

Disproportionate microvascular burden emerging at younger ages in early- versus late-onset type 2 diabetes: an age-standardized analysis in Northern China

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Abstract

Background

The incidence of early-onset type 2 diabetes (diagnosed before 40 years of age) is rising rapidly worldwide and is thought to be more aggressive than late-onset disease. However, the long-term burden of chronic complications and the factors associated with microvascular damage in younger patients remain incompletely characterized, particularly in Chinese populations. We compared the metabolic profile and age-standardized complication burden between early- and late-onset disease and examined factors independently associated with microvascular complications.

Methods

We retrospectively analyzed 1,940 patients hospitalized with type 2 diabetes at a tertiary hospital in Northern China between 2018 and 2025, classified as early-onset (diagnosed < 40 years; $n = 1,116$) or late-onset (diagnosed ≥ 40 years; $n = 824$). Crude and age-standardized complication prevalence were calculated by direct standardization to the 2020 Chinese Census population. Restricted cubic spline models characterized the non-linear relationship between age at diagnosis and complication risk, and multivariable logistic regression identified factors independently associated with microvascular complications.

Results

Compared with the late-onset group, patients with early-onset disease had poorer glycemic control, greater insulin resistance, higher body mass index, more adverse lipid profiles, and higher serum uric acid (all $P < 0.001$). Although crude rates of macrovascular disease and neuropathy were lower in the early-onset group, the age-standardized microvascular burden was substantially higher, for both diabetic nephropathy (24.0% vs. 8.8%) and diabetic retinopathy (21.0% vs. 7.5%). Diabetic nephropathy prevalence among early-onset patients aged 40–49 years (24.6%) exceeded that among late-onset patients aged ≥ 70 years (21.5%). Restricted cubic spline analysis showed a sharp non-linear increase in macrovascular and neuropathic risk after age 40. Younger age at diagnosis, longer diabetes duration, higher body mass index, higher glycated hemoglobin, and higher serum uric acid were each independently associated with microvascular complications.

Conclusions

In this single-center cohort, early-onset type 2 diabetes was associated with a greater metabolic burden and a disproportionately higher age-standardized microvascular burden than late-onset disease, with renal complications emerging at younger ages. Serum uric acid was independently associated with microvascular complications, suggesting that risk assessment in early-onset diabetes should extend beyond traditional glucose-centered measures and support earlier, comprehensive evaluation in this population.

Background

Over the past six decades, the epidemiology of type 2 diabetes mellitus (T2DM) has shifted markedly, with a rising incidence among younger people. Once regarded as a disease of middle and older age, T2DM is now increasingly diagnosed in children, adolescents, and young adults worldwide [1–5]. Although multiple factors contribute to this trend, the rising prevalence of obesity in youth is widely regarded as the principal driver [6]. As a result, early-onset type 2 diabetes (EOD), typically diagnosed before 40 years of age, has become a substantial global public health concern [7].

Accumulating evidence suggests that EOD is not simply an earlier presentation of late-onset type 2 diabetes (LOD), but a more aggressive clinical phenotype. Compared with LOD, patients with EOD tend to show greater insulin resistance and higher levels of pro-inflammatory markers [8, 9], together with a more rapid decline in β -cell function, with reported annual loss rates exceeding those of adult-onset disease [10–14]. These features are associated with earlier glycemic deterioration and a shorter interval to insulin requirement.

Because diagnosis occurs at a younger age, patients with EOD accumulate a longer lifetime exposure to hyperglycemia, which has been linked to earlier development of microvascular and macrovascular complications and to increased premature mortality [15–17]. Despite this, young adults are under-represented in clinical research, as most large randomized controlled trials enroll predominantly older participants. The resulting scarcity of evidence contributes to “clinical inertia”, in which management lags behind the disease’s rapid progression [18].

Two gaps are particularly relevant. First, although serum uric acid is increasingly implicated in cardiometabolic disease, it has not been systematically evaluated as a risk factor for microvascular complications in EOD. Second, direct comparisons of complication burden between EOD and LOD are confounded by the large difference in age between the two groups, which crude prevalence rates do not address. In addition, given known ethnic differences in obesity thresholds and β -cell vulnerability, data from Chinese populations are needed. In this hospital-based study from Northern China, we therefore compared the metabolic profile and the age-standardized burden of chronic complications between EOD and LOD, used restricted cubic spline models to characterize the non-linear relationship between age at diagnosis and complication risk, and used multivariable logistic regression—with particular attention to serum uric acid—to identify factors independently associated with microvascular complications.

Methods

Study design and participants

This was a retrospective, single-center, cross-sectional study conducted in the Department of Endocrinology and Metabolism, Tianjin Medical University General Hospital (Tianjin, China). We screened 8,680 patients hospitalized with type 2 diabetes mellitus (T2DM) between January 2018 and September 2025. Patients were excluded if oral glucose tolerance test (OGTT) data were unavailable ($n = 5,791$) or for any of the following ($n = 949$): positive glutamic acid decarboxylase antibodies (GADA); a diagnosis of gestational, monogenic, secondary, or unspecified diabetes; incomplete medical records; or serious comorbidities (advanced cardiac, cerebral, or hepatic disease, or malignancy). The remaining 1,940 patients were classified by age at diagnosis as early-onset (EOD, < 40 years; $n = 1,116$) or late-onset (LOD, ≥ 40 years; $n = 824$). To limit bias, eligibility criteria were applied uniformly across the study period, and all complications were ascertained using predefined, standardized diagnostic criteria applied identically to the EOD and LOD groups. This study was performed in line with the Declaration of Helsinki and received approval from the Ethics Committee of Tianjin Medical University General Hospital (Approval number: IRB2020-YX-027-01; extended approval: IRB2020-YX-027-07). The study is reported in accordance with the STROBE guideline for observational studies.

Data collection and measurements

Demographic and clinical data (age, sex, diabetes duration, smoking status, and family history of diabetes) were extracted from electronic medical records. Physical examinations were performed by trained staff using standardized protocols. Blood pressure was measured with an automated sphygmomanometer after at least 10 min of rest. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Venous blood samples were obtained after an overnight fast of at least 8 h and analyzed in the hospital’s ISO-certified central laboratory. Glycated hemoglobin (HbA1c) was measured by high-performance liquid chromatography. Fasting plasma glucose, 2-hour postprandial

plasma glucose, serum uric acid, total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were measured on an automated biochemical analyzer, and fasting insulin by chemiluminescence immunoassay. Insulin resistance and β -cell function were estimated using the homeostatic model assessment (HOMA-IR and HOMA- β , respectively).

Definitions of complications and comorbidities

Diabetic nephropathy was defined as a persistent urinary albumin-to-creatinine ratio ≥ 30 mg/g and/or an estimated glomerular filtration rate < 60 mL/min/1.73 m² (CKD-EPI equation), confirmed on at least two occasions over a 3–6-month period. Diabetic retinopathy was diagnosed by digital fundus photography and graded independently by two ophthalmologists according to the International Clinical Diabetic Retinopathy Severity Scale. Diabetic peripheral neuropathy (DPN) was defined by characteristic symptoms together with at least two abnormal signs (reduced vibration perception, diminished ankle reflexes, or loss of 10-g monofilament sensation), after excluding non-diabetic causes. Atherosclerotic cardiovascular disease (ASCVD) was defined by a documented history or imaging evidence of coronary artery disease, ischemic stroke, or peripheral arterial disease. Obesity was defined as BMI ≥ 28.0 kg/m² (Working Group on Obesity in China criteria); hypertension as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or use of antihypertensive medication; hyperlipidemia and hyperuricemia according to standard clinical thresholds or relevant pharmacological treatment; and metabolic dysfunction-associated steatotic liver disease as imaging evidence of hepatic steatosis without secondary causes. In the analysis of risk factors, microvascular complications were defined as the presence of diabetic nephropathy and/or diabetic retinopathy.

Statistical analysis

Analyses were performed using SPSS version 26.0 and R version 4.3.1. Continuous variables are presented as mean $\pm$ standard deviation or median [interquartile range] according to their distribution and compared using the independent-samples *t* test or Mann–Whitney *U* test, respectively; categorical variables are presented as frequencies (percentages) and compared using the chi-square or Fisher's exact test. No a priori sample-size calculation was performed; all eligible patients during the study period were included. Patients with incomplete clinical records were excluded at enrollment (Fig. 1); analyses were therefore performed on complete cases, and no imputation was undertaken. To account for the difference in age structure between the EOD and LOD groups, age-standardized complication prevalence was calculated by direct standardization to the 2020 Chinese Census population. Trends across age groups were assessed by logistic regression with age group modeled as a continuous variable. Restricted cubic splines with four knots were used to characterize potential non-linear relationships between age at diagnosis and complication risk, adjusted for sex, diabetes duration, BMI, and HbA1c. To identify factors independently associated with microvascular complications, variables with $P < 0.10$ in univariate logistic regression were entered into a multivariable logistic regression model with backward stepwise selection. A two-sided P value < 0.05 was considered statistically significant.

Use of large language models

During the preparation of this manuscript, the authors used a large language model–based tool (Claude, Anthropic) solely to improve the language and readability of the text. The tool was not used to generate, analyze, or interpret data, to design the study, or to draw scientific conclusions. The authors reviewed and edited all output and take full responsibility for the content of the manuscript.

Results

Study population and baseline characteristics

Of 8,680 patients hospitalized with type 2 diabetes during the study period, 1,940 met the eligibility criteria and were included (Fig. 1): 1,116 with early-onset disease (EOD) and 824 with late-onset disease (LOD). Patients with EOD were diagnosed at a younger age than those with LOD (33.05 ± 4.62 vs. 53.28 ± 8.42 years) and had a longer median diabetes duration (7.50 [4.00, 18.00] vs. 4.00 [2.00, 5.00] years; $P < 0.001$). The EOD group also had a higher proportion of men (58.4% vs. 51.8%; $P = 0.004$), a positive family history of diabetes (52.7% vs. 46.5%; $P = 0.008$), and current smokers (36.1% vs. 29.7%; $P = 0.003$) (Table 1).

Table 1
Baseline clinical characteristics of patients with EOD and LOD.

