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Impact of diabetes duration on heart failure in Korean patients without clinical cardiovascular disease

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Abstract

We aimed to investigate the association between diabetes duration and the subsequent occurrence of heart failure (HF) in type 2 diabetes mellitus (T2DM) patients without clinical cardiovascular disease.

In this single-center, observational cohort study, a total of 3724 T2DM patients were stratified by diabetes duration into three 5-year interval subgroups. The primary outcomes were the occurrence of new-onset HF and all-cause mortality.

HF incidence ($P < .001$) and mortality ($P = .001$) were significantly higher in patients with a longer duration of diabetes (≥ 10 years) than in those with a shorter duration (< 5 years). On multivariate analysis, diabetes duration ≥ 10 years was not independently associated with all-cause mortality compared with duration < 5 years, but there was a nonsignificant increased risk of HF in patients with a diabetes duration ≥ 10 years ($P = .056$). Poor glycemic control was associated with an increased risk of HF and mortality; statin use was associated with a significantly decreased risk of mortality.

Our study indicated that a longer duration of diabetes is associated with an increased risk of new-onset HF occurrence and all-cause mortality in T2DM patients without clinical cardiovascular disease.

Abbreviations: CI = confidence interval, CVD = cardiovascular disease, EF = ejection fraction, HbA1c = glycated hemoglobin, HF = heart failure, HR = hazard ratio, LV = left ventricular, MI = myocardial infarction, T2DM = type 2 diabetes mellitus.

Keywords: cardiovascular diseases, diabetes mellitus, risk factors

1. Introduction

The prevalence of type 2 diabetes mellitus (T2DM) is increasing worldwide, in parallel with increasing numbers of overweight and obese individuals and a growing population of older adults, who have the highest incidence of diabetes.[1,2] Diabetes is associated with long-term cardiac and cerebrovascular morbidity and up to a 3-fold increase in mortality; however, improved medical treatment was shown to reduce the incidence of diabetes-related morbidity and mortality between 1990 and 2010.[3,4]

Despite this improvement, diabetes remains a significant risk factor for the development of cardiovascular disease (CVD).[5–8] Although some studies have assessed the association between diabetes duration and risk of CVD,[9,10] the impact of diabetes duration on the risk of new-onset heart failure (HF) in T2DM patients without previous clinical CVD is less understood. Specifically, few studies have examined the HF risk in T2DM patients receiving both medical treatment and risk factor modification with respect to diabetes duration.

This study investigated the association between diabetes duration and the subsequent occurrence of HF in Asian T2DM patients without clinical CVD who received both current medical treatment and risk factor modification. The clinical variables associated with new-onset HF in these patients were also investigated.

2. Subjects and methods

2.1. Study design and population

This single-center, retrospective, observational study analyzed data extracted from patient medical records. The present study protocol was reviewed and approved by the institutional review board of Asan Medical Center (IRB No. 2015–0691), which waived the need for informed consent. A total of 6485 consecutive Asian T2DM patients >50 years old who first visited the Diabetes Center outpatient clinic between January 2009 and December 2012 were eligible, regardless of diabetes duration. In this study, we excluded subjects fulfilling criteria for prediabetes based on American Diabetes Association guidelines.[11] Only patients with baseline cardiovascular screening (cardiac enzyme levels, 12-lead electrocardiogram, and carotid

duplex ultrasonography) were included. Exclusion criteria centered on evidence of CVD, and included previous myocardial infarction (MI), angina, HF, valvular heart disease, cerebral infarction, and severe carotid bifurcation stenosis [≥70% stenosis based on North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria] requiring carotid revascularization. In addition, patients with a history of coronary or carotid revascularization, known malignancy, and known chronic renal failure with dialysis were also excluded. Patients with poor adherence to medication or risk factor modification were excluded. Poor adherence to medication was defined as failure to take regular medications prescribed for diabetes, hypertension, or dyslipidemia resulting in sustained hyperglycemia, hypertension, and hyperlipidemia, respectively. Poor adherence to risk factor modification was defined as failure to quit smoking within 6 months of study inclusion. As previously described,[12] the diagnosis of T2DM was based on plasma glucose criteria, and diabetes duration was estimated as the difference between the patient's current age and age at diabetes onset. Clinical variables and long-term outcomes were entered in an Excel database and retrospectively analyzed.

2.2. Identification of risk factor variables and modification

Risk factor variables were defined as previously described.[12–14] Past smoking was defined as smoking before study inclusion but cessation within 6 months of inclusion. Significant carotid stenosis was defined as both >50% and <70% narrowing of the diameter of the common carotid artery, carotid bifurcation, or internal carotid artery based on NASCET criteria. In our Diabetes Center, the modification of each risk factor was individually evaluated following the Standards of Medical Care of the American Diabetes Association.[15,16] During follow-up and surveillance, prophylactic revascularization was considered in patients with radiologic evidence of significant coronary artery stenosis in the absence of myocardial ischemia or carotid plaque progression resulting in ≥70% stenosis in the absence of cerebral infarction.

2.3. Primary outcomes and follow-up

The primary outcomes included the occurrence of new-onset HF and all-cause mortality. We considered prophylactic revascularizations for asymptomatic coronary or carotid artery stenosis as one of the risk factor modifications and did not include them as a study outcome in the absence of periprocedural complications. Coronary computed tomography angiography, with or without diagnostic coronary angiography, and Doppler echocardiography were performed when signs or symptoms suggestive of CVD were identified. Only the first temporal event of each outcome was included in the analysis.

HF was categorized by systolic or diastolic dysfunction. Diagnosis was based on the Framingham score (2 major criteria or 1 major and 2 minor criteria) and evidence of systolic or diastolic dysfunction on Doppler echocardiography.[17] Patients with signs or symptoms of HF and a left ventricular (LV) ejection fraction (EF) ≤50% were considered to have HF with reduced EF, or systolic HF. Patients with signs or symptoms of HF, LVEF >50%, and evidence of diastolic LV dysfunction were considered to have HF with preserved EF, or diastolic HF.[17] Diastolic dysfunction was defined by the ratio of passive transmitral LV inflow velocity to tissue Doppler imaging velocity of the medial mitral annulus during passive filling (E/e'), with a ratio >15 considered to be dysfunction.[17–19]

Follow-up visits were scheduled at approximately 6-month intervals, and all medication adjustments were made by the patient's health care provider in our Diabetes Center. Follow-up laboratory evaluations including cardiac enzyme levels and 12-lead electrocardiograms were performed depending on individual CVD risk factors.

2.4. Statistical analysis

Categorical variables are reported as frequency or percentage, and continuous variables are reported as mean ± standard deviation. Categorical variables were compared using Chi-square tests with the Bonferroni correction for multiple comparisons, and continuous variables were compared using 1-way analysis of variance with Tukey test for multiple comparisons. Diabetes duration was stratified by 5-year increments, with groups of < 5 years, 5 to 10 years, or ≥10 years, to evaluate threshold effects. The cumulative probability of events was estimated with Kaplan–Meier analysis and was compared with the cumulative probability estimated with the log-rank test. Univariate and multivariate analyses of the association of clinical variables with each endpoint were conducted with Cox proportional hazards modeling using the event of interest and period from study enrollment to the date of the event or last follow-up as the outcome. Univariate Cox proportional hazard regression models were fitted to calculate hazard ratios (HRs) with 95% confidence intervals (95% CIs) to estimate the association of clinical variables with the occurrence of primary outcomes. Variables with a $P < .1$ on univariate analysis were included in multivariate Cox proportional hazard regression models using the backward elimination method. P values were 2-tailed; $P < .05$ was considered statistically significant. Statistical analyses were performed using SPSS Version 21.0 (SSPS, Inc., Chicago, IL).

3. Results

3.1. Study population

Of the 6485 consecutive T2DM patients treated at our Diabetes Center who were >50 years old, we excluded 1704 patients (26.3%) with prior CVD, 74 (1.1%) with a history of coronary or carotid revascularization, 366 (5.6%) with known malignancy, and 73 (1.1%) with known chronic renal failure and dialysis. A further 544 patients (8.4%) were excluded from the analysis either because they were lost to follow-up (376 patients, 5.8%) or because of poor adherence to medication or risk factor modification (168 patients, 2.6%). The remaining 3724 patients (57.4%) without clinical CVD at baseline who had received both medical treatment for diabetes and risk factor modification with regular 6-month interval follow-up were included in the study evaluation. Eligible patients were stratified into 3 groups, based on diabetes duration < 5, 5 to 10, and ≥10 years. The mean duration of diabetes at baseline was 8.8 ± 7.4 years.

Baseline characteristics are presented in Table 1. Patients with longer diabetes duration were more likely to be older ($P < .001$), female ($P < .001$), and obese ($P = .001$) than patients with shorter diabetes duration. Longer-duration patients also had a higher prevalence of hypertension ($P < .001$), chronic kidney disease ($P < .001$), and significant carotid artery stenosis ($P = .033$), and a lower prevalence of past smoking ($P = .002$). They showed worse glycemic control, reflected by the glycated hemoglobin (HbA1c) levels ($P < .001$), and worse chronic kidney disease, reflected by the serum creatinine ($P < .001$) and estimated glomerular

Table 1

Baseline characteristics of the study population stratified by diabetes duration.

	Diabetes duration			
	<5 y	5–10 y	≥10 y	P
Number of patients	1313 (35.3)	911 (24.5)	1500 (40.3)	
Diabetes duration, y	1.8±1.4	7.0±1.4	15.9±6.2	
Mean age, y	60.0±7.3[a]	61.4±7.5[b]	63.6±8.1[c]	<.001
Male sex	843 (64.2)[a]	525 (57.6)[b]	848 (56.5)[b]	<.001
Body mass index, kg/m^2	25.0±3.2[a]	25.1±3.1[a]	24.7±3.2[b]	.001
Risk factor				
Hypertension	588 (44.8)[a]	518 (56.9)[a]	896 (59.7)[b]	<.001
Dyslipidemia	365 (27.8)	245 (26.9)	364 (24.3)	.088
Past smoking[*]	162 (12.3)[a]	91 (10.0)[a,b]	125 (8.3)[b]	.002
Chronic kidney disease	15 (1.1)[a]	21 (2.3)[a]	79 (5.3)[b]	<.001
Carotid stenosis[†]	70 (5.3)[a]	54 (5.9)[a,b]	115 (7.7)[b]	.033
Laboratory data				
HbA1c (%)[‡]	6.8±0.9[a]	7.2±1.0[b]	7.5±1.0[c]	<.001
Creatinine, mg/dL[§]	0.9±0.3[a]	0.9±0.3[a]	1.0±0.3[b]	<.001
eGFR, mL/min/1.73 m$^{2[§]}$	76.8±13.0[a]	75.2±14.4[b]	72.0±16.4[c]	<.001
Total cholesterol, mg/dL[§]	177.0±39.9[a]	165.4±32.2[b]	163.1±34.0[b]	<.001
HDL, mg/dL[§]	50.8±13.3	50.6±12.6	51.2±13.5	.523
LDL, mg/dL[§]	105.7±34.0[a]	95.4±27.6[b]	93.8±28.2[b]	<.001
TG, mg/dL[§]	137.9±82.0[a]	134.5±73.2[b]	125.2±74.5[b]	<.001
Medication use				
Antiplatelet	662 (50.4)[a]	565 (62.0)[b]	1010 (67.3)[c]	<.001
Statin	586 (44.6)[a]	494 (54.2)[b]	774 (51.6)[b]	<.001
Hypertension medication	539 (41.1)[a]	467 (51.3)[b]	816 (54.4)[b]	<.001
ACE inhibitor	44 (3.4)[a]	36 (4.0)[a,b]	78 (5.2)[b]	.046
ARB	335 (25.5)[a]	343 (37.7)[b]	581 (38.7)[b]	<.001
Insulin	108 (8.2)[a]	95 (10.4)[a]	419 (27.9)[b]	<.001
Follow-up, mo	50.0±20.4[a]	46.8±17.3[b]	45.8±15.2[b]	<.001

Continuous data are means±standard deviations; categorical data are numbers (%).

ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker, eGFR = estimated glomerular filtration rate, HbA1c = glycated hemoglobin, HDL = high-density lipoprotein cholesterol, LDL = low-density lipoprotein cholesterol, TG = triglycerides.

[a,b,c] Non-significant difference between groups.

[*] Past smoking was defined as cessation within 6 months of enrollment.

[†] ≥50% luminal narrowing.

[‡] Mean values during follow-up.

[§] Baseline values after study enrollment.

filtration rate (P < .001) levels. Total cholesterol (P < .001), low-density lipoprotein cholesterol (P < .001), and triglyceride (P < .001) levels were significantly lower in patients with a longer duration of diabetes. The proportion of patients taking antiplatelet medications, statins, antihypertensives, and insulin increased with diabetes duration (P < .001).

3.2. Association of diabetes duration and primary outcomes

During the mean follow-up period of 47.6±17.8 months, the new-onset HF incidence was 3.0% in patients with a diabetes duration < 5 years, 4.1% in those with a duration of 5 to 10 years, and 6.4% in those with a duration ≥10 years (Table 2). The difference between patients with ≥10 years' duration of T2DM and < 5 years' duration was statistically significant (P < .001). The risks of both diastolic HF (P < .001) and all-cause mortality (P = .001) increased with a longer duration of diabetes (≥10 years) than a shorter duration of diabetes (<5 and 5–10 years). During the study period, 82 patients underwent prophylactic revascularizations (2.2%) for asymptomatic significant coronary or carotid artery stenosis; no instances of periprocedural major adverse cardiac events occurred in these patients. Kaplan–Meier analysis revealed that patients with a longer duration of diabetes had a higher risk of HF (P < .001) and

all-cause mortality (P < .001) than those with a shorter duration (Fig. 1).

3.3. Analysis of clinical variables associated with primary outcomes

Multivariate Cox proportional hazard regression analyses adjusting for confounding variables indicated that a diabetes duration of ≥10 years compared with < 5 years was not independently associated with all-cause mortality (HR 1.82;

Table 2

Incidence of primary outcome occurrence among the study population stratified by diabetes duration.

	Diabetes duration			
	<5 y	5–10 y	≥10 y	P
Number of patients	1313 (35.3)	911 (24.5)	1500 (40.3)	
Heart failure	39 (3.0)[a]	37 (4.1)[a,b]	96 (6.4)[b]	<.001
Systolic heart failure	2 (0.2)	3 (0.3)	5 (0.3)	.600
Diastolic heart failure	37 (2.8)[a]	34 (3.7)[a]	91 (6.1)[b]	<.001
Death[*]	11 (0.8)[a]	6 (0.7)[a]	34 (2.3)[b]	.001

Values are presented as numbers (%).

[a,b,c] Non-significant difference between groups.

