

Vascular complications in early-onset type 2 diabetes in China: An emerging challenge

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Received: February 4, 2026; Accepted: June 3, 2026; Published Online: June 4, 2026; <https://doi.org/10.59717/j.xinn-med.2026.100248>

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Citation: Chen X., Ke D., Sun J., et al. (2026). Vascular complications in early-onset type 2 diabetes in China: An emerging challenge. *The Innovation Medicine* 4:100248.

Early-onset type 2 diabetes (T2D), defined as T2D diagnosed before the age of 40 years, is increasingly prevalent with substantial health and socio-economic implications, particularly in Asian populations. China accounts for one-quarter of the world's diabetes population. As of 2023, an estimated 233 million individuals in China were living with diabetes.¹ In recent years, early-onset T2D is increasingly common in China. From 1990 to 2021, the percentage growth in prevalence of early-onset T2D was 240.0%, and in 2021, the number of early-onset T2D cases was 22.6 million in China, second globally after India.² Compared to late-onset T2D, early-onset T2D is characterized by a prolonged duration and more rapid progression of vascular complications. For example, participants with early-onset T2D had a higher age-standardized prevalence of nonfatal cardiovascular diseases than those with late-onset T2D (11.4% vs 4.4%) in 14 provinces in China.³ Vascular complications, mainly including macrovascular and microvascular complications, consequently substantially impair the quality of life and work capacity among young adults. Therefore, addressing the vascular complications of early-onset T2D is particularly urgent for China.

Accumulating evidence has demonstrated that individuals with early-onset T2D have almost twice the risk of microvascular (e.g., retinopathy, nephropathy, neuropathy) and macrovascular (e.g., coronary heart disease, stroke) complications compared with late-onset T2D during the first 10 years of follow-up.² Our previous studies have shown that proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) in early-onset T2D have significantly higher levels of glucose, lipid, and inflammatory biomarkers, and poorer visual prognosis.⁴ Further retinal imaging and aqueous humor analysis revealed distinctive clinical manifestations, biomarker profiles, and responses to treatment among these individuals. For instance, these patients have higher prevalence of retinal microaneurysms, haemorrhages, cotton-wool spots, and microvascular abnormalities, and lower visual improvement following vitrectomy or anti-VEGF therapy.⁴ Optical coherence tomography (OCT) analyses in our cohort of 380 patients with DME further demonstrated that patients with early-onset T2D complicated by DME had greater central macular thickness and a higher proportion of severe or atrophic DME (Table 1). As the "window" of systemic vascular lesions, the accelerated progression and clinical manifestation in retinopathy suggest that comprehensive vascular screening and appropriate interventions should be implemented as early as possible for the patients with early-onset T2D.

Beyond the epidemiological burden, emerging evidence suggests that early-onset T2D represents a particularly aggressive biological phenotype, characterized by severe obesity-related insulin resistance, excess visceral adiposity, and accelerated β -cell decline, which together may increase cumulative glycemic exposure. Hyperglycemia and insulin resistance can further promote oxidative stress, chronic inflammation, endothelial dysfunction, and maladaptive vascular remodeling, providing a mechanistic basis for the earlier onset and faster progression of retinal, renal, and neural complications. Notably, endothelial dysfunction has been demonstrated in youth-onset T2D within 5 years of diagnosis, even in the absence of severe hyperglycemia or dyslipidemia. Emerging biomarkers and translational tools under investigation include inflammatory cytokines, vascular injury markers, extracellular vesicles or exosomal cargo, and imaging-based assessments of endothelial function, although their clinical utility in routine care remains to be established. These findings support earlier risk stratification and more proactive prevention and management strategies in early-onset T2D.

Nevertheless, current preventive strategies and management of vascular complications in early-onset T2D in China are still very limited. First, although China has established large prospective cohorts, such as the China Kadoorie Biobank, patients with early-onset T2D represent only a small subgroup within these cohorts. This limits statistical power for subgroup analyses and makes it difficult to comprehensively evaluate multiple vascular outcomes, including retinal, renal, and neural complications, in a nationally representative manner. Future studies should better leverage existing cohorts for subgroup analyses while also developing dedicated or pooled cohorts to address these data gaps. Second, vascular screening for younger people with diabetes remains limited in China. Fundus photography and urinary albumin testing have not yet been systematically incorporated into routine medical examinations and basic health insurance coverage for early-onset T2D, and implementation may be hindered by fragmented care and concerns about cost. International experience suggests that earlier screening can still be feasible and economically justified when embedded within existing diabetes care. For example, the UK National Health Service offers diabetic eye screening to all people with diabetes aged 12 years and older, and the program is evaluated within a framework requiring benefit at a reasonable cost to the health system. Singapore has also shown that telemedicine-based retinal screening in primary care can achieve similar health outcomes at lower cost. Third, both public awareness and clinicians predominantly focus on the middle-aged and older T2D patients for vascular complications, ignoring the high risk among early-onset T2D patients due to long disease duration and rapid progression of complications. Fourth, the prevalence of obesity is increasing among young Chinese adults. Many also show an Asian-specific "lean phenotype" with a low body mass index but high visceral fat. In addition, genetic risks for β -cell dysfunction and insulin resistance are common. These factors further raise the risk of vascular complications in early-onset T2D, which demand prompt attention.