Characteristic	EOD (n = 1116)	LOD (n = 824)	P value
Demographic characteristics			
Current age (years)	44.66 ± 14.44	57.40 ± 9.06	< 0.001
Age at diagnosis (years)	33.05 ± 4.62	53.28 ± 8.42	< 0.001
Diabetes duration (years)	7.50 [4.00, 18.00]	4.00 [2.00, 5.00]	< 0.001
Male sex, n (%)	652 (58.4%)	427 (51.8%)	0.004
Family history of diabetes, n (%)	588 (52.7%)	383 (46.5%)	0.008
Current smoker, n (%)	403 (36.1%)	245 (29.7%)	0.003
Metabolic risk factors			
BMI (kg/m ²)	28.34 ± 3.55	27.01 ± 2.99	< 0.001
SBP (mmHg)	128.92 ± 14.68	136.47 ± 24.04	< 0.001
DBP (mmHg)	86.20 ± 11.78	83.98 ± 11.44	< 0.001
TG (mmol/L)	3.74 ± 2.46	2.80 ± 2.65	< 0.001
TC (mmol/L)	5.34 ± 1.50	5.00 ± 1.32	< 0.001
LDL-C (mmol/L)	2.88 ± 0.79	2.47 ± 0.73	< 0.001
HDL-C (mmol/L)	1.01 ± 0.33	1.15 ± 0.44	< 0.001
Uric acid (μmol/L)	371.0 [309.7, 437.0]	325.0 [279.0, 380.0]	< 0.001
Insulin resistance and beta-cell function markers			
FPG (mmol/L)	8.93 ± 3.14	7.98 ± 2.50	< 0.001
2hFPG (mmol/L)	16.27 ± 4.09	14.89 ± 4.09	< 0.001
HbA1c (%)	9.01 ± 1.83	7.70 ± 1.17	< 0.001
Fasting insulin (mIU/L)	20.93 [12.84, 31.47]	15.60 [10.17, 25.33]	< 0.001
HOMA-IR	7.89 [4.61, 12.69]	5.18 [3.07, 9.21]	< 0.001
HOMA-β	44.05 [25.78, 75.33]	37.28 [22.54, 65.59]	0.001
Comorbidities			
Hypertension, n (%)	439 (39.3%)	386 (46.8%)	0.002
Hyperlipidemia, n (%)	386 (34.6%)	235 (28.5%)	0.005
Hyperuricemia, n (%)	305 (27.3%)	180 (21.8%)	0.015
MASLD, n (%)	331 (29.7%)	195 (23.7%)	0.004
Complications			
ASCVD, n (%)	146 (13.1%)	164 (19.9%)	< 0.001
DN, n (%)	192 (17.2%)	100 (12.1%)	< 0.001

Characteristic	EOD (n = 1116)	LOD (n = 824)	P value
Demographic characteristics			
DR, n (%)	176 (15.8%)	90 (10.9%)	0.003
DPN, n (%)	230 (20.6%)	270 (32.8%)	0.003

Notes: Data are presented as mean $\pm$ standard deviation for normally distributed continuous variables, median [interquartile range] for skewed continuous variables, and number (percentage) for categorical variables.

Abbreviations: 2hFPG, 2-hour postprandial plasma glucose; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; DBP, diastolic blood pressure; DN, diabetic nephropathy; DPN, diabetic peripheral neuropathy; DR, diabetic retinopathy; EOD, early-onset diabetes; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HOMA- β , homeostatic model assessment of β -cell function; HOMA-IR, homeostatic model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; LOD, late-onset diabetes; MASLD, metabolic dysfunction-associated steatotic liver disease; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.

Metabolic phenotype and comorbidities

Patients with EOD had a greater metabolic burden than those with LOD (Table 1). They had a higher body mass index (28.34 ± 3.55 vs. 27.01 ± 2.99 kg/m²) and higher serum uric acid (371.0 [309.7, 437.0] vs. 325.0 [279.0, 380.0] μ mol/L), higher triglycerides, total cholesterol, and LDL-cholesterol, and lower HDL-cholesterol (all $P < 0.001$). Glycemic control and insulin sensitivity were also poorer in the EOD group, with higher HbA1c ($9.01 \pm 1.83\%$ vs. $7.70 \pm 1.17\%$) and HOMA-IR (7.89 [4.61, 12.69] vs. 5.18 [3.07, 9.21]; both $P < 0.001$). The EOD group had a lower prevalence of hypertension (39.3% vs. 46.8%; $P = 0.002$) but higher rates of hyperlipidemia (34.6% vs. 28.5%; $P = 0.005$), hyperuricemia (27.3% vs. 21.8%; $P = 0.015$), and metabolic dysfunction-associated steatotic liver disease (29.7% vs. 23.7%; $P = 0.004$).

Age-standardized burden and age-related patterns of complications

Crude and age-standardized complication prevalence are shown in Table 2. Although the crude prevalence of atherosclerotic cardiovascular disease (ASCVD; 13.1% vs. 19.9%) and diabetic peripheral neuropathy (DPN; 20.6% vs. 32.8%) was lower in the EOD group, direct standardization to the 2020 Chinese Census population revealed a substantially higher microvascular burden in the EOD group, for both diabetic nephropathy (DN; 24.0% vs. 8.8%) and diabetic retinopathy (DR; 21.0% vs. 7.5%). The prevalence of all complications increased with age in both groups (P for trend < 0.001). Notably, the prevalence of DN among EOD patients aged 40–49 years (24.6%) exceeded that among LOD patients aged ≥ 70 years (21.5%); in the ≥ 70 -year stratum, the EOD group also had higher rates of DN (37.3% vs. 21.5%), DR (42.2% vs. 19.0%), and DPN (67.5% vs. 55.7%) than the LOD group (Table 2).

Table 2
Age-specific, crude, and age-standardized prevalence of chronic complications in EOD and LOD.

