Management of type 1 diabetes

Type 1 diabetes and metabolic syndrome: The special risks of "double diabetes"

Adrian Scott
Consultant Physician in Diabetes and General Medicine, Northern General Hospital, Sheffield

I've argued for some time that, from the patient's perspective, having type 1 diabetes is one of the most demanding long-term conditions. For many patients, their mantra may be "Forget empowerment – why can't my doctor sort out my diabetes?".

Well, imagine you have type 1 diabetes and find out that your gene pool is even worse than you thought! Your grandparents (and maybe even a parent) are apple shaped and have type 2 diabetes. You wake up one morning, leap out of bed and step nimbly on to the bathroom scales only to find that your belly is obscuring the view. This, and any other associated feature of the metabolic syndrome, puts you at a much higher risk of macrovascular disease than the person with type 1 diabetes with a normal BMI (or waist circumference).

The paper by Merger and colleagues (summarised alongside) highlights the growing coexistence of the two most common types of diabetes and the impact this has on complication prevalence. Metabolic syndrome in type 1 diabetes is associated with increased prevalence of macro- and microvascular complications, even in those with good glycaemic control. People with "double diabetes" are a special risk population and lifestyle modifications, such as physical exercise, healthy diet and weight reduction, are essential therapeutic strategies in order to improve quality of life and survival.

This often overlooked association deserves more attention, with a particular focus on vascular risk modification. We are likely to see many more people with double diabetes over the next decade or so. ■

Diabetes Care

Beta-cell function: TrialNet analysis

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 After onset of T1D, insulin secretion is generally measured through stimulated C-peptide from a mixed-meal tolerance test (MMTT).

2 To understand the natural history of residual insulin secretion and relate it to other clinical measures of beta-cell secretory function, data from 407 participants in five TrialNet studies were analysed.

3 All had baseline stimulated C-peptide values of ≥0.2 nmol/L from MMTTs. Values from MMTTs, HbA_{1c} and insulin doses were obtained every 6 months for up to 4 years.

4 The percentage of participants with stimulated C-peptide of ≥0.2 nmol/L or detectable C-peptide of ≥0.017 nmol/L diminished over 4 years and was influenced by age. The most rapid decline was seen in the first year.

5 The relationships between C-peptide and HbA_{1c} or insulin doses varied over time and with age. Combined clinical variables, such as insulin-dose adjusted HbA_{1c} (IDAA1C) and the relationship of IDAA1C to C-peptide, were not reliable predictors of C-peptide responses.

6 The authors conclude that C-peptide should remain the primary endpoint in beta-cell function.

Hao W, Gitelman S, DiMeglio LA et al (2016) Fall in C-peptide during first 4 years from diagnosis of type 1 diabetes: variable relation to age, HbA_{1c} and insulin dose. *Diabetes Care* **39**: 1664–70

Diabetes Res Clin Pract

Prevalence of double diabetes in T1D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓✓

1 Autoimmune T1D is often thought of as being distinct from metabolic syndrome (MS) and T2D, where insulin resistance and a relative insulin deficiency are the key features.

2 There are increasing numbers of people with T1D presenting with signs of MS, such as abdominal obesity, arterial hypertension and dyslipidaemia. The combined presentation of features of T1D and T2D is sometimes referred to as "double diabetes" (DD).

3 In this cross-sectional study, the data of 31 119 adults with T1D from the DPV registry in Germany were analysed. Of these, 7926 (25.5%) met the criteria for DD. A subgroup of people with well-controlled diabetes (HbA_{1c} <53 mmol/mol [7%]) was also identified.

4 People with DD showed a significantly higher prevalence of macrovascular disease than those without DD (8% vs 3%; $P<0.0001$). Although less pronounced, this effect remained highly significant in those with well-controlled diabetes (2.6% vs 1.4%; $P<0.0001$).

5 A similar effect was seen with microvascular comorbidities. Retinopathy and nephropathy were significantly more prevalent in the group with DD compared to the group without. This increase was also seen in the subgroup with well-controlled diabetes.

6 The results indicate that MS is an independent risk factor in T1D for the development of macro- and microvascular comorbidities. People with T1D at risk of developing MS should be identified so that therapeutic strategies can be put in place.

Merger SR, Kerner W, Stadler M et al (2016) Prevalence and comorbidities of double diabetes. *Diabetes Res Clin Pract* **119**: 48–56

Diabetes Care

Home use of closed-loop control

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓✓✓

1 The study set out to evaluate the safety and efficacy of the DiAs–USS Virginia artificial pancreas (AP) system in the home environment.

