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Research Article

Characteristics of Type 1 Diabetes Patients Aged 60 and Older in Shanghai, China

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Abstract

Aims: This study provided data to demonstrate the characteristics of Type 1 Diabetes Mellitus (T1DM) in individuals aged 60 years or older in a modern city in China to help health professionals optimize diabetes management.

Research Design and Methods: A total of 370 patients with T1DM were evaluated. Clinical characteristics of T1DM were analysed according to the age at enrolment (≤18 years old, 18–60 years old, ≥60 years old), and chronic complications in T1DM patients aged ≥60 years old compared to those in overall T1DM patients were also analysed by diabetes duration.

Results: T1DM patients aged 60 years and older displayed high level of HbA1c (9.5±2.1%) and SBP (130.6±18.3 mmHg). Macrovascular complications were more commonly seen in T1DM patients aged 60 years and older. When stratified by diabetes duration, albuminuria and impaired GFR were remarkably increased in T1DM patients aged 60 years and older with a diabetes duration of more than 30 years. However, all chronic complications in overall T1D were increased with shorter diabetes duration.

Conclusion: In T1DM patients aged 60 years and older, glycaemia and blood pressure were poorly controlled; age was associated with macrovascular complications, diabetes duration was associated with diabetic Kidney Disease (DKD), and this effect was weaker in those individuals. More efforts were required to control blood pressure and blood glucose in T1D patients aged 60 years and older to improve life expectancy and quality of life.

Keywords: Type 1 diabetes mellitus; Aged; Characteristics

Abbreviations

T1DM, Type 1 Diabetes Mellitus; DKD, Diabetic Kidney Disease; CHD, Coronary Heart Disease; PAD, Peripheral Artery Disease; CGM, Continuous Glucose Monitoring; BMI, Body Mass Index; WHR, Waist-To-Hip Ratio; ACE-I/ARB, Angiotensin-Converting Enzyme Inhibitor/Angiotensin Receptor Antagonist; HDL-C, High-Density Lipoprotein-Cholesterol; LDL-C, Low-Density Lipoprotein-Cholesterol; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; Hba1c, Glycosylated Haemoglobin.

Introduction

The Incidence Of Type 1 Diabetes (T1DM) has been increasing worldwide [1-3] and T1DM has become one of the largest global public health problems. The incidence of T1DM has shown considerable differences among countries, and China was ranked as one of the countries with the lowest incidence of T1DM among children, according to the DIAMOND investigation [3]. However, recent studies have found that the incidence of type 1 diabetes has increased rapidly in China during the past two decades [4-6] and most new-onset T1DM patients are adults [4-7]. In addition, Shanghai is one of the cities in China with developed economic and medical standards. According to the statistics of the Shanghai Municipal Statistics Bureau, in 2017, the average life expectancy of Shanghai's registered population was 83.37 years, including 80.98 years for men and 85.85 years for women [8]. Consequently, elderly people with type 1 diabetes are a growing population in Shanghai, China, but investigations of these individuals are lacking.

Despite improvements in treatments for diabetes allowing people with type 1 diabetes to live longer, life expectancy for T1DM patients remains 11-13 years less than that of the general population [9,10]. The prevention of diabetic complications to shorten the lifespan gap between T1DM patients and unaffected persons is a very urgent matter. Most research in T1DM has concentrated on young patients and ignored elderly patients. However, T1DM patients aged 60 years and older present widely heterogeneous health statuses and individual medical complexities, and management strategies for these patients should be individualized [11]. In this study, we analysed the clinical features of T1DM to find common differences in clinical, biochemical, therapeutic and chronic complications in T1DM patients aged 60 years and older compared to those aged ≤18 years and 18-60 years. Furthermore, we aimed to provide diabetes healthcare providers a reference for improving the management of diabetes and decreasing disease-associated complications and burden.