Age group	N	ASCVD		DN		DR		DPN		
		EOD	LOD	EOD	LOD	EOD	LOD	EOD	LOD	EOD
< 40 years	554	0	16 (2.9%)	—	13 (2.3%)	—	23 (4.2%)	—	33 (6.0%)	—
40–49 years	195	180	22 (11.3%)	16 (8.9%)	48 (24.6%)	18 (10.0%)	35 (17.9%)	4 (2.2%)	40 (20.5%)	39 (21.7%)
50–59 years	144	303	27 (18.8%)	39 (12.9%)	52 (36.1%)	27 (8.9%)	41 (28.5%)	33 (10.9%)	53 (36.8%)	87 (28.7%)
60–69 years	140	262	46 (32.9%)	83 (31.7%)	48 (34.4%)	38 (14.5%)	42 (30.0%)	38 (14.5%)	48 (34.3%)	100 (38.2%)
≥ 70 years	83	79	35 (42.2%)	26 (32.9%)	31 (37.3%)	17 (21.5%)	35 (42.2%)	15 (19.0%)	56 (67.5%)	44 (55.7%)
Crude rate, n (%)	1116	824	146 (13.1%)	164 (19.9%)	192 (17.2%)	100 (12.1%)	176 (15.8%)	90 (10.9%)	230 (20.6%)	270 (32.8%)
Age-standardized rate	—	—	17.7%	14.0%	24.0%	8.8%	21.0%	7.5%	26.9%	23.4%
P for trend	—	—	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Notes: Data are presented as n (%) unless otherwise indicated. Age groups reflect patients' current age at the time of data collection. Age-standardized rates were calculated by direct standardization using the 2020 Chinese Census population as the reference. *P* for trend was calculated using logistic regression models with age group treated as a continuous variable.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; DN, diabetic nephropathy; DPN, diabetic peripheral neuropathy; DR, diabetic retinopathy; EOD, early-onset diabetes; LOD, late-onset diabetes.

Restricted cubic spline analysis characterized the relationship between age at diagnosis and complication risk (Fig. 2). The risk of DN was approximately linear across the age range (*P* for non-linearity = 0.201), whereas the risks of ASCVD and DPN rose sharply and non-linearly, particularly after age 40 (*P* for non-linearity = 0.005 and 0.002, respectively).

When stratified by diabetes duration (Fig. 3), DN prevalence was numerically higher in the EOD group in both the short-duration (< 10 years: 9.3% vs. 8.3%) and long-duration (≥ 10 years: 31.4% vs. 28.0%) strata, although these differences were not statistically significant (Fig. 3A). DR prevalence did not differ significantly between groups in either stratum (< 10 years: 6.0% vs. 5.4%; ≥10 years: 33.1% vs. 33.5%; Fig. 3B). In contrast, ASCVD and DPN were significantly more prevalent in the LOD group early in the disease course, consistent with their stronger dependence on chronological age (Fig. 3C, D).

Factors independently associated with microvascular complications

In the EOD cohort, factors associated with microvascular complications (defined as diabetic nephropathy and/or diabetic retinopathy) were examined by logistic regression (Table 3). In the multivariable model, younger age at diagnosis (odds ratio [OR] 0.952; 95% confidence interval [CI] 0.931–0.974), longer diabetes duration (OR 1.120; 95% CI 1.100–1.140), higher body mass index (OR 1.067; 95% CI 1.014–1.124), higher HbA1c (OR 1.503; 95% CI 1.345–1.681), and higher serum uric acid (OR 1.007; 95% CI 1.005–1.009) were each independently associated with microvascular complications

(all $P < 0.05$); systolic blood pressure, total cholesterol, and LDL-cholesterol were retained in the model but were not statistically significant.

Table 3
Univariate and multivariate logistic regression analyses of risk factors for microvascular complications in patients with early-onset type 2 diabetes.

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Sex (male vs. female)	1.202 (0.908, 1.590)	0.199		
Family history (yes vs. no)	0.961 (0.731, 1.263)	0.775		
Current smoker (yes vs. no)	1.387 (1.052, 1.830)	0.021		
Age at diagnosis (years)	0.860 (0.839, 0.882)	< 0.001	0.952 (0.931, 0.974)	< 0.001
Diabetes duration (years)	1.093 (1.079, 1.108)	< 0.001	1.120 (1.100, 1.140)	< 0.001
BMI (kg/m ²)	1.062 (1.021, 1.104)	0.003	1.067 (1.014, 1.124)	0.013
SBP (mmHg)	0.990 (0.979, 1.001)	0.084	0.988 (0.974, 1.003)	0.117
DBP (mmHg)	1.025 (1.013, 1.037)	< 0.001		
FPG (mmol/L)	0.976 (0.933, 1.021)	0.294		
2hFPG (mmol/L)	0.989 (0.956, 1.023)	0.516		
FINS (mIU/L)	1.001 (0.996, 1.005)	0.755		
HOMA-IR	1.001 (0.992, 1.011)	0.761		
HOMA-β	1.000 (0.998, 1.002)	0.878		
HbA1c (%)	1.330 (1.228, 1.440)	< 0.001	1.503 (1.345, 1.681)	< 0.001
TG (mmol/L)	0.939 (0.883, 1.000)	0.049		
TC (mmol/L)	1.134 (1.038, 1.240)	0.006	1.099 (0.975, 1.239)	0.123
LDL-C (mmol/L)	1.270 (1.077, 1.496)	0.004	1.186 (0.943, 1.491)	0.144
HDL-C (mmol/L)	1.250 (0.925, 1.689)	0.146		
UA (μmol/L)	1.006 (1.005, 1.008)	< 0.001	1.007 (1.005, 1.009)	< 0.001

Notes: In the multivariate analysis, a backward stepwise selection method was applied; variables with $P < 0.10$ in the univariate analysis were entered. Empty cells indicate variables not retained in the final model.

