Young adult-onset type 2 diabetes

Adverse outcomes and potential solutions

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Until recently, type 2 diabetes was considered a lifestyle disease of mature people and less serious than type 1 diabetes. Young adult-onset type 2 diabetes has been revealed to be an aggressive condition with a high risk of diabetes complications and premature death, a risk greater than for those with type 1 diabetes.

The prevalence of young adult-onset type 2 diabetes worldwide has been increasing in parallel with the increase in childhood obesity. Type 2 diabetes is being increasingly diagnosed in young people, particularly in Indigenous populations.[1,2] There is often a perception that type 1 diabetes is the most severe form of diabetes and type 2 diabetes is a milder condition of poor lifestyle and remedied more easily. However, recent evidence suggests an aggressive course and a worse prognosis for patients with young adult-onset type 2 diabetes. This article discusses the challenges in the diagnosis, prognosis and treatment of young adult-onset type 2 diabetes with particular reference to the young adult population between the ages of 18 and 30 years.

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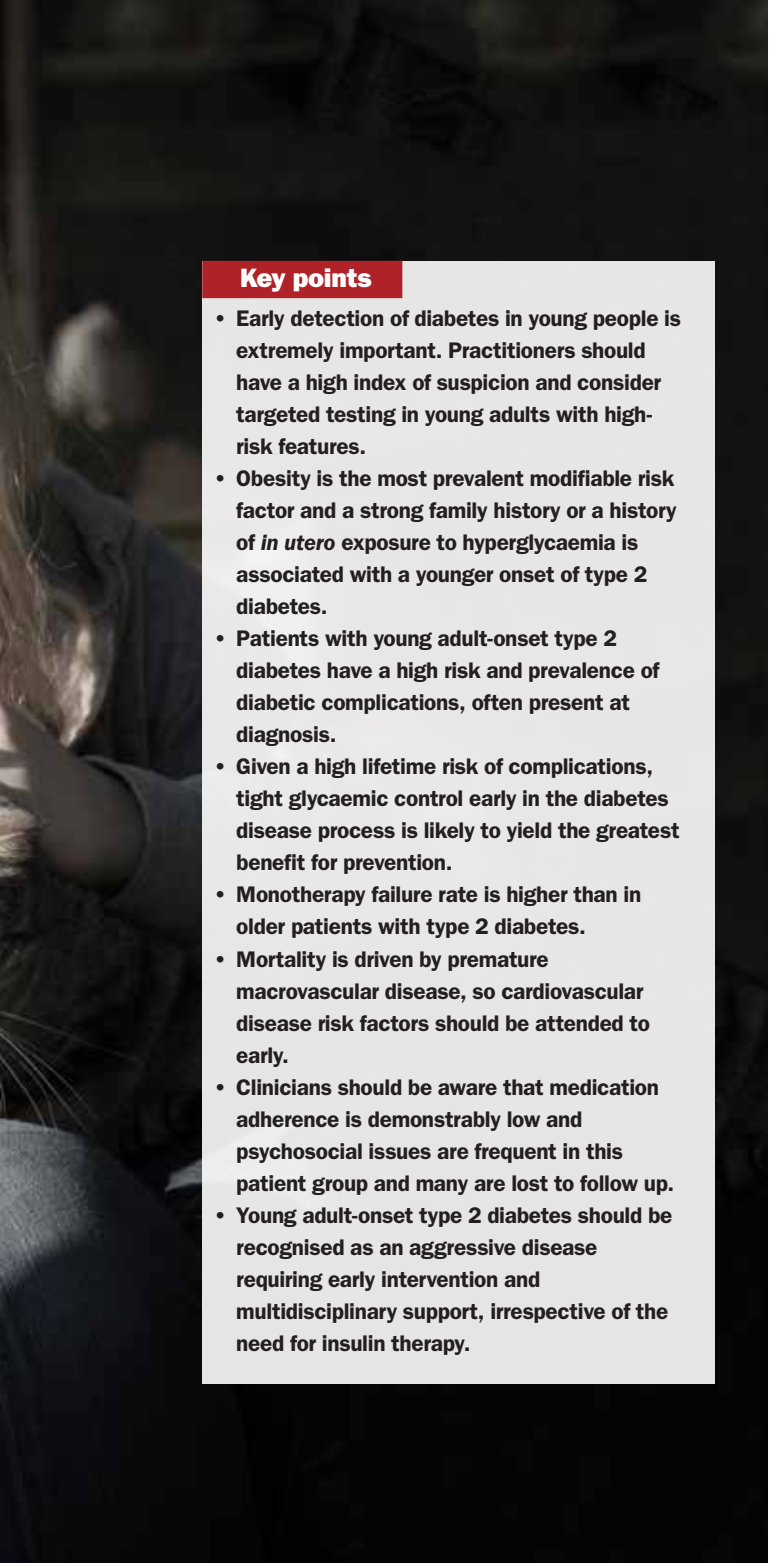
Risk factors

The risk factors for developing type 2 diabetes at a younger age are similar to those for older adults. Obesity is the most prevalent modifiable risk factor. A strong family history and exposure to a hyperglycaemic uterine environment from maternal diabetes are also associated with the development of type 2 diabetes at a younger age.[3] Although early detection of diabetes in the young is extremely important, general screening is unlikely to be cost effective. Practitioners should have a high index of suspicion and consider targeted testing in young adults with high-risk features (see the Box).[4]



Key points

- **Early detection of diabetes in young people is extremely important. Practitioners should have a high index of suspicion and consider targeted testing in young adults with high-risk features.**
- **Obesity is the most prevalent modifiable risk factor and a strong family history or a history of *in utero* exposure to hyperglycaemia is associated with a younger onset of type 2 diabetes.**
- **Patients with young adult-onset type 2 diabetes have a high risk and prevalence of diabetic complications, often present at diagnosis.**
- **Given a high lifetime risk of complications, tight glycaemic control early in the diabetes disease process is likely to yield the greatest benefit for prevention.**
- **Monotherapy failure rate is higher than in older patients with type 2 diabetes.**
- **Mortality is driven by premature macrovascular disease, so cardiovascular disease risk factors should be attended to early.**
- **Clinicians should be aware that medication adherence is demonstrably low and psychosocial issues are frequent in this patient group and many are lost to follow up.**
- **Young adult-onset type 2 diabetes should be recognised as an aggressive disease requiring early intervention and multidisciplinary support, irrespective of the need for insulin therapy.**

What type of diabetes is it?

It can be challenging to differentiate between type 1 and type 2 diabetes on clinical grounds; age is no longer a useful guide and obesity is now seen increasingly in type 1 diabetes. The common clinical features are listed in the Table.[5] Most cases of young adult-onset type 2 diabetes present with obesity and are asymptomatic or mildly symptomatic without weight loss. Confusingly, diabetic ketoacidosis, a classic manifestation of type 1 diabetes, can also be seen in young adult-onset type 2 diabetes.[6] Insulin therapy should be initiated urgently in patients with acute metabolic derangement although those with type 2 diabetes may not require ongoing insulin therapy, but this may take some months to clarify.

Tests may be helpful to distinguish between type 1 and type 2 diabetes. In patients with type 2 diabetes, C-peptide levels are often elevated indicating substantial residual insulin secretory capacity. The presence of beta-cell autoimmune markers, such as islet-cell antibodies or glutamic acid decarboxylase antibodies suggest a contributing autoimmune aetiology. About 10% of patients with clinically apparent type 2 diabetes have antibodies present but may not require insulin therapy for some time.[7] There have been multiple terms used to describe this condition including 'latent autoimmune diabetes in adults'.[8] For such patients who are not already commenced on insulin, ongoing clinical follow up is important.

An alternative consideration in young adults is a type of monogenic diabetes known as 'maturity-onset diabetes of the young' (MODY), caused by a single gene abnormality. It is characterised by an autosomal dominant inheritance pattern and continued secretion of endogenous insulin. MODY is rare, but recognition is important because cases are often misdiagnosed as type 1 or type 2 diabetes and treated inappropriately.[9] Genetic testing is available and suggestive features are given in the Table. A full discussion on MODY is beyond the scope of this article, but is reviewed elsewhere.[10]

Complications in young adult-onset type 2 diabetes

Diabetes duration is one of the strongest predictors for the development of diabetes complications, therefore patients with young adult-onset type 2 diabetes have a high lifetime risk of complications. There may also be a greater inherent susceptibility to complications in youth.[11] Alarmingly, and in contrast to the situation in type 1 diabetes, complications are often present early, even at diagnosis. Patients with young adult-onset type 2 diabetes have higher rates of albuminuria and neuropathy, and similar rates of retinopathy compared with age-matched patients with type 1 diabetes.[12,13] Therefore, screening for complications should start at diagnosis, regardless of their young age. There is also a high prevalence of cardiovascular risk factors including dyslipidaemia, hypertension and albuminuria evident as early as the teenage years. Progression is as rapid, if not more so than, as in older adults with type 2 diabetes.

Mortality

Of great concern is recent evidence of a twofold increase in mortality risk in patients with young adult-onset type 2 diabetes compared with those with type 1 diabetes, despite a similar age of onset.[12] Most of these deaths were due to premature cardiovascular disease, some occurring as early as the third decade of life. It is important to recognise the potentially poor outcomes for this patient group, regardless of the need for insulin therapy.

High-risk characteristics to prompt screening for type 2 diabetes in young adults

Diabetes screening of asymptomatic young adults is suggested for those who are overweight (BMI ⩾25 kg/m^2, or lower for some ethnicities) and have one of the following additional risk factors:

- physical inactivity
- family history of type 2 diabetes in a first-degree relative
- high-risk race or ethnicity (e.g. Asian, Indian, Aboriginal, African American, Pacific Islander)
- previous gestational diabetes
- signs or conditions associated with insulin resistance: acanthosis nigricans, hypertension, dyslipidaemia, polycystic ovarian syndrome, previous dysglycaemia or cardiovascular disease.

Continue testing at least at three-year intervals or more frequently if warranted by the clinical picture.

Adapted from American Diabetes Association. Standards of Medical Care in Diabetes. Diabetes Care 2014; 37: S14-80.[4]

Management

Management of glycaemia

Given the high lifetime risk of complications in patients with young adult-onset type 2 diabetes, tight glycaemic control early in the diabetes disease process is likely to yield the greatest benefit for prevention. Accordingly, in adults more stringent targets have been recommended for those with long life expectancy.[14] Target HbA_{1c} levels of 6.0% (42 mmol/mol) or less are generally recommended for young adults with diabetes of short duration and no clinical cardiovascular disease who are being treated with lifestyle measures and metformin.[15] A higher individualised HbA_{1c} target may be more appropriate in people with comorbidities and higher hypoglycaemia risk.

Lifestyle management is important but not enough

Patients with newly diagnosed young adult-onset type 2 diabetes should be started on an intensive lifestyle modification program incorporating healthy eating and regular physical activity. The optimal lifestyle modifications have not been well established but limiting screen time and high calorie beverages have been recommended for adolescents and would be relevant to the young adult population as well.[16] Although lifestyle management is the cornerstone of treatment, studies suggest that in youth only about 10% can achieve adequate metabolic control with lifestyle measures, even with weight loss.[16]

Pharmacological management

The recommendation for the early use of metformin from the time of diagnosis is based on the low success rate with diet and exercise alone in youth, and metformin remains first-line therapy in this group. The results of the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study, which looked at treatment options for type 2 diabetes, demonstrated a much more aggressive course in youth than in adults, with decreased durability of glycaemic control with metformin monotherapy and more rapid deterioration in beta-cell function as compared with adults.[17]

Given the risk of complications and high monotherapy failure rate, clinicians should review patients frequently and guard against therapeutic inertia. Second-line options for young adults include: insulin, sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 agonists and sodium glucose cotransporter-2 inhibitors. The choice of second-line therapy should be individualised and take into account factors such as efficacy, hypoglycaemia risk, weight gain, route of administration and potential teratogenicity. Metformin and insulin are the only antidiabetic agents currently approved by the Australian Therapeutic Goods Administration for use in adolescents. Bariatric

Table. Typical clinical characteristics of type 1 diabetes, type 2 diabetes and maturity-onset diabetes of the young (MODY)[5]

Characteristics	Type 1 diabetes	Type 2 diabetes	MODY
Age of onset	From six months to young adulthood	From puberty onwards	Neonatal and postpubertal
Clinical presentation	Acute and fast	Variable: slow to fast, mild (often insidious) to severe	Variable
Autoimmune	Yes	No	No
Presence of ketosis	Common	Uncommon	Common in neonates with diabetes, otherwise uncommon
Frequency of obesity	Same as population	Higher than population	Same as population
Presence of acanthosis nigricans	No	Yes	No
Percentage of all diabetes in young people	90%	Less than 10% (except in Japan 60 to 80%)	1 to 3%
Percentage with parents with diabetes	2 to 4%	80%	90%

Adapted from Craig ME, et al. Pediatric Diabetes 2009; 10(Suppl 12): 3-12.[5]

surgery has been suggested as an early alternative intervention for patients who are morbidly obese, but currently there is limited data on the long-term outcomes of the procedure in patients with young adult-onset type 2 diabetes.

Management of other cardiovascular risk factors and comorbidities

In view of the risk of premature cardiovascular death in this group of young adults, it follows that cardiovascular risk factors should be attended to early in the disease; however, these risk factors are not being addressed adequately for many young people. Currently, there are few trials examining primary prevention in diabetic populations of this age, so risk-reduction strategies are extrapolated from studies in older adults and any treatment strategies need to be individualised. Assuming that lifestyle interventions and agents such as angiotensin-converting enzyme (ACE) inhibitors and statins are as effective in young adults as in older adults, the message should now be to intervene early to manage hypertension, dyslipidaemia and albuminuria, not waiting till middle age. The Australian Diabetes Society recommends adult targets for blood pressure in the absence of proteinuria of less than 130/80 mmHg, and the primary lipid target in the absence of clinical macrovascular disease of LDL-cholesterol of less than 2.5 mmol/L, although these may be reviewed in the light of more contemporary evidence.[15,18,19] Of course, many agents are contraindicated in pregnancy, and women of childbearing age should be appropriately counselled.

Clinicians should be aware that medication adherence is demonstrably low in young adults and many are lost to follow up. Additionally, given the burden of psychosocial issues associated with a chronic disease in youth, clinicians need to be alert to the possible presence of depression and other coexisting psychological conditions.

A multidisciplinary approach to treatment

Management challenges and information needs in patients with young adult-onset type 2 diabetes are different from older adults with type 2 diabetes or children with type 1 diabetes. Multidisciplinary teams may improve outcomes and GPs are encouraged to maintain contact with specialist centres and enlist other disciplines according to individual patient needs.

Conclusion

The rising prevalence of young adult-onset type 2 diabetes predicts an increasingly common presentation to the GP. Recognition of high-risk individuals will aid early detection. Young adult-onset type 2 diabetes should be recognised as an aggressive disease requiring early intervention and multidisciplinary support, irrespective of the need for insulin. **ET**

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

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