Diabetes

Prediabetes associated with increased risk of CVD and all-cause mortality

A meta-analysis has shown an association between prediabetes and raised risk of all-cause mortality and incident cardiovascular disease (CVD) in the general population as well as patients with atherosclerotic heart disease.

The investigators searched electronic databases for suitable studies up to April 2020. Prospective cohort studies or post hoc analyses of clinical trials of adults where blood glucose was evaluated at baseline and adjusted risks were reported for all-cause mortality and CVD were included.

Retrospective or case-control studies were excluded, as were studies that did not control for other variables or those that followed up for less than a year.

The American Diabetes Association (ADA), WHO and International Expert Committee all use different thresholds to define where normoglycaemia ends and prediabetes begins (see table 1, below) with the ADA having the lowest threshold. Prediabetes was defined as present or absent for any or all of the definitions listed in table 1, below.

A total of 129 eligible studies were found, giving 10,069,955 individuals for analysis with a median follow-up of 9.4 years. Prediabetes was associated with an increased risk of all-cause mortality and CVD, irrespective of which definition was used. Impaired fasting glucose showed a greater risk than impaired fasting glycaemia. The risk was greater in individuals with preexisting atherosclerotic heart disease.

Compared with normoglycaemia the absolute risk difference (cases per 10,000 person years) conferred by prediabetes in the general population for the following was:

- All-cause mortality 7.36 (95% CI: 9.59-12.51)
- Composite CVD 8.75 (95% CI: 6.41-10.49)
- Coronary heart disease 6.59 (95% CI: 4.53-8.65)
- Stroke 3.68 (95% CI: 2.1-5.26)

For patients with atherosclerotic heart disease respective figures were:

- All-cause mortality 66.19 (95% CI: 38.6-99.25)
- Composite CVD 189.77 (95% CI: 117.97-271.84)
- Coronary heart disease 40.62 (95% CI: 5.42-78.53)
- Stroke 8.54 (95% CI: -32.43 to 61.45)

An association was found between prediabetes diagnosed using any criteria and an increased risk of death or CVD. This gives a small but significant risk elevation in the general population, but a much higher risk in patients with preexisting atherosclerotic heart disease.

The association with stroke is much weaker in both groups, so the role of prediabetes in cerebrovascular disease is less clear.

This was a large study population, but the authors note that lack of individual data may mean that confounders cannot be ruled out. Transition to diabetes as a cause of increased death and disease is another possible influence on the association, as is the inclusion of patients with low blood sugar, thought to be a risk factor for diabetes in a J shaped curve.

'Screening and proper management of prediabetes might contribute to primary and secondary prevention of CVD,' the study authors state.

Prediabetes programmes are currently available in the UK, and the population is offered routine health check screening. This research adds to the evidence that this is an important public health intervention.

DR MATTHEW LOCKYER

Cai X, Zhang Y, Li M et al. Association between prediabetes and risk of all cause mortality and cardiovascular disease: updated meta-analysis. *BMJ* 2020;370:m2297

Table 1

Definitions of normoglycaemia and prediabetes according to different guidelines

Guideline	Normoglycaemia	Prediabetes
ADA	FPG < 5.6 mmol/L (< 100 mg/dL)	IFG-ADA:FPG 5.6-6.9 mmol/L (100-125 mg/dL)
WHO	FPG < 6.1 mmol/L (< 110 mg/dL)	IFG-WHO:FPG 6.1-6.9 mmol/L (110-125 mg/dL)
OGTT 2 hr PG	2 hr PG < 7.8 mmol/L (< 140 mg/dL)	IGT:2 hr PG 7.8-11.1 mmol/L (140-199 mg/dL)
ADA HbA_{1c}	HbA_{1c} < 39 mmol/mol (5.7%)	HbA_{1c} 39-46 mmol/mol (5.7-6.4%)
IEC HbA_{1c}	HbA_{1c} < 42 mmol/mol (6%)	HbA_{1c} 42-46 mmol/mol (6.0-6.4%)

2 hr PG = two hour postload plasma glucose ADA = American Diabetes Association FPG = fasting plasma glucose
HbA_{1c} = glycated haemoglobin IGT = impaired glucose tolerance IEC = International Expert Committee
IFG = impaired fasting glucose IFG-ADA = impaired fasting glucose (ADA definition)
IFG-WHO = impaired fasting glucose (WHO definition) OGTT = oral glucose tolerance test