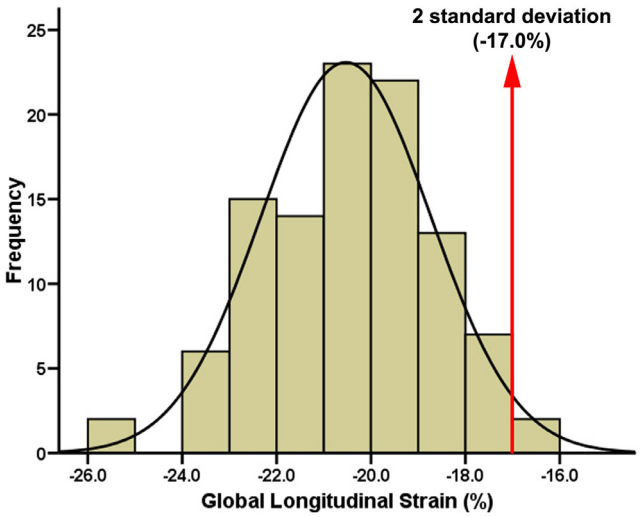

Figure 1. Distribution of LV global longitudinal strain values in the normal controls. The mean LV global longitudinal strain was −20.5 ± 1.8%. Therefore, the normal global longitudinal strain cut-off value was −17.0% (based on 2 standard deviations below the mean).

Results

The mean age of the 104 normal healthy volunteers was 50 ± 9 years, and 56.7% were male. The mean heart rate, systolic and diastolic blood pressures were 68 ± 11 beats/-min, 123 ± 12 mm Hg, and 82 ± 9 mm Hg respectively. All normal healthy volunteers had normal echocardiograms by virtue of the inclusion criteria. The mean LV mass index, LVEDVI, LVESVI, and LVEF were 69.2 ± 12.4 g/m^2, 52.9 ± 8.1 mL/m^2, 12.5 ± 3.8 mL/m^2, and 57.8 ± 4.6%, respectively. The mean LV global longitudinal strain for the healthy volunteers was −20.5 ± 1.8%. Although there was no correlation between LV global longitudinal strain and age, there was a significant gender difference (men −19.8 ± 1.6%, women −21.4 ± 1.7%, p <0.001). To define subclinical myocardial dysfunction, the lower limit of normal is calculated as 2 standard deviations from the mean. Therefore, in order to simplify and increase clinical utility, the lower cut-off value of −17% for LV global longitudinal strain was used (Figure 1). Thus, all diabetic individuals with normal LVEF but LV global longitudinal strain worse than −17% (less negative) were considered to have subclinical LV systolic dysfunction.

Table 1 outlines the clinical, biochemical and echocardiographic characteristics of the 397 diabetic individuals. Using the LV global longitudinal strain cut-off value of −17.0%, 178 (44.8%) diabetic individuals had evidence of subclinical LV systolic dysfunction.

After a mean follow-up period of 3.6 ± 1.6 years (median 3.5 years, 25th and 75th percentile 2.8 and 4.5 years respectively), 46 diabetic individuals died. Patients who died were significantly older (68.3 ± 11.7 vs 57.1 ± 11.8 years, p < 0.001), and had lower hemoglobin (13.2 ± 1.6 vs 13.9 ± 1.6 g/dL, p = 0.009) and lower GFR (63.5 ± 34.0 vs 86.3 ± 26.3 mL/min/1.73m^2, p <0.001). On echocardiography, patients who died had significantly higher LV mass index (108.9 ± 23.9 vs 91.8 ± 22.9 g/m^2, p <0.001) and worse LV global longitudinal strain (−15.4 ± 2.3 vs −17.5 ± 2.2%, p <0.001) compared with patients who were alive. There were no significant differences in LV volumes or LVEF. The Kaplan Meier survival curves in Figure 2 show the patients with subclinical LV systolic dysfunction had significantly lower survival compared with patients with preserved LV systolic function (log rank p <0.001), and significantly lower survival compared with the general population (SMR 2.61, 95% CI 1.78 to 3.68, one-sided log rank p <0.001). A SMR above unity indicates that the mortality of the study cohort is higher than the general population, adjusted for age distribution, gender, and calendar time. Thus, diabetic individuals with subclinical myocardial dysfunction were 161% more likely to die on follow-up compared with the general population. In contrast, there was no difference in survival between diabetic individuals with preserved LV systolic function and the general population (SMR 0.94, 95% CI 0.52 to 1.58, one-sided log rank p = not significant).