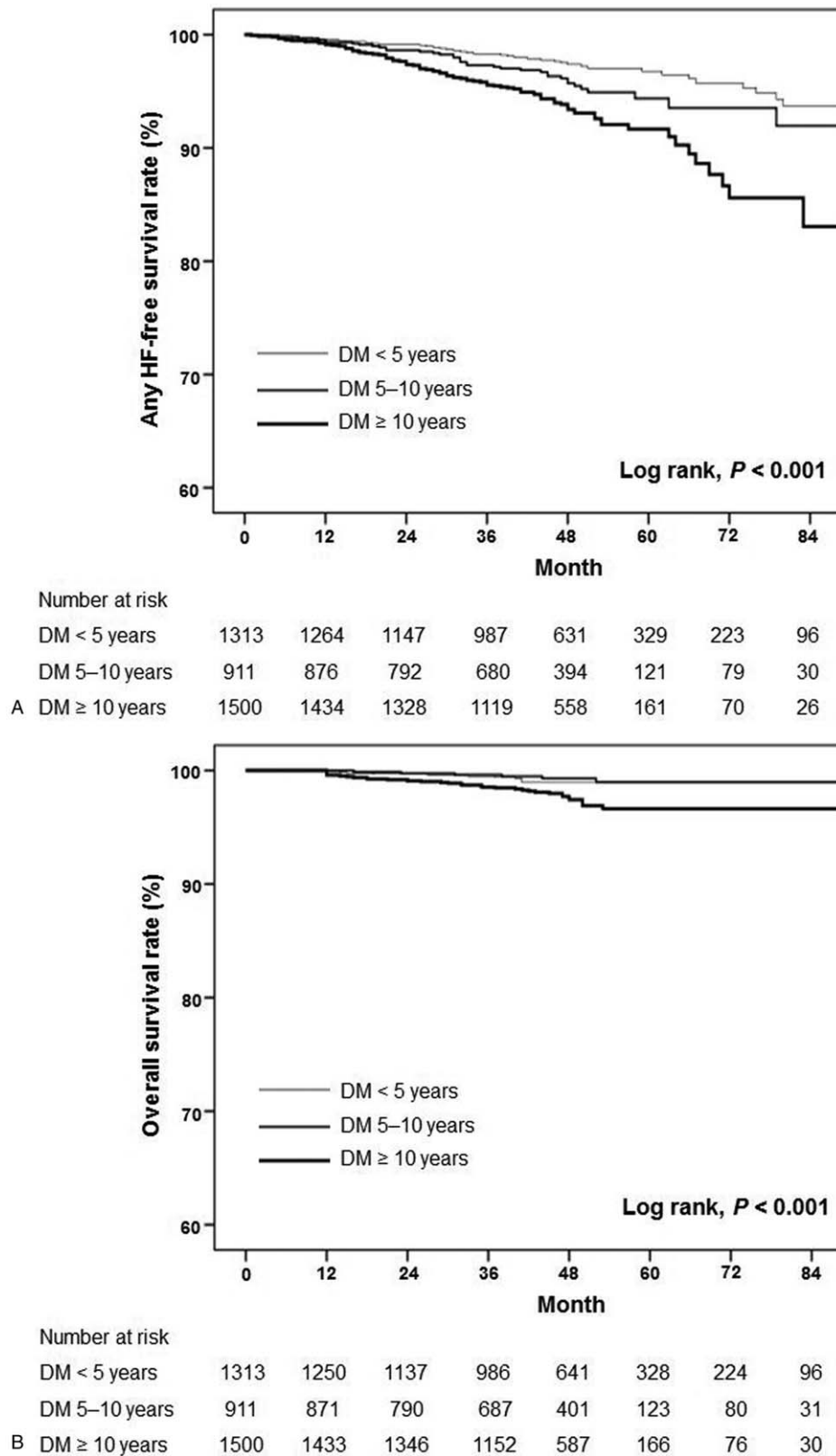[*] All-cause mortality during follow-up period.

Figure 1. Kaplan–Meier analysis of cumulative event-free rates of (A) HF and (B) mortality stratified by diabetes duration. DM = diabetes mellitus, HF = heart failure.

95% CI 0.88–3.76; *P* = .105) (Table 3), but there was a nonsignificant increased risk of new-onset HF in patients with a diabetes duration ≥10 years (HR 1.48; 95% CI 0.99–2.20; *P* = .056) (Table 4). Poor glycemic control, as reflected by HbA1c level, was independently associated with HF (HR 1.19; 95% CI 1.07–1.33; *P* = .001) and all-cause mortality (HR 1.32; 95% CI 1.04–1.68; *P* = .023). Statin use was significantly associated with a decreased risk of mortality (HR 0.31; 95% CI 0.17–0.59; *P* < .001).

Table 3

Clinical variables associated with all-cause mortality.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age	1.07 (1.04–1.11)	< .001	1.06 (1.02–1.09)	.001
Male sex	1.49 (0.82–2.69)	.188	NA	NA
BMI	1.01 (0.92–1.09)	.902	NA	NA
Hypertension	1.06 (0.61–1.84)	.839	NA	NA
Dyslipidemia	0.41 (0.19–0.92)	.029	NA	NA
Past smoking*	1.40 (0.63–3.12)	.405	NA	NA
CKD	5.09 (2.29–11.30)	< .001	3.23 (1.43–7.32)	.005
Carotid stenosis†	0.65 (0.16–2.66)	.546	NA	NA
Hypertension medication	1.01 (0.59–1.76)	.961	NA	NA
ACE inhibitor	0.05 (0.00–18.56)	.315	NA	NA
ARB	1.18 (0.67–2.07)	.578	NA	NA
Antiplatelet	0.87 (0.50–1.52)	.632	NA	NA
Statin	0.33 (0.18–0.62)	.001	0.31 (0.17–0.59)	< .001
Insulin	2.05 (1.12–3.74)	.020	NA	NA
HbA1c	1.41 (1.13–1.76)	.003	1.32 (1.04–1.68)	0.023
Creatinine	2.03 (1.31–3.15)	.002	NA	NA
eGFR	0.98 (0.97–1.00)	.027	NA	NA
Diabetes duration				
<5 y	Reference			
5–10 y	0.80 (0.30–2.15)	.654	0.73 (0.27–1.97)	.529
≥ 10 y	2.78 (1.41–5.48)	.003	1.82 (0.88–3.76)	.105

ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker, BMI = body mass index, CI = confidence interval, CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate, HbA1c = glycated hemoglobin, HR = hazard ratio, NA = not applicable.

* Past smoking was defined as cessation within 6 months of enrollment.

† ≥ 50% luminal narrowing.

4. Discussion

Diabetes duration is a well-known indicator for future CVD risk,[20–23] and indeed, we show that new-onset HF incidence and all-cause mortality are significantly higher in patients with a longer duration of diabetes. Furthermore, our multivariate analyses indicate that a diabetes duration of ≥10 years compared with a duration of <5 years was not independently associated with HF and all-cause mortality in T2DM patients with no prior

Table 4

Clinical variables associated with heart failure.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age	1.08 (1.06–1.10)	< .001	1.07 (1.05–1.09)	< .001
Male sex	0.50 (0.37–0.68)	< .001	0.57 (0.42–0.78)	< .001
BMI	1.02 (0.97–1.06)	.501	NA	NA
Hypertension	2.11 (1.52–2.92)	< .001	1.46 (1.04–2.05)	.029
Dyslipidemia	0.90 (0.64–1.26)	.543	NA	NA
Past smoking*	0.86 (0.52–1.44)	.572	NA	NA
CKD	4.46 (2.77–7.19)	< .001	2.58 (1.57–4.24)	< .001
Carotid stenosis†	2.64 (1.75–3.99)	< .001	1.75 (1.14–2.69)	.011
Hypertension medication	2.06 (1.50–2.82)	< .001	NA	NA
ACE inhibitor	1.24 (0.63–2.42)	.534	NA	NA
ARB	1.46 (1.08–1.98)	.015	NA	NA
Antiplatelet	2.29 (1.60–3.28)	< .001	NA	NA
Statin	1.45 (1.07–1.96)	.018	NA	NA
Insulin	2.60 (1.88–3.61)	< .001	NA	NA
HbA1c	1.38 (1.21–1.56)	< .001	1.19 (1.07–1.33)	.001
Creatinine	1.84 (1.37–2.47)	< .001	NA	NA
eGFR	0.97 (0.96–0.98)	< .001	NA	NA
Diabetes duration				
<5 y	Reference			
5–10 y	1.55 (0.99–2.44)	.057	1.20 (0.76–1.90)	.427
≥ 10 y	2.61 (1.79–3.80)	< .001	1.48 (0.99–2.20)	.056

ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker, BMI = body mass index, CI = confidence interval, CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate, HbA1c = glycated hemoglobin, HR = hazard ratio, NA = not applicable.

* Past smoking was defined as cessation within 6 months of enrollment.

† ≥ 50% luminal narrowing.

clinical CVD, who also received medical treatment and risk factor modification for diabetes. Poor glycemic control was significantly associated with an increased risk of new-onset HF and all-cause mortality; statin use was significantly associated with a decreased risk of mortality.

Our study cohort was chosen to reflect healthy T2DM patients, and our results may therefore not apply to the general T2DM population. For this reason, we could not compare our findings to those of other population-based studies.[24,25] Compared with the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial cohort with a similarly aged population of adults with both T2DM and no prior CVD,[26] our rate of death from any cause was extremely low, because we analyzed only the first event of each outcome.