In addition to the general recommendations, it is important to consider the heterogeneity of early-onset T2D in different populations, such as adolescents and females. For adolescents, recent studies have shown that adolescent obesity is strongly associated with an increased risk of developing T2D at an earlier age, with rapid disease progression and more severe complications compared to adults. Early identification and intervention in high-risk adolescents, including family-based weight management programs and early screening for vascular complications, are essential to delay the onset of diabetes and prevent early vascular damage. For females, those with a previous history of gestational diabetes mellitus (GDM) are at significantly higher risk of developing early-onset T2D. A systematic review and meta-analysis found that the risk of progression to early-onset T2D in women following GDM was 10-fold higher (hazard ratio 9.51; 95% CI 7.14–12.67) compared to women without GDM.⁵ It is crucial to optimize glycemic control during these periods to reduce the long-term risk of T2D and its associated vascular complications. Furthermore, women diagnosed with early-onset T2D should receive tailored care throughout four reproductive phases, including not planning pregnancy, planning pregnancy, pregnancy, and postpartum. Timely management of these four phases is essential to ensure better maternal and fetal outcomes and prevent vascular complications.

China has started the "Healthy China 2030" plan, which promotes comprehensive prevention and control of chronic diseases, with a focus on prevention. It is imperative to systematically and proactively incorporate vascular

Table 1. Characteristics between early-onset and late-onset DME patients.

Characteristics	Total (n=380)	Early-onset (n=154)	Late-onset (n=226)	P
Age (year)	56.00 [49.00,61.00]	49.50 [39.00,56.00]	59.00 [55.00,63.00]	<0.001
BMI (kg/m ²)	23.90 [21.80, 26.10]	24.20 [22.35, 26.63]	23.30 [21.40, 25.70]	0.014
Male (%)	212 (55.8)	92 (59.7)	120 (52.8)	0.240
Ethnicity (%)	351 (92.3)	144 (93.5)	207 (91.6)	>0.999
Smoking	64 (16.8)	35 (22.9)	29 (13.4)	0.025
Age at T2D diagnosis (year)	43.0 (10.4)	33.06 (6.28)	49.69 (6.47)	<0.001
Duration of T2D (year)	12.00 [5.00,16.00]	15.00 [8.00,20.00]	10.00 [4.00,15.00]	<0.001
Right eye (%)	177 (46.6)	70 (45.5)	107 (47.4)	0.796
CT (μm)	288.3 (77.6)	296.8 (79.8)	282.4 (75.7)	0.080
CMT (μm)	335.00 [256.00,476.25]	369.50 [267.00,529.25]	308.00 [248.00,438.75]	<0.001 [†]
DME classification (%) [*]				<0.001 [‡]
Mild	69 (18.02)	15 (9.7)	54 (23.9)	
Moderate	257 (67.89)	107 (69.5)	150 (66.4)	
Severe or atrophic	54 (14.2)	32 (20.8)	22 (9.7)	

Abbreviations: OCT, optical coherence tomography; DME, diabetic macular edema; CMT, central macular thickness; CT, choroidal thickness. Data were presented as median [interquartile range], mean (standard deviation), or number (%). Continuous variables were compared using the Wilcoxon rank-sum test or Student's *t* test depending on their distribution, while categorical variables were compared using the χ^2 test.

^{*}Based on the OCT-based classification criteria for DME proposed by European investigators in 2020, DME was classified into four types in this study: mild DME, moderate DME, severe DME, and atrophic maculopathy.

[†]For CMT, the *P* value was obtained from multivariable linear regression with log-transformed CMT, adjusted for age, BMI, sex, smoking, and diabetes duration. After adjustment, early-onset T2D was associated with 0.25 higher log-transformed CMT (β : 0.25, 95% CI: 0.11, 0.40).

[‡]For DME, the *P* value was obtained from a multivariable ordinal logistic regression, adjusted for age, BMI, sex, smoking, and diabetes duration. After adjustment, early-onset T2D was associated with more severe DME classification (OR: 5.6, 95% CI: 2.5, 12.8).

health in early-onset T2D into national strategies for chronic disease prevention and youth health. It is recommended that Chinese healthcare policymakers place greater emphasis on health education, nutritional counselling, physical exercise, and comprehensive management of other risk factors to reduce vascular complications. Multi-level preventive approaches should be implemented, including primary prevention across the general population, secondary prevention among high-risk younger adults, and tertiary prevention for diagnosed early-onset T2D patients to prevent vascular complications. Specifically, primary prevention should prioritize obesity prevention and healthier lifestyles in children, adolescents, and young adults; secondary prevention should strengthen earlier risk assessment and vascular screening in younger adults with obesity, family history of diabetes, or metabolic abnormalities; and tertiary prevention should focus on intensified management of glycaemia, blood pressure, lipids, body weight, and early retinal, renal, and neural injury in patients with early-onset T2D. Only by building a coordinated prevention and management system across all three levels can China effectively curb the rising burden of vascular complications in early-onset T2D, protect young adults' health, and support the goals of Healthy China.

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FUNDING AND ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (82471103, 82404266) and National Key Research and Development Program of China (2024YFC2510803). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

AUTHOR CONTRIBUTIONS

All authors contributed to and approved the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.