Materials and Methods

Subjects

We retrospectively collected data from 370 type 1 diabetes patients in the Endocrinology Department of Xinhua Hospital affiliated with

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Shanghai Jiaotong University School of Medicine between January 2007 and April 2019. Those with type 2 diabetes, pregnancy, surgery, serious trauma, and secondary or pancreatic exocrine diseases were excluded. Finally, 370 patients were analysed and divided into three groups according to age at enrolment (≤18 years old, 18–60 years old, ≥60 years old). A diagnosis of diabetes was based on the diagnostic criteria of the American Diabetes Association [12]. Type 1 diabetes was diagnosed by the typical presentation of disease, the absolute dependence on insulin treatment for survival, the presence of undetectable fasting C-peptide concentrations, and the presence of anti–islet cell autoantibodies. Current and past medical histories, personal backgrounds, and the use of medications were investigated for all subjects.

Clinical parameter collection

C-peptide was assayed with an automated analyser (ADVIA Centaur XP, Siemens, Berlin, German). Blood glucose and lipids were measured with an autoanalyzer (Hitachi 7600, Tokyo, Japan). Haemoglobin A1c (HbA1c) was detected by high-performance liquid chromatography (BIO-RAD VARIANT II, California, USA), urine albumin was detected by nephelometric immunoassay (BN Prospec; Siemens), and urine creatinine was measured using a chromatographic stable isotope dilution electrospray Mass Spectrometry Mass Spectrometry (MSMS) method on an AB SCIEX API5000. Data were collected on clinical presentation (age, sex, family history of diabetes, BMI, etc.) and biological parameters, including plasma glucose, blood lipids, HbA1c, C-peptide, uric acid, serum creatinine, Albumin-To-Creatinine Ratio (ACR), and estimated glomerular filtration rate (eGFR; calculated using MDRD) [13]. All of the blood samples were collected once at the time of admission in a fasting state except for the 2 h plasma glucose and C-peptide. Macrovascular complications, including Coronary Heart Disease (CHD), stroke and Peripheral Artery Disease (PAD), and microvascular complications consisted of Diabetic Kidney Disease (DKD), including albuminuria defined as ACR ≥30 μg/mg and impaired GFR defined as eGFR<60 ml/min/1.73 m^2, retinopathy and peripheral neuropathy. All diabetic complications were evaluated during hospitalization.

Statistical Analyses

Continuous measures were summarized by mean ± standard deviation [unless the data were non-normally distributed, then median and Interquartile Range (IQR) was used] and categorical variables by percentages. Continuous variables with normality and homogeneity of variance were analysed using one-way ANOVA; otherwise, the Kruskal-Wallis test and Mann-Whitney U test were used for continuous variables. The chi-square test was used for categorical variables. Two-tailed p values <0.05 were considered significant. Statistical analyses were performed in SPSS version 22 (IBM Corp, Armonk, NY, USA).

Results

Participant characteristics

Participant characteristics are shown in (Table 1) Of the 370 patients, 76, 215 and 79 were categorized as T1DM patients aged ≤18 years, T1DM patients aged 18-60 years, and T1DM patients aged≥60 years old. The age at enrolment of T1DM patients aged ≥60 years old was 66±5.3 years, and the age at T1DM onset was 53±12.6 years. The duration of T1DM in T1DM patients aged≥60 years old (10 (4,20) years) was significantly longer than that in T1DM patients aged ≤18 years (0.6 (0,4) years, p<0.0001) and T1DM patients aged 18-60 years (6 (1,12) years, p=0.001). The percentage of current smokers in T1DM patients aged ≥60 years old (30%) was higher than that in T1DM patients aged ≤18 years (0%) and similar to that in T1DM patients aged 18-60 years (26%). BMI was higher in T1DM patients aged ≥60 years old (21.5±3.2) than in T1DM patients aged ≤18 years (19±3.5, p<0.0001), while it was similar to that in T1DM patients aged 18-60 years (21.1±3.2, p=0.386), but the percentage of overweight or obesity

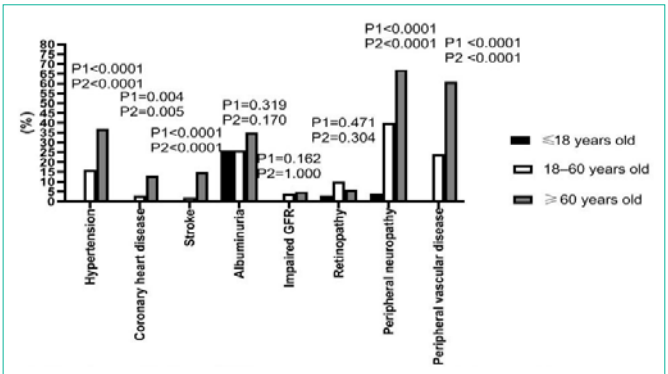

Figure 1: Chronic complications of T1D among age subgroups, p1>60 years old versus<18 years old: p2,>60 years old versus 18-60 years old.

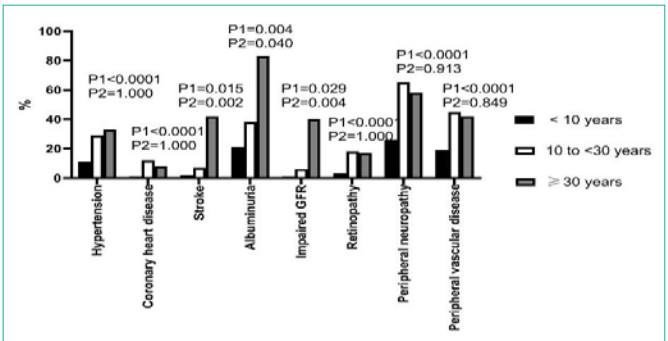

Figure 2: Chronic complications in overall T1D by duration group (<10 years, 10 to <30 years and >30 years), p1, 10 to <30 years versus <10 years:p2, 10 to <30 years versus>30 years.

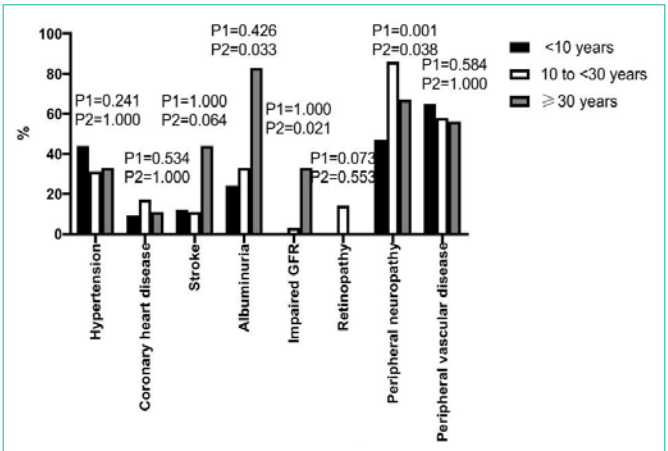

Figure 3: Chronic Complications in T1D patients aged 60 years and older by duration group (<10 years, 10 to <30 years and >30 years), p1, 10 t0<30 years versus<10 years; p2, 10to<30 years versus>30 years.

Table 1: Participant and clinical characteristics comparison by age subgroups.