Table 2 outlines the all significant univariable determinants of all-cause mortality on follow-up (including presence of subclinical LV systolic dysfunction, age, hemoglobin, GFR, and LV mass index). On multivariate Cox proportional-hazards models, the presence of subclinical LV systolic dysfunction (HR 2.83, 95% CI 1.40 to 5.71, p = 0.004) in diabetic individuals was independently associated with increased all-cause mortality on follow-up after adjusting for baseline clinical and echocardiographic characteristics. Similarly, when LV global longitudinal strain was modeled as a continuous variable, it was still independently associated with increased all-cause mortality on follow-up (HR 1.29, 95% CI 1.14 to 1.46, p <0.001) (Table 3).

Figure 3 graphically illustrates the IDI and continuous NRI between the baseline Cox model 1 (age, GFR, hemoglobin, and LV mass index [thick line]) and Cox model 2 (model 1 + subclinical myocardial dysfunction [thin line]). The identification of subclinical LV systolic dysfunction significantly improved the predictive value of the Cox model based on the IDI (point estimate 0.054, 95% CI 0.002 to 0.163, p = 0.040) and continuous NRI (point estimate 0.362, 95% CI 0.062 to 0.587, p = 0.013).

Table 1
Clinical, biochemical and echocardiographic characteristics of diabetic patients

Variable	Diabetic population (n = 397)	Preserved LV systolic function (n = 219)	Subclinical LV systolic dysfunction (n = 178)	p Value
Age (years)	58 ± 12	58 ± 12	59 ± 12	0.34
Men	63.7%	62.6%	65.2%	0.59
Body mass index (kg/m^2)	28.8 ± 5.5	27.3 ± 5.0	30.5 ± 5.7	<0.001
Systolic blood pressure (mm Hg)	141 ± 22	139 ± 20	143 ± 23	0.032
Diastolic blood pressure (mm Hg)	81 ± 11	80 ± 11	83 ± 12	0.023
Hyperlipidemia	50.0%	48.6%	51.7%	0.54
Hypertension	57.8%	55.7%	60.5%	0.34
Smoker	16.9%	15.6%	18.5%	0.44
Hemoglobin (g/dL)	13.8 ± 1.6	13.9 ± 1.6	13.8 ± 1.7	0.56
HbA1c (%)	7.3 ± 1.5	7.1 ± 1.5	7.6 ± 1.4	0.013
GFR (mL/min/1.73m^2)	83.8 ± 28.1	86.3 ± 27.4	80.7 ± 28.7	0.052
Heart rate (beats/min)	74 ± 13	72 ± 13	75 ± 12	0.05
Transmitral E velocity (m/s)	0.66 ± 0.17	0.70 ± 0.18	0.65 ± 0.18	0.014
Transmitral E/A ratio	0.98 ± 0.33	1.00 ± 0.34	0.91 ± 0.28	0.005
Deceleration time (ms)	197 ± 54	198 ± 54	201 ± 54	0.60
LV mass index (g/m^2)	93.8 ± 23.7	91.2 ± 23.2	96.7 ± 23.9	0.016
LVEDVI (mL/m^2)	46.0 ± 11.2	45.9 ± 10.7	46.2 ± 11.8	0.75
LVESVI (mL/m^2)	18.7 ± 5.6	18.1 ± 5.1	19.6 ± 6.0	0.007
LVEF (%)	59.5 ± 5.4	60.8 ± 5.3	57.9 ± 5.0	<0.001
Global longitudinal strain (%)	−17.3 ± 2.3	−18.9 ± 1.5	−15.3 ± 1.4	<0.001

*p value by unpaired Student's *t* test and Chi-square test for continuous and categorical variables, respectively. EDVI = end-diastolic volume index; ESVI = end-systolic volume index; EF = ejection fraction; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; LV = left ventricular.

Figures 4 and 5 are the decision curve analyses illustrating the net clinical benefit of identifying subclinical LV systolic dysfunction and LV global longitudinal strain respectively. In these figures, the net benefit in risk stratifying diabetic individuals using echocardiography to identify subclinical LV systolic dysfunction is represented by the y-axis, and plotted over varying thresholds of risk for death at 5 years on the x-axis. This is compared against the 2 "extreme theoretical" clinical strategies: perform echocardiograms in all diabetic individual (gray solid line) vs not performing any echocardiograms in all diabetic individual (black solid line). Both figures demonstrate that using LV global longitudinal strain either as a categorical variable (i.e., presence of subclinical LV systolic dysfunction, Figure 4) or continuous variable (Figure 5) to inform clinical decisions will lead to superior predictive outcomes when the threshold probability of death at 5 years is above 8% (arrow, Figure 4) to 10% (arrow, Figure 5). Importantly, once the patient's 5-year probability of death is >50% to 70%, there is no net benefit in identifying subclinical LV systolic dysfunction or quantifying LV global longitudinal strain respectively on echocardiogram.