2 Thirty adult participants with T1D from six centres in four countries completed the study. They each spent 0–3 weeks using continuous glucose monitoring (CGM) followed by 2 weeks using both the study pump and CGM to record a baseline. There followed 2 weeks of overnight closed-loop control (CLC) system use and 2 weeks of 24-hours-per-day and 7-days-per-week (24/7) CLC system use.

3 The following glycaemic control parameters were significantly improved during overnight-only CLC compared with baseline: time in hypoglycaemia (1.1% vs 3.0%); time in target (75% vs 61%); and variability (30% vs 36%; all $P<0.001$).

4 There were similar improvements with 24/7 CLC compared with baseline: time in hypoglycaemia (1.7% vs 4.1%); time in target (73% vs 65%); and variability (34% vs 38%; all $P<0.001$).

5 Overnight-only CLC did not reduce hypoglycaemia during the day, whereas 24/7 CLC did provide this additional benefit. There were no serious adverse effects, such as severe hypoglycaemia or diabetic ketoacidosis, during the trial.

6 Use of this portable and wireless hybrid AP system in the home was safe and effective during this trial. Further studies are required to establish safety and clinical outcomes over time. Studies in children and those with hypoglycaemia unawareness are ongoing.

Anderson SM, Raghinaru D, Pinsker JE et al (2016) Multinational home use of closed-loop control is safe and effective. *Diabetes Care* **39**: 1143–50

Diabetes Care

Hypoglycaemia: risk of mortality and CVD

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 These investigators identified a cohort of 10 411 individuals with T1D registered in Taiwan's National Health Insurance Research Database from 1997–2011.

2 Taking all-cause mortality and cardiovascular disease (CVD) incidence as outcomes, the investigators conducted two nested case–control studies within the cohort. The study enrolled 564 individuals who had died from any cause (non-survivors) and 1615 control subjects, as well as 743 CVD case subjects and 1439 control subjects.

3 Compared with the controls, non-survivors and CVD case subjects were more likely to have experienced severe hypoglycaemia. Those with a history of severe hypoglycaemia within 1 year of the outcome were 2.74 times more likely to die and 2.02 times more likely to develop CVD.

4 Although the strength of the association was attenuated, all-cause mortality was still significantly associated with severe hypoglycaemia occurring within 1–3 years (adjusted odds ratio [aOR], 1.94 [95% confidence interval (CI), 1.39–2.71]) and 3–5 years (aOR, 1.68 [95% CI, 1.15–2.44]) of the outcome.

5 However, severe hypoglycaemia occurring 1–3 years and 3–5 years before CVD incidence did not significantly increase the risk of CVD incidence.

6 Clinicians should be aware of the possible risks of all-cause mortality and CVD incidence in the following year after an individual experiences severe hypoglycaemic events.

Lu CL, Shen HN, Hu SC et al (2016) A population-based study of all-cause mortality and cardiovascular disease in association with prior history of hypoglycemia among patients with type 1 diabetes. *Diabetes Care* **39**: 1571–8

Diabetes Care

Autoantibody reversion in TEDDY

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓✓

1 This study examined how frequently beta-cell autoantibodies (a key feature of preclinical T1D) reverted in a cohort of at-risk children and whether reversion has any effect on T1D risk.

2 Participants ($n=8503$) were children up to 10 years of age at genetic high risk for T1D and were enrolled in the TEDDY (The Environmental Determinants of Diabetes in the Young) study. They were monitored for insulin autoantibody, GAD antibody and insulinoma antigen-2 antibodies.

3 Overall, 596 (7%) of the children developed one or more persistent autoantibody.

4 Reversion (two or more negative tests after persistence) was relatively frequent for autoantibodies to GAD65 (19%) and insulin (29%). It was largely restricted to those who had single autoantibodies (24%) and was rare in those who had developed multiple autoantibodies (<1%).

5 Most reversion of single antibodies occurred within 2 years of seroconversion, and was associated with HLA genotype, age and decreasing titre.

6 Children who reverted from single autoantibodies to autoantibody negative had, from birth, a risk for T1D of 0.14 per 100 person-years; those who never developed autoantibodies, 0.06 per 100 person years; and those who remained single-autoantibody positive, 1.8 per 100 person-years.

7 In those who had developed multiple beta-cell autoantibodies, T1D risk remained high even when individual autoantibodies reverted.

Vehik K, Lynch KF, Schatz DA et al (2016) Reversion of beta-cell autoimmunity changes risk of type 1 diabetes: TEDDY study. *Diabetes Care* **39**: 1535–42

"The often overlooked association between T1D and metabolic syndrome deserves more attention, with a particular focus on vascular risk modification."