Abbreviations: 2hFPG, 2-hour postprandial plasma glucose; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; FINS, fasting insulin; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-β, homeostasis model assessment of β-cell function; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; UA, uric acid.

Discussion

In this hospital-based cohort from Northern China, early-onset type 2 diabetes was characterized by a more adverse metabolic profile than late-onset disease, including poorer glycemic control, greater insulin resistance, higher body mass index, and more pronounced dyslipidemia. These observations are consistent with recent NHANES (1999–2020) and NHIS (2016–2022) analyses, in which individuals with early-onset disease had worse metabolic profiles, including higher body mass index and HOMA-IR, than those with later-onset disease [19, 20], and with large studies from China and India reporting greater difficulty in glycemic management and a higher complication burden in this group [21, 22]. Obesity-related insulin resistance, chronic glucotoxicity, and lipotoxicity are thought to place sustained stress on β -cells and may contribute to the more rapid disease progression observed in early-onset disease [23, 24].

The most salient finding was that, after direct age-standardization, the microvascular burden was substantially higher in the early-onset group despite their younger age, particularly for diabetic nephropathy and retinopathy. This pattern is in keeping with prospective data from the TODAY study and other cohorts, in which microvascular complications develop early in young-onset disease [24, 25], and with the UK Prospective Diabetes Study (UKPDS 92), in which younger-onset disease was associated with a higher incidence of complications—most markedly microvascular disease—over up to 30 years of follow-up [12]. Recent reviews have likewise highlighted the premature development of complications in early-onset type 2 diabetes as a growing public-health concern [6, 9].

A particularly notable observation was that the prevalence of diabetic nephropathy among early-onset patients aged 40–49 years (24.6%) exceeded that among late-onset patients aged ≥ 70 years (21.5%), indicating that renal complications may emerge at considerably younger ages in early-onset disease. In multivariable analysis, younger age at diagnosis remained independently associated with microvascular complications after adjustment for diabetes duration, body mass index, and HbA1c, consistent with a meta-analysis of 26 observational studies reporting a 3–5% reduction in cardio-renal risk per additional year of age at diagnosis [26]. One interpretation is that earlier and prolonged exposure to a dysmetabolic environment may reflect a “metabolic memory” phenomenon, in which earlier glycemic and metabolic exposure is associated with adverse renal outcomes independently of later control [27, 28]; this remains hypothesis-generating in a cross-sectional study. The true duration of exposure may also be underestimated, as type 2 diabetes can be present for several years before clinical diagnosis [31, 32].

Duration-stratified analysis added further nuance. Within duration strata, the between-group differences in microvascular prevalence were attenuated: diabetic nephropathy was numerically higher in the early-onset group in both strata but did not reach statistical significance, and diabetic retinopathy did not differ significantly between groups in either stratum. The more pronounced EOD–LOD difference in microvascular burden therefore emerged after age-standardization and in the age-stratified comparisons rather than within duration strata, suggesting that age at diagnosis, rather than diabetes duration alone, is an important determinant of microvascular risk in this cohort [8]. The restricted cubic spline analysis showed relatively stable risk before age 40 followed by a sharper, non-linear increase in macrovascular and neuropathic risk thereafter, compatible with a phased pattern in which microvascular complications appear early and macrovascular risk accumulates with advancing age. These observations are in line with registry data linking earlier age at diagnosis to higher cardiovascular and mortality risk [29, 30].

Multivariable analysis also identified serum uric acid as a factor independently associated with microvascular complications in the early-onset cohort. Although landmark studies such as the UKPDS and TODAY have advanced the understanding of early-onset disease, serum uric acid has been less consistently examined in this context. In our cohort the median serum uric acid (371.0 $\mu\text{mol/L}$) was near the upper end of the physiological range, suggesting that even subclinical elevations may warrant attention. Experimentally, elevated uric acid has been associated with afferent arteriolar changes and activation of the renin–angiotensin system, mechanisms that may contribute to microvascular injury, glomerulosclerosis, and retinal damage [33, 34]. Each one-year decrease in age at diagnosis was associated with approximately 4.8% higher odds of microvascular complications; whether serum uric acid and age at diagnosis interact could not be determined in the present analysis and warrants dedicated study.

This study has several strengths and limitations. Strengths include a relatively large, well-characterized single-center cohort with standardized laboratory measurements, the use of direct age-standardization to enable a fairer comparison between groups of differing age structure, and the use of restricted cubic spline models to characterize non-linear age–risk relationships. The inclusion of serum uric acid addresses a relatively under-examined factor in early-onset disease. Several limitations should be acknowledged. First, the retrospective, cross-sectional design precludes causal inference and does not allow assessment of temporal sequence. Second, recruitment from a single tertiary hospital may introduce selection bias toward more severe cases, limiting generalizability. Third, the cohort comprised only Chinese individuals, so the findings may not extend to other populations. Finally, some variables were derived from medical records, and unmeasured confounding cannot be excluded. Prospective, multicenter studies in diverse populations are needed to confirm these associations and to clarify the role of serum uric acid in microvascular risk.

Conclusions

In this single-center cohort from Northern China, early-onset type 2 diabetes was associated with a greater metabolic burden and a disproportionately higher age-standardized burden of microvascular complications than late-onset disease, with diabetic nephropathy and retinopathy emerging at younger ages. Younger age at diagnosis, longer diabetes duration, higher body mass index, higher HbA1c, and higher serum uric acid were each independently associated with microvascular complications. These findings suggest that risk assessment in early-onset type 2 diabetes should extend beyond traditional glucose-centered measures to incorporate serum uric acid, and support earlier and more comprehensive risk evaluation in this population. Given the retrospective, single-center design, prospective multicenter studies are needed to confirm these associations.