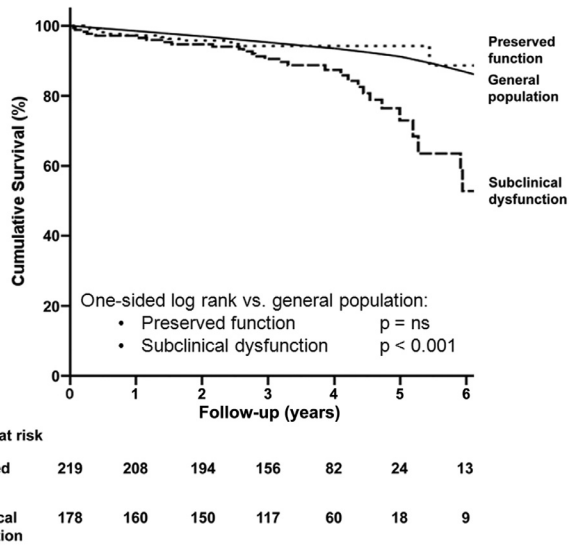

Figure 2. Kaplan Meier survival curves for diabetic individuals with subclinical LV systolic dysfunction and preserved LV systolic function compared with the general population. There was no significant difference in long-term survival for diabetic individuals with preserved LV systolic function and the general population (p = ns). In contrast, diabetic individuals with normal LVEF but with subclinical LV systolic dysfunction had significantly lower long-term survival compared with the general population (p <0.001).

Discussion

It is well recognized that LVEF is a poor marker for identifying myocardial dysfunction as it remains well preserved until significant impairment of longitudinal, circumferential and radial deformations.[3] Depending on the echocardiographic modality used, the prevalence of myocardial dysfunction in diabetics ranged from 21% to 63%.[12,13] In the present study, up to 45% of diabetic individuals had evidence of subclinical LV systolic dysfunction as defined by 2D speckle tracking LV global longitudinal strain. This was identical to a previous publication by Holland et al.[14]

IMyocardial dysfunction in diabetics has a multifactorial pathophysiology. Proposed mechanisms include metabolic derangements, autonomic dysfunction, abnormal calcium homeostasis, endothelial dysfunction, altered structural proteins and interstitial fibrosis.[15,16] As such, the diabetic myocardium has accentuated cellular damage, reduced structural and function reserve, and is more prone to future

Table 2
Univariable and multivariable Cox proportional hazard models for all-cause mortality in diabetic patients

Variable	Univariable		Multivariable	
	Hazard ratio (95% CI)	p Value	Hazard ratio (95% CI)	p Value
Presence of subclinical LV systolic dysfunction	2.78 (1.48−5.23)	0.002	2.83 (1.40−5.71)	0.004
Age (per 10 year increase)	1.89 (1.43−2.50)	<0.001	1.44 (1.08−1.91)	0.013
LV mass index (per 10 g/m^2 increase)	1.14 (1.03−1.26)	0.012		
GFR (per 10 mL/min/1.73m^2 decrease)	1.29 (1.14−1.45)	<0.001	1.18 (1.03−1.35)	0.015
Hemoglobin (per 1 g/dL decrease)	1.25 (1.06−1.47)	0.008		

CI = confidence interval; GFR = glomerular filtration rate; LV = left ventricular.

Table 3
Univariable and multivariable Cox proportional hazard models for all-cause mortality in diabetic patients

Variable	Univariable		Multivariable	
	Hazard ratio (95% CI)	p Value	Hazard ratio (95% CI)	p Value
LV global longitudinal strain (per unit [1%] worsening)	1.37 (1.22−1.54)	<0.001	1.29 (1.14−1.46)	<0.001
Age (per 10 year increase)	1.89 (1.43−2.50)	<0.001	1.37 (1.03−1.82)	0.029
LV mass index (per 10 g/m^2 increase)	1.14 (1.03−1.26)	0.012		
GFR (per 10 mL/min/1.73m^2 decrease)	1.29 (1.14−1.45)	<0.001	1.16 (1.02−1.32)	0.021
Hemoglobin (per 1 g/dL decrease)	1.25 (1.06−1.47)	0.008		