	≤18 years old	18–60 years old	≥60 years old	P1	P2
Subjects -N (%)	76 (21%)	215 (58%)	79 (21%)	-	-
Age at enrolment (years)	12.8±3.9	41±12.9	66±5.3	0	0
Age of T1DM onset (years)	11±6.5	33.3±13.2	53±12.6	0	0
Duration of diabetes (years)	0.6 (0,4)	6 (1,12)	10 (4,20)	0	0.001
Sex (male %)	45%	49%	58%	0.093	0.153
Family history (%)	32%	35%	35%	0.611	0.929
Current smoker (%)	0%	26%	30%	0	0.459
BMI (kg/m^2)	19±3.5	21.1±3.2	21.5±3.2	0	0.386
WHR (cm/cm)	0.9±0.1	0.9±0.1	1±0.8	0.707	0.443
Overweight or obesity (%)	9	17	21	0.08	0.426
Antihypertensive use (%)	0	14	29	0	0.006
ACE-I/ARB use (%)	0	9	17	0.001	0.056
Statin use (%)	0	10	18	0.001	0.057
Aspirin use (%)	2	4	18	0.003	0
Time to insulin use from diagnosis (years)	0 (0, 0)	0 (0, 0.1)	0 (0, 2)	0	0.017
Insulin dose (U/kg of body weight/day)	0.81±0.28	0.62±0.23	0.58±0.21	0	0.209
Pump use (%)	33	8	4	0	0.177
≥3 Insulin injections daily/ pump use (%)	84	82	85	0.945	0.572

BMI, body mass index; WHR, waist-to-hip ratio; ACE-I/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor antagonist.
P1, ≥60 years old versus ≤18 years old; P2 ≥60 years old versus 18-60 years old

and WHR showed no difference among the age groups. There were no significant differences in the proportion of males or family history of diabetes. The use of antihypertensive medications and aspirin in T1DM patients aged ≥60 years old (29% and 18%, respectively) were higher than that in T1DM patients aged ≤18years (0, p<0.0001; 2%, p=0.003, respectively) and T1DM patients aged 18-60 years (14%, p=0.006; 4%, p<0.0001, respectively), Statin use was higher in T1DM patients aged ≥60 years old than in T1DM patients aged ≤18years and was similar to that in T1DM patients aged 18-60 years. Time to insulin use from diagnosis in T1DM patients aged ≥60 years old was longer than that in T1DM patients aged ≤18 years and T1DM patients aged 18-60 years (0 (0, 2) years versus 0 (0, 0) years, p<0.0001; 0 (0, 2) years versus (0, 0.1) years, p=0.017; respectively). Compared to T1DM patients aged ≤18 years, fewer T1DM patients aged ≥60 years used an insulin pump (4% versus 33%, p<0.0001), and those who did needed a lower insulin dose (0.58±0.21 versus 0.81±0.28, p<0.0001). Intensive therapy percentages were similar among subgroups.

Clinical Outcomes

Table 2 presents the clinical outcomes in the age subgroups. T1DM patients aged≥60 years old showed reduced fasting C-peptide (0.01 (0, 0.11) versus 0.13 (0.04, 0.35), p<0.0001), postprandial 2-hour C-peptide (0.01 (0, 0.21) versus 0.18 (0.04, 0.36, p=0.001), and HbA1c (9.5±2.1 versus 11.7±2.9, p<0.0001) levels compared to T1DM patients aged ≤18years upon admission and showed lower fasting C-peptide (0.01 (0, 0.11) versus 0.04 (0, 0.22), p=0.019) and HbA1c (9.5±2.1 versus 10.3±12.9, p=0.044) levels, as well as similar postprandial 2-hour C-peptide levels, compared to T1DM patients aged 18-60 years. HDL-C, serum uric acid, and serum creatinine levels were higher in T1DM patients aged ≥60 years old (1.6±0.5, 261±89 and 56 (51, 69), respectively) than in T1DM patients aged ≤18 years (1.4±0.4, p=0.004; 216.1±74.8, p=0.013; 36 (31, 45), p<0.0001, respectively) but similar to T1DM patients aged 18-60 years. Fasting glucose, postprandial 2-hour glucose, total cholesterol, LDL-C and triglyceride levels among age subgroups were similar. A significantly higher proportion of T1DM patients aged ≥60 years old (28%) had SBP≥140 mmHg than T1DM patients aged ≤18years (3%, p<0.0001) and T1DM patients aged 18-60 years (12%, p=0.001). Furthermore, the proportion of individuals with DBP≥90 mmHg was higher among T1DM patients aged ≥60 years old (9%) than among T1DM patients aged ≤18years (1%, p=0.032) but was not different from that of T1DM patients aged 18-60 years (10%, p=0.733). The incidence of ketoacidosis in T1DM patients aged ≥60 years old (17%) was lower than that in T1DM patients aged ≤18 years (51%, p<0.0001) and T1DM patients aged 18-60 years (38%, p<0.0001).