Abbreviations

2hFPG

2-hour postprandial plasma glucose

ASCVD

atherosclerotic cardiovascular disease

BMI

body mass index

CI

confidence interval

CKD-EPI

Chronic Kidney Disease Epidemiology Collaboration

DBP

diastolic blood pressure

DN

diabetic nephropathy

DPN

diabetic peripheral neuropathy

DR

diabetic retinopathy

eGFR

estimated glomerular filtration rate

EOD

early-onset type 2 diabetes

FINS

fasting insulin
FPG
fasting plasma glucose
GADA
glutamic acid decarboxylase antibody
HbA1c
glycated hemoglobin
HDL-C
high-density lipoprotein cholesterol
HOMA-IR
homeostatic model assessment of insulin resistance
HOMA- β
homeostatic model assessment of β -cell function
LDL-C
low-density lipoprotein cholesterol
LOD
late-onset type 2 diabetes
MASLD
metabolic dysfunction-associated steatotic liver disease
NHANES
National Health and Nutrition Examination Survey
NHIS
National Health Interview Survey
OGTT
oral glucose tolerance test
OR
odds ratio
RCS
restricted cubic spline
SBP
systolic blood pressure
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
T2DM
type 2 diabetes mellitus
TC
total cholesterol
TG
triglycerides
UA
uric acid
UACR
urinary albumin-to-creatinine ratio
UKPDS
UK Prospective Diabetes Study.

Declarations

Ethics approval and consent to participate

This study was performed in line with the Declaration of Helsinki and received approval from the Ethics Committee of Tianjin Medical University General Hospital (Approval number: IRB2020-YX-027-01; extended approval: IRB2020-YX-027-07). The committee waived informed consent because the study was retrospective, and all data were anonymized to protect patient confidentiality.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because of hospital data-protection policies and patient privacy but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

No specific funding was received for this study.

Authors' contributions

PA, TL, and YL performed the statistical analyses, interpreted the data, and drafted the manuscript. RL, HW, and HS contributed to data curation and cleaning. YF and QS collected the clinical data. ML conceived and designed the study, supervised the work, and critically revised the manuscript. All authors read and approved the final manuscript. PA, TL, and YL contributed equally to this work.

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Figures

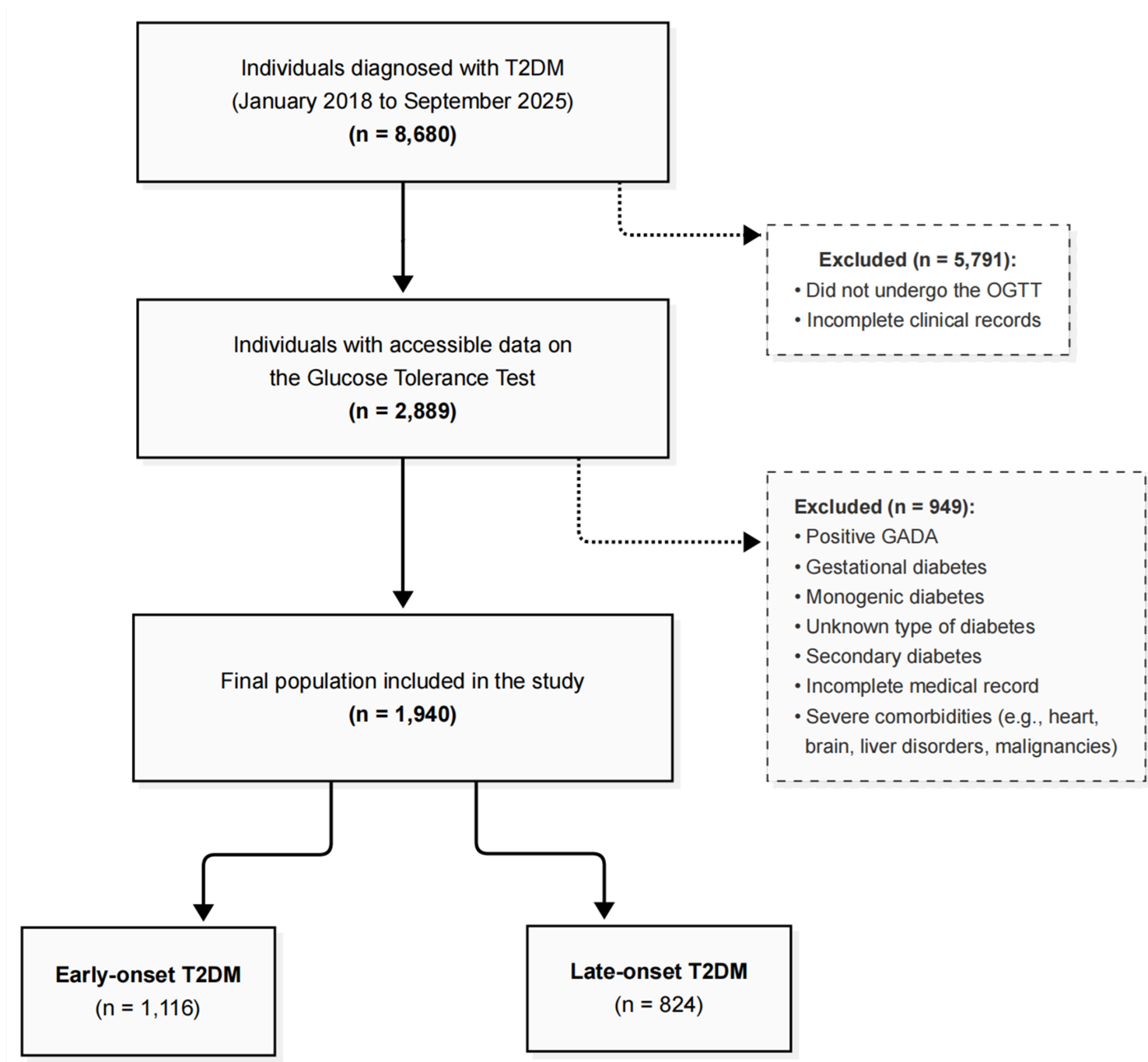


Figure 1

Flowchart of study participant selection.