CI = confidence interval; GFR = glomerular filtration rate; LV = left ventricular.

decompensation and eventual failure when exposed to adverse cardiac events. This was highlighted in the seminal work by From et al that showed increased incidence of new-onset heart failure in diabetic patients with preclinical diastolic dysfunction.[17] Although it is traditionally held that diastolic dysfunction precedes systolic dysfunction, recent work suggested that subclinical LV systolic dysfunction detected by LV global longitudinal strain may be the first sign of diabetic heart disease instead.[18] Even though it is clear that prognosis is very poor once clinical heart failure is established,[19] there is a paucity of research data on prognosis of the earlier subclinical dysfunction stage.

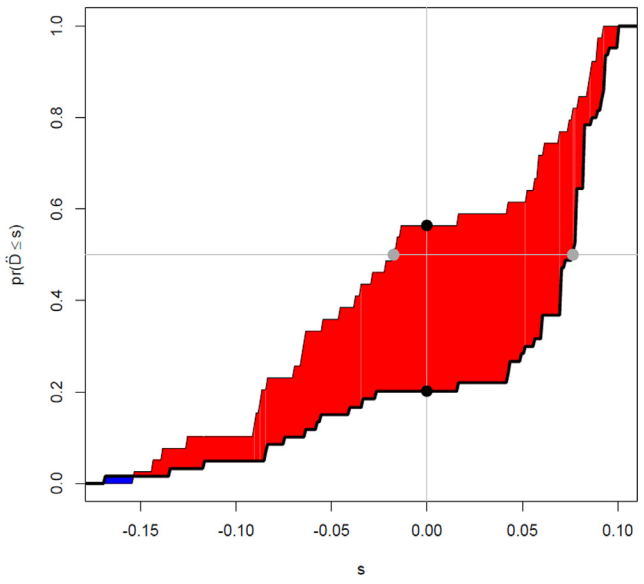

Figure 3. Graphical representation of the incremental prognostic value of subclinical LV systolic dysfunction in predicting all-cause mortality in the overall multivariable Cox regression model in diabetic individuals at 5 years. Model 1 (age, GFR, hemoglobin, and LV mass index) and model 2 (model 1+ subclinical myocardial dysfunction as categorical variable) are represented by the thick and thin lines, respectively. The difference between the 2 curves (area under the curve) represents the IDI, and the distances between the 2 black dots vertically and the 2 gray dots horizontally represents the continuous NRI and difference in medians for the 2 curves respectively. The larger the separation between the 2 curves, the larger the improvement in model performance when including subclinical LV systolic dysfunction as a prognostic marker.

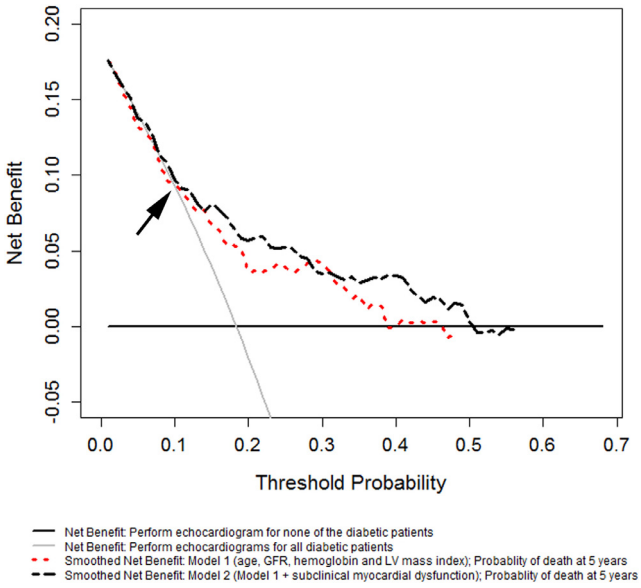

Figure 4. Decision curve analysis for model 1 (age, GFR, hemoglobin, and LV mass index) and model 2 (model 1 + subclinical LV systolic dysfunction as categorical variable). Once the threshold probability of death approaches 10% (arrow), performing echocardiograms to identify subclinical LV systolic dysfunction (model 2) provide a superior net clinical benefit across a large range of death risk at 5 years follow-up. GFR: glomerular filtration rate, LV: left ventricular.

