

Cardiovascular and major journals



Systolic blood pressure in diabetes: Should recommended targets be lowered?

Marc Evans
Consultant Physician, Llandough Hospital, Cardiff

Hypertension guidelines are reviewing their recommended target for systolic blood pressure in diabetes, aiming for below 130 mmHg instead of below 140 mmHg. There is a relative lack of clinical trial data supporting this potential target. Many observational data sets have suggested a J-shaped association between blood pressure and cardiovascular events, although such observations are always limited by confounding comorbidities.

The objective of the study by Adamsson Eryd and colleagues (summarised alongside) was to compare the risk associated with systolic blood pressure that meets current recommendations (that is, below 140 mmHg) with the risk associated with lower levels in patients who have type 2 diabetes and no previous cardiovascular disease. This was a Swedish population-based record-linked cohort study from nationwide clinical registries between 2006 and 2012, with a mean follow-up of 5 years. The study included 187 106 patients who had had type 2 diabetes for at least a year, were aged 75 years or younger, and had no previous cardiovascular or other major disease.

The index date was defined as the first examination after the patient had been included in the diabetes register, with all individuals being followed from the index date until a first event, death or the end of follow-up on 31 December 2013.

The group of patients with the lowest systolic blood pressure (110–119 mmHg) had a significantly lower risk of non-fatal acute myocardial infarction (adjusted hazard ratio, 0.76; 95% confidence interval, 0.64–0.91; $P=0.003$), total acute myocardial infarction (0.85; 0.72–0.99; $P=0.04$), non-fatal cardiovascular disease (0.82; 0.72–0.93; $P=0.002$), total cardiovascular disease (0.88;

0.79–0.99; $P=0.04$), and non-fatal coronary heart disease (0.88; 0.78–0.99; $P=0.03$) compared with the reference group (130–139 mmHg). Furthermore, there was no indication of a J-shaped relation between systolic blood pressure and any of the endpoints, with the exceptions of heart failure and total mortality. A secondary analysis illustrated a J-shaped association between systolic blood pressure and cardiovascular events in patients with established cardiovascular disease, with an apparent risk inflection at a systolic blood pressure <130 mmHg.

This study supports, therefore, the potential benefit of reducing systolic blood pressure well below 130 mmHg in people with type 2 diabetes and no established comorbidities and, as such, could inform treatment paradigms with respect to blood pressure targets in type 2 diabetes. Its main strength is the large number of participants, including patients from a nationwide diabetes register, with a high participation rate evaluating data derived from routine practice. This study did not evaluate the effect of blood pressure variations during the study period and, importantly, did not include patients >75 years of age. Thus, it cannot inform on blood pressure management in elderly patients with type 2 diabetes.

In summary, this population-based study demonstrated that systolic blood pressure levels well below currently advocated targets were associated with reduced cardiovascular risk in patients with type 2 diabetes in a primary prevention setting. Furthermore, it also highlights that any potential association between low blood pressure and increased mortality is likely to be caused by concomitant disease rather than antihypertensive treatment. ■

BMJ

T2D without CVD: BP recommendations

Readability /////
Applicability to practice /////
WOW! Factor /////

1 Current guidelines recommend a systolic blood pressure (SBP) target of below 140 mmHg for people with T2D, as evidence supporting the previous target of below 130 mmHg was inconclusive. Studies have indicated a J-shaped relationship between blood pressure and cardiovascular events, with an increased risk at the highest and lowest levels.

2 This study compared the risk associated with the current recommendations with that associated with the lower levels in patients with T2D and no previous cardiovascular disease (CVD) or other major disease.

3 Individuals from the Swedish national diabetes register meeting the criteria ($n=187\ 106$) were assigned to six groups according to SBP achieved and followed for a mean of 5.0 years.

4 The group with the lowest SBP (110–119 mmHg) was associated with a significantly lower risk of non-fatal myocardial infarction, total acute myocardial infarction, non-fatal CVD, total CVD and non-fatal coronary heart disease than the reference group (130–139 mmHg).

5 There was no evidence of a J-shaped relationship between SBP and the endpoints, other than for heart failure and total mortality. However, a secondary analysis did show such a relationship when individuals who had previous disease were included.

6 The association between low SBP and increased mortality could be caused by concomitant disease rather than antihypertensive treatment.

Adamsson Eryd S, Gudbjörnsdóttir S, Manhem K et al (2016) Blood pressure and complications in individuals with type 2 diabetes and no previous cardiovascular disease: national population based cohort study. *BMJ* **354**: i4070

Int J Cardiol

Retinopathy and atrial fibrillation risk

Readability ★★★★
 Applicability to practice ★★★★
 WOW! Factor ★★★★

- 1 People with T2D have a 40% increased risk of developing atrial fibrillation (AF) compared to those without diabetes.
- 2 The impact of diabetic retinopathy (DR) on the risk of AF is controversial. These authors evaluated the association between DR and the incidence of AF in a population-based cohort study.
- 3 Using a Korean register, 40 500 adults with T2D but without AF were identified. From screening codes, participants were classified as being without DR (non-DR; $n=30\,178$), with DR (DR; $n=8920$) or with proliferative DR (PDR; $n=1402$). Baseline comorbidities were also evaluated.
- 4 During a mean follow-up of 5.9 years, 1261 people (3.1%) developed AF. Those with DR and PDR were more likely to have a higher incidence of AF than those without DR ($P<0.001$), and there was a positive, graded relationship between increasing severity of DR and incidence of AF.
- 5 Adjusted hazard ratios (HRs) for AF in the DR and PDR groups were 1.14 (95% confidence interval [CI], 1.00–1.30) and 1.46 (95% CI, 1.13–1.87) compared to the non-DR group.
- 6 End-stage renal disease (ESRD) was an independent predictor of the development of AF. The risk of AF increased in those with DR and ESRD (HR, 2.39; 95% CI, 1.31–3.96; $P<0.001$) and in those with PDR and ESRD (HR, 3.59; 95% CI, 1.96–5.97; $P<0.001$).
- 7 The authors conclude that physicians should monitor AF carefully in this population because of the associated risk of stroke.

Lee SR, Choi EK, Rhee TM et al (2016) Evaluation of the association between diabetic retinopathy and the incidence of atrial fibrillation: a nationwide population-based study. *Int J Cardiol* **223**: 953–57

JAMA

Glucose-lowering drugs in T2D: a meta-analysis

Readability ★★★★
 Applicability to practice ★★★★
 WOW! Factor ★★★★

- 1 American Diabetes Association (ADA) guidelines for T2D recommