



Young-Onset Type 2 Diabetes - Time to Realign Clinical Priorities

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Traditionally considered as a disease of the middle-aged, type 2 diabetes (T2D) has become increasingly more prevalent in children, adolescence and young adults below the age of 40 [1,2]. Of concern, this evolution of young-onset T2D is a global phenomenon. Obesity is a major predisposing factor as the age of onset is inversely associated with body mass index [3], reflecting the consequences of sedentary lifestyle afflicting different nations and cultural backgrounds. Young-onset T2D subjects share similar pathophysiological aetiology of beta-cell failure and insulin resistance with the middle-aged counterparts, and this metabolic dysfunction has been observed within the first two decades of life [4].

In recent years, increasing evidence has supported the hypothesis that young-onset T2D is more likely to develop premature microvascular and macrovascular complications than older-onset subjects [5,6]. Despite the young age of onset (including children and adolescence), clustering of multiple risk factors such as obesity, hypertension and dyslipidaemia is common [7]. The consequence of this exposure to adverse metabolic milieu at a young age is evident. This young cohort developed significant burden of complications by their 40s [6,8], at a much earlier stage of their lives compared to the older-onset subjects, a testimony to the high life time risk for complications. Moreover, the young-onset T2D subjects were less likely to respond to oral diabetes medications as the rate of beta-cell function decline was greater than the older-onset cohort (20-35% vs 6% decline per year) [9-11], an indication that achieving good glycaemic control will be a challenge.

Since type 1 diabetes (T1D) is the most prevalent type of diabetes in young people, it would be clinically pertinent to ascertain which type of diabetes is more deleterious when its onset occurred in the young. Recent studies have compared the characteristics of diabetes-related complications in young-onset T1D and T2D [12-16]. Not only the cardiometabolic risk profile (obesity, hypertension, dyslipidaemia) was more adverse in the T2D cohort, the burden of cardiovascular disease, neuropathy and nephropathy were also greater in this population. Cardiovascular mortality was 2-fold higher than T1D with these deaths occurring at significantly shorter diabetes duration [12]. Clearly, these data provide strong evidence that T2D in the young is not a benign condition.

The clinical management of young-onset T2D faces many challenges involving both healthcare professionals and patients. There is lack of robust evidence to prove that intensive treatment of glycaemia and cardiovascular risk factors will lead to better outcomes in this population, in contrast to T1D [17] and older-

onset T2D [18]. This has led to suboptimal administration of cardio-protective treatment, particularly relating to primary prevention of cardiovascular disease [19], perhaps compounded by the clinicians' misperception of this young cohort being low risk. Furthermore, poor adherence to medical care is not uncommon in young-onset T2D resulting in poor control of glycaemia and cardiovascular risk factors [20], thus, increasing the risk for complications.

There is a clear need for future research to focus specifically on young-onset T2D. Demonstrating the link between intensive risk factor management and improved complication and mortality outcomes is essential. A better understanding of the underlying process of accelerated beta-cell dysfunction may help to determine the most appropriate therapeutic choice to achieve glycaemic durability. The role and effectiveness of newer agents such as GLP-1 agonist and SGLT-2 inhibitor in reducing obesity and improving diabetes control need to be explored, particularly with the reduced efficacy of metformin in this young cohort [9]. Ascertaining the appropriate clinical service provision and structured education models that are responsive to the medical, emotional and psychological needs of young-onset T2D is important to improve engagement and adherence to treatment and healthy lifestyle.

The phenotypic landscape of T2D has changed, perhaps irrevocably, and this raises clinical and societal concerns. The cost of diabetes care is already a considerable burden on healthcare budget [21] which will most likely increase as the younger segment of the population develops significant complications at an economically-productive age. To tackle this problem, a cohesive approach from the government, society, public health and clinicians is required to promote healthy lifestyle in the general population to prevent diabetes, screening at risk young individuals for early diabetes detection, timely medical care to reduce complications and recognising young-onset T2D as a high risk condition. Successful achievement of these goals will be dependent upon concerted realignment of clinical priorities by all parties involved, with no room for inertia.

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