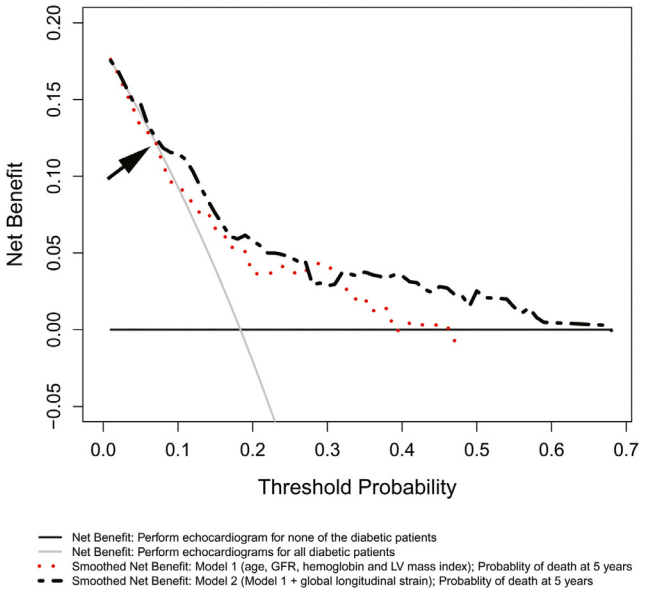

Figure 5. Decision curve analysis for model 1 (age, GFR, hemoglobin, and LV mass index) and model 2 (model 1 + LV global longitudinal strain as continuous variable). Once the threshold probability of death approaches 8% (arrow), quantifying LV global longitudinal strain (model 2) provide a superior net clinical benefit across a large range of death risk at 5 years follow-up. GFR: glomerular filtration rate, LV: left ventricular.

To our knowledge, only 2 previous publications have demonstrated adverse long-term prognosis associated with subclinical LV systolic dysfunction using LV global longitudinal strain.[14,20] Holland et al included 230 diabetic patients and showed increased all-cause mortality and hospitalization in patients with subclinical LV systolic dysfunction compared with those with preserved LV global longitudinal strain.[14] However, the primary outcome was primarily driven by hospitalization, and the causes of hospitalizations were unknown. Liu et al included 247 diabetic patients and showed that an impaired LV global longitudinal strain was associated with an increased incidence of cardiovascular events defined as a composite of acute coronary syndrome, cerebrovascular stroke, cardiovascular death and hospitalization for heart failure.[20] In contrast, the present study is the largest to date to include 397 diabetic patients with a primary end-point of all-cause mortality. Not only did our results corroborate the previous 2 publications demonstrating similar adverse prognosis associated with subclinical LV systolic dysfunction, it is also first to show diabetic individuals with preserved LV systolic function had similar long-term survival rates as the general population.

In studies by Holland et al[14] and Liu et al[20], the "incremental" prognostic value of LV global longitudinal strain were based on the Chi square change in the multivariable Cox model, which is a statistical measure of the overall model performance related to the concept of "goodness-of-fit" (i.e., a better model results in smaller distances between predicted and observed outcomes).[21] However, it fails to inform the doctor and patient if the test is clinically useful. In contrast, the use of a decision curve analysis in the present study illustrated the net clinical benefit of identifying subclinical LV systolic dysfunction (binary data, Figure 4) and LV global longitudinal strain (continuous data, Figure 5) in diabetic individuals over the baseline prediction model (age, GFR, hemoglobin, and LV mass index) by incorporating the clinical consequences across a large range of all-cause mortality risk. As the relative weights of benefits and harms in identifying subclinical LV systolic dysfunction in asymptomatic diabetic population will differ individually, the decision curve analysis allows the setting of individual patient's thresholds for predicting the probability of death at 5 years. It showed that the identification of subclinical LV systolic dysfunction is only of incremental net clinical benefit if the risk of death at 5 years is between 10% and 50%. As for quantification of LV global longitudinal strain as a continuous variable, the incremental net clinical benefit is present if the risk of death at 5 years is between 8% and 70%. Therefore, the identification of subclinical LV systolic dysfunction provided superior net clinical benefit across a wide range of probabilities of death at 5 years.

Although the present study included healthy volunteers and diabetic individuals across 3 different institutions, all diabetic individuals were recruited from a single center. Subgroup analyses based on cardiovascular and noncardiovascular mortality were not available. Finally, by virtue of the study design, we did not evaluate the progression of subclinical LV systolic dysfunction over time. However, that research was previously reported by our group.[22]

Disclosures

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