Chronic Diabetes Complications Of T1DM By Age Subgroups

Chronic complications of T1DM by age subgroups are shown in (Figure 1) hypertension (37% versus 0, aged ≥60 years old versus aged ≤18 years, p<0.0001; 37% versus 16%, aged ≥60 years old versus aged 18-60 years, p<0.0001), CHD (13% versus 0, aged≥60 years old versus aged ≤18 years, p=0.004; 13% versus 3%, aged ≥60 years old versus aged 18-60 years, p=0.005), stroke (15% versus 0, aged ≥60 years old versus ≤18 years, p<0.0001; 15% versus 2%, aged ≥60 years old versus aged 18-60 years, p<0.0001), peripheral neuropathy (67% versus 4%, aged ≥60 years old versus aged ≤18 years, p<0.0001; 67% versus 40%, aged≥60 years old versus 18-60 years, p<0.0001), PVD (61% versus 0, aged≥60 years old versus aged ≤18 years, p<0.0001; 61% versus 24%, aged≥60 years old versus aged 18-60 years, p<0.0001) were more commonly seen in T1DM patients aged 60 years and older compared to T1DM patients aged ≤18 years and T1DM patients aged 18-60 years. Retinopathy (6%), albuminuria (35%), and impaired GFR (5%) in T1DM patients aged 60 years and older were similar to those in T1DM patients aged ≤18 years and T1DM patients aged 18-60 years.

Diabetic Complications by Duration Group (0 To<10 Years, 10 To <30 Years And ≥30 Years)

For T1DM patients aged≥60 years old, diabetes complications include hypertension (31% versus 44%, p=0.241), CHD (17% versus 9%, p=0.534), and stroke (11% versus 12%, p=1), albuminuria (33% versus 24%, p=0.426), impaired GFR (3% versus 0, p=1), retinopathy (14% versus 0%, p=0.073) and peripheral vascular disease (58% versus 65%, p=0.584) in patients in the 10 to <30 year group displayed the same frequency as those in the 0 to <10 year group. Only peripheral neuropathy (86% versus 47%, p=0.001) presented a higher percentage. For the overall patient group, all of the diabetes complications in those with a duration of 10 to <30 years had a higher frequency than in those with a duration of 0 to <10 years. For T1DM patients aged≥60 years old, hypertension (33% versus 31%, p=1), CHD (11% versus 17%, p=1), stroke (44% versus 11%, p=0.064), retinopathy (0 versus 14%, p=0.553), peripheral neuropathy (67% versus 86%, p=0.380) and PVD (56% versus 58%, p=1) still showed no change in patients with a duration ≥30 years and those with a duration 10 to <30 years.

Table 2: Clinical outcome comparison in age subgroups.