Of 8,680 patients hospitalized with a diagnosis of type 2 diabetes mellitus (T2DM) between January 2018 and September 2025, 5,791 were excluded due to missing oral glucose tolerance test (OGTT) data and 949 were excluded for clinical reasons (presence of glutamic acid decarboxylase antibodies [GADA]; diagnosis of gestational, monogenic, secondary, or unspecified diabetes; incomplete medical records; or serious comorbidities). The remaining 1,940 eligible patients were classified as early-onset T2DM (EOD; diagnosed at age <40 years; n = 1,116) or late-onset T2DM (LOD; diagnosed at age ≥40 years; n = 824).

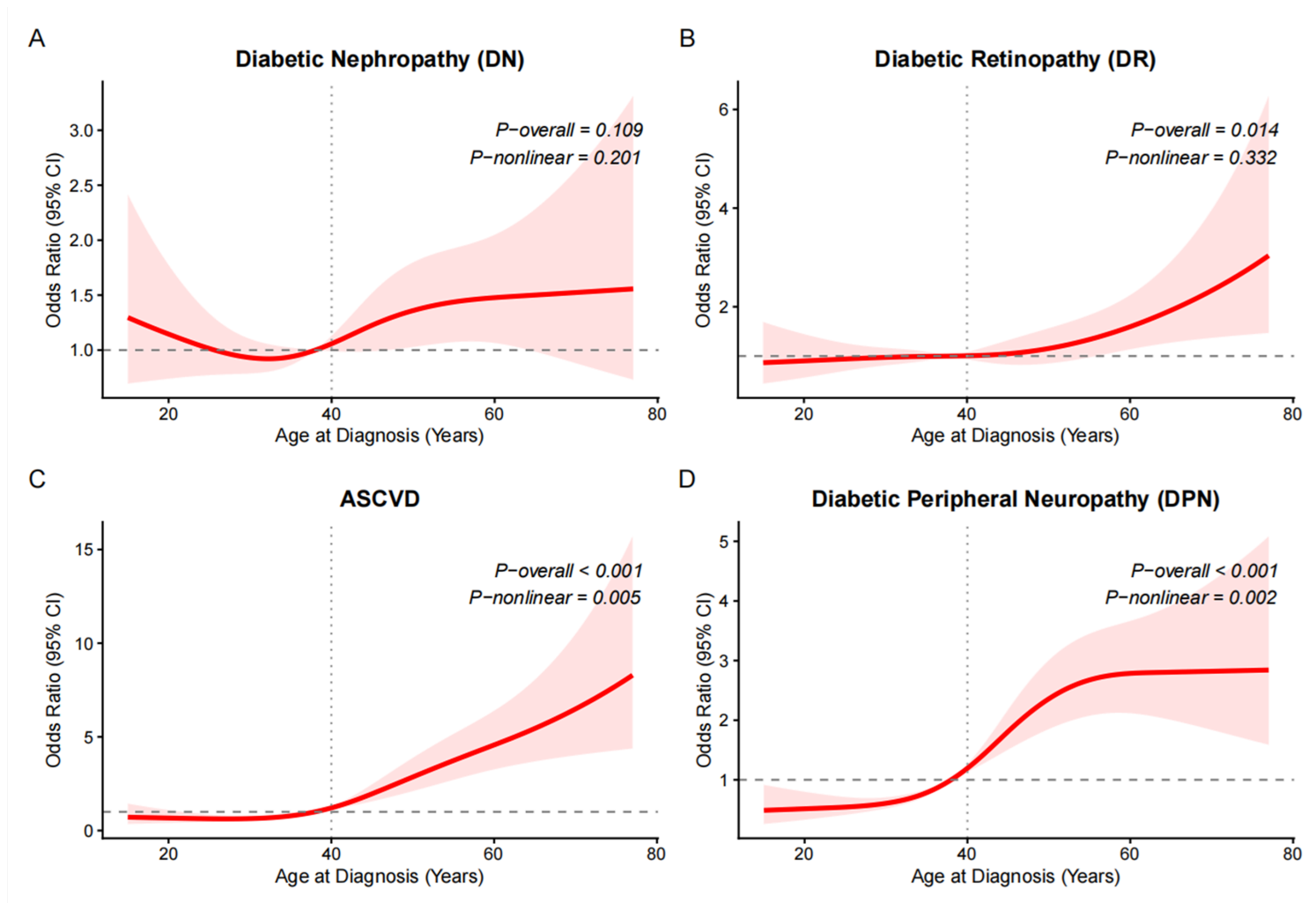


Figure 2

Association between age at diagnosis and risk of diabetic complications: restricted cubic spline analysis.