DM is known to have independent adverse effects on diastolic dysfunction and increase the risk of HF.[19] Framingham Heart Study data have shown that HF is 2 to 5 times more frequent in diabetes patients than in age-matched control subjects.[19] Diabetes duration may also be associated with worsening LV diastolic dysfunction, but data on the impact of medication or risk factor modification are not yet available.[19] Predisposing conditions for diastolic HF include older age, female sex, diabetes and obesity, arterial hypertension, and LV hypertrophy.[17] As the present study population includes more predisposing conditions with a longer duration of diabetes, and as no therapy has been shown to improve outcomes in patients with diastolic HF,[18] the incidence of diastolic HF significantly increased in patients with a longer duration of diabetes, despite medical treatment and risk factor modification. Diabetes duration ≥10 years showed a trend toward an increased risk of HF but was not associated with all-cause mortality. The presence of DM alone may be associated with diastolic dysfunction and loss of diastolic reserve, possibly increasing susceptibility to diastolic HF.[27]

Controversy persists regarding the target HbA1c level and its impact on the subsequent occurrence of CVD in diabetic patients. Two previous large trials failed to find any cardiovascular benefit from intensive control (HbA1c < 6.0–6.5%) compared with standard control (HbA1c: 7.0–7.9%).[26,28] Because intensive control was not shown to reduce CVD occurrence, the American Heart Association, American College of Cardiology, and American Diabetes Association recommend a HbA1c goal of 7% and leave the decision to pursue tighter control on an individualized basis up to the physician.[29] Although we did not determine a target HbA1c level to prevent the subsequent occurrence of HF and increased mortality, the association of poor glycemic control with HF and increased mortality suggests that the degree of hyperglycemia may be involved in HF pathogenesis in our patients. Patients with T2DM have an increased prevalence of lipid abnormalities, which increases their risk of CVD.[16] Multiple clinical trials have demonstrated beneficial effects of statin therapy on CVD outcomes in subjects with and without MI.[30] Recently updated guidelines recommend that moderate-intensity statin therapy be considered in addition to lifestyle therapy for all diabetes patients ≥40 years old.[15,16] In our analysis, statin use was associated with a decreased risk of all-cause mortality. A prospective trial is needed to determine whether better glycemic control and statin use can improve clinical outcomes in T2DM patients without clinical CVD.

This study has some limitations of note. First, its retrospective design is subject to selection and information biases. Hence, the primary outcome incidence may have been underestimated. In addition, the baseline differences may have affected the incidence of primary outcome between the study populations stratified by diabetes duration. Patients with a longer duration of diabetes were older with a higher prevalence of comorbidities and poorer glycemic control than those with a shorter duration; in addition, they were more often female, and had a lower prevalence of past smoking in addition to significantly lower low-density lipoprotein cholesterol levels and a higher proportion of antiplatelet medication and statin use. Moreover, despite efforts to optimize risk factor variables, we sometimes failed to achieve management goals defined by the annually updated Standards of Medical Care in Diabetes by the American Diabetes Association[15,16] during the study period. Second, our study cohort included only patients of Asian descent, and because there may be racial or ethnic differences in the prevalence of HF and mortality in T2DM patients, our findings should be interpreted with caution when generally applied. Third, the baseline diabetes duration was estimated using self-reported ages, which may have included some inaccuracies from patient recall. Patients may have met criteria for prediabetes, which also increases the risk of CVD, for varying numbers of years. Furthermore, the analysis of the association between diabetes duration and the risk of primary outcome occurrence is complicated by the association of longer diabetes duration with older age, and residual confounding effects of this association cannot be excluded. Fourth, Doppler echocardiography was performed when any signs or symptoms suggestive of new-onset HF were identified, but we could not evaluate subclinical diastolic dysfunction, which may decrease the generalizability of the results. Lastly, the mean duration of follow-up was 47.6 ± 17.8 months, which may not have been long enough to accurately assess the primary outcomes.

In conclusion, a longer duration of diabetes is not a significant risk factor associated with an increased occurrence of new-onset HF and all-cause mortality in T2DM patients without previous clinical CVD. However, despite medical treatment for diabetes and risk factor modification for atherosclerotic CVD, patients with a longer duration of diabetes have an increased likelihood of new-onset HF and greater all-cause mortality.

Author contributions

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