	≤18 years old	18–60 years old	≥60 years old	P1	P2
Fasting glucose (mmol/L)	10.2 (6.8, 13.1)	9.6 (6.2, 13.2)	8.7 (5.7, 13.2)	0.181	0.445
Postprandial 2-hour glucose (mmol/L)	14.9±5.3	14.1±5.5	14.9±6.4	0.986	0.351
Fasting C-peptide (nmol/L)	0.13 (0.04, 0.35)	0.04 (0, 0.22)	0.01 (0, 0.11)	0	0.019
Postprandial 2-hour C-peptide (nmol/L)	0.18 (0.04, 0.36)	0.04 (0.01, 0.2)	0.01 (0, 0.21)	0.001	0.231
Total cholesterol (mmol/L)	4.3±0.9	4.5±1.2	4.6±1.2	0.175	0.819
HDL-C (mmol/L)	1.4±0.4	1.6±0.5	1.6±0.5	0.004	0.212
LDL-C (mmol/L)	2.4±0.7	2.5±0.9	2.5±0.9	0.46	0.851
Triglyceride (mmol/L)	0.9 (0.7, 1.3)	0.9 (0.6, 1.3)	0.9 (0.7, 1.2)	0.34	0.632
Serum uric acid (μmol/L)	216.1±74.8	280.5±117.3	261±89	0.013	1
Serum creatinine (μmol/L)	36 (31, 45)	54 (43, 66)	56 (51, 69)	0	1
HbA1c (%)	11.7±2.9	10.3±12.9	9.5±2.1	0	0.044
<7.5% (<58 mmol/mol) (%)	8	15	15	0.247	0.904
<8.0% (<64 mmol/mol) (%)	10	24	22	0.037	0.803
<8.5% (<69 mmol/mol) (%)	17	31	34	0.015	0.615
SBP (mmHg)	109.2±12.9	121.6±15.7	130.6±18.3	0	0
≥140 mmHg (%)	3	12	28	0	0.001
≥130 mmHg (%)	8	33	56	0	0
DBP (mmHg)	68.8±9.4	74±10.3	75.3±11.3	0	0.367
≥90 mmHg (%)	1	10	9	0.032	0.733
≥80 mmHg (%)	18	31	37	0.009	0.318
Ketoacidosis (%)	51	38	17	0	0

HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycosylated haemoglobin
P1, ≥60 years old versus ≤18 years old; P2 ≥60 years old versus 18-60 years old

However, albuminuria (83% versus 33%, p=0.033) and impaired GFR (33% versus 3%, p=0.021) were significantly higher in those with a duration ≥30 years than in those with a duration 10 to <30 years. The results of this analysis are presented in (Figure 2 and Figure 3).

Discussion

Our aim of this study was to explore the characteristics of T1DM patients aged 60 years and older compared with those of T1DM patients aged ≤18 years and T1DM patients aged 18-60 years in Shanghai, China. We found that the blood glucose and blood pressure in T1DM patients aged 60 years and older in our study were poorly controlled, as reflected by elevated HbA1c, SBP and DBP. In addition, we reported more hypertension, CHD, stroke, PAD and peripheral neuropathy in T1DM patients aged 60 years and older than in T1DM patients aged ≤18 years and T1DM patients aged 18-60 years. DKD and retinopathy presented no significant differences among the age subgroups. Stratification by diabetes duration indicated that a duration of more than 30 years was an important driver of the development of albuminuria and impaired GFR in T1DM patients aged 60 years and older, although other diabetic complications were not closely related to diabetic duration in T1DM patients in this age group. However, all diabetic complications in the overall T1DM study population increased rapidly, even after only 10 years of diabetes.

T1DM patients aged 60 years and older were susceptible to poor glycaemic and blood pressure control. In our study, T1DM patients aged 60 years and older showed more severe insulin deficiency than both T1DM patients aged ≤18 years and T1DM patients aged 18-60 years; moreover, patients in this group had more diabetic complications and comorbidities and required multiple insulin injections and the use of many medicines. In addition, accumulating evidence has demonstrated that T1DM patients aged 60 years and older are prone to severe hypoglycaemia [14,15]. Not only does a low HbA1c level have an increased risk for hypoglycaemia [14], but higher HbA1c goals alone are not sufficient to prevent hypoglycaemia in older patients with T1DM [16]. All of these reasons cause glycaemic and blood pressure management to be quite challenging for these individuals. Fortunately, many studies demonstrated that Continuous Glucose Monitoring (CGM) was beneficial for better glycaemic control [17-20] in T1DM patients aged 60 years and older. All of these factors underlie more attention and individualized management strategies for older adults with T1DM, and achieving better glycaemic and blood pressure control is possible in these individuals.