Solid lines represent multivariable-adjusted odds ratios (ORs) with 95% confidence intervals (CIs) shown as shaded areas. The horizontal dashed line indicates OR = 1.0; the vertical dotted line marks the reference age of 40 years. All models were adjusted for sex, diabetes duration, body mass index (BMI), and glycated hemoglobin (HbA1c). $P\text{-overall}$ indicates the significance of the overall association; $P\text{-nonlinear}$ indicates the test for departure from linearity. **(A)** Diabetic nephropathy (DN; $P\text{-overall} = 0.109$, $P\text{-nonlinear} = 0.201$). **(B)** Diabetic retinopathy (DR; $P\text{-overall} = 0.014$, $P\text{-nonlinear} = 0.332$). **(C)** Atherosclerotic cardiovascular disease (ASCVD; $P\text{-overall} < 0.001$, $P\text{-nonlinear} = 0.005$). **(D)** Diabetic peripheral neuropathy (DPN; $P\text{-overall} < 0.001$, $P\text{-nonlinear} = 0.002$).

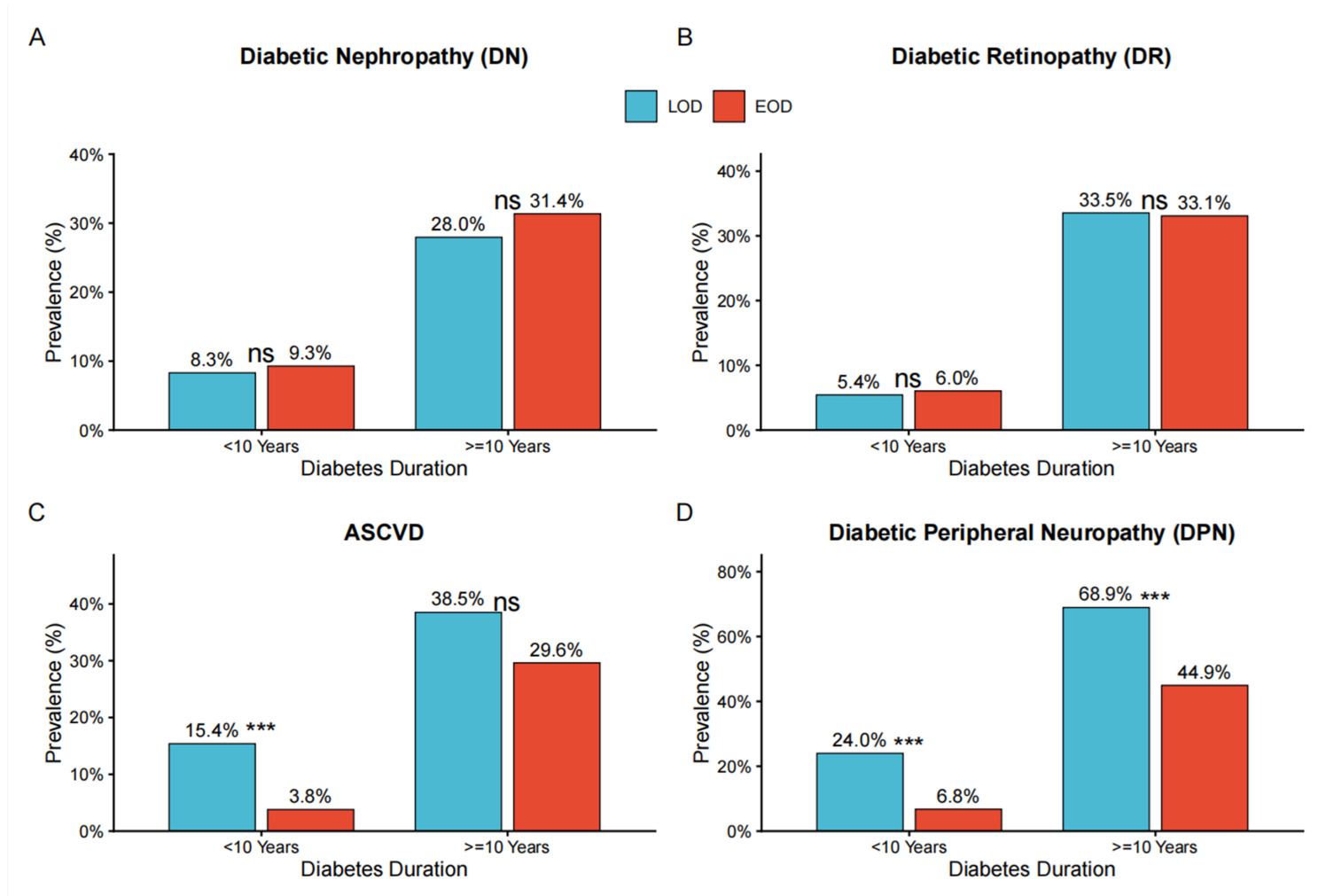


Figure 3

Prevalence of chronic complications in early-onset and late-onset T2DM stratified by diabetes duration.

Patients were stratified into two diabetes duration groups (<10 years and ≥10 years) and compared between EOD (age at diagnosis <40 years) and LOD (age at diagnosis ≥40 years). Complication prevalence (%) is shown above each bar. Between-group differences within each duration stratum were assessed using the chi-square or Fisher's exact test, as appropriate. **(A)** Diabetic nephropathy (DN). **(B)** Diabetic retinopathy (DR). **(C)** Atherosclerotic cardiovascular disease (ASCVD). **(D)** Diabetic peripheral neuropathy (DPN). Significance levels: *** $P < 0.001$; ns, not significant.

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