Macrovascular complications in patients with T1DM are commonly seen [21] and remain the major cause of premature morbidity and mortality [9-22]. In this study, we reported more CHD, stroke and PVD in T1DM patients aged 60 years and older than in T1DM patients aged ≤18years and T1DM patients aged 18-60 years, which was consistent with previous studies demonstrating that the development of Cardiovascular Disease (CVD) increased

dramatically with age in patients with diabetes, although most of these individuals had type 2 diabetes [23-25]. Mechanisms underlying the reason why older adults with T1DM had more CVD were not clear until now. At the cellular and molecular level, many theories have supported the pathogenesis of ageing-related CVD, including oxidative stress, inflammation, DNA damage, telomere shortening, genomic instability, epigenetic defects, metabolic disarray and mitochondrial dysfunction [26-28].Regarding clinical factors, a large prospective observational study demonstrated that blood pressure, LDL-C, smoking, albuminuria and HbA1c were cardiovascular risk factors in patients with T1DM and that the more risk factors were targeted, the fewer major adverse cardiovascular outcomes occurred [29]. In our study, glycaemia and blood pressure in T1DM patients aged 60 years and older were poor, and intervention in these factors might reduce the development of CVD.

The current study found that unlike macrovascular complications, age was not significantly associated with microvascular complications. A randomized controlled trial in patients with type 2 diabetes demonstrated that only diabetes duration was independently associated with microvascular events and that this effect was stronger in the youngest patients [30]. In our study, we also confirmed that a long diabetes duration increased the risk for developing DKD with a slower progression in T1DM patients aged 60 years and older.

DKD is the leading cause of end-stage renal disease, and it also increases the risk of CVD and death [31-33]. In the Diabetes Control and Complications Trial (DCCT) and Epidemiology of Diabetes Interventions and Complications (EDIC) study, after 30 years of T1DM, less albuminuria and a slower decline in GFR were observed than reported earlier with intensive therapy in early and other risk factor interventions [34-36]. Another study on type 1 diabetes reported that lower blood pressure was associated with a lower risk of microalbuminuria and milder declines in renal function [37]. Furthermore, a study comparing treatments and chronic complications in the United States T1DM Exchange and the German/Austrian DPV registries in T1DM patients aged ≥60 years old with T1DM found fewer chronic complications in the T1DMX might be related to greater use of antihypertensive medications (including ACE-I and ARBs), statins and aspirin [38]. In our study, long-term poor glycaemic and blood pressure control in T1DM patients aged 60 years and older were the main risk factors for DKD, the use of ACE-I or ARBs may explain part of the slower development of DKD in T1DM patients aged 60 years and older. In our study, retinopathy showed little relation to diabetes duration, which might be related to the limited sample size.

Some limitations of our study should be noted. First, the study subjects lacked data on CGM. Since CGM can reflect glycaemic excursions and hypoglycaemic events, these two factors have an important impact on glucose control and mortality, especially for T1DM patients aged 60 years and older. Second, in T1DM patients aged 60 years and older with a long diabetes duration, glycaemic and blood pressure control was not available during early T1DM. Third, this was a single-centre study with limitations of study number and region; thus, multicentre studies should be performed to further clarify the characteristics of T1DM patients aged 60 years and older.

In conclusion, glycaemia and blood pressure in T1DM patients aged 60 years and older were poorly controlled. In T1DM patients aged 60 years and older, age was associated with macrovascular complications, and diabetes duration of more than 30 years was an important driver of developing albuminuria and impaired GFR in T1DM patients aged 60 years and older with a slower progression. However, age was not a risk factor for Chronic Kidney Disease (CKD). Further studies are needed to better understand the risk factors for developing chronic disease in T1DM patients aged 60 years and older and to determine how to improve management strategies in T1DM patients aged 60 years and older to achieve long-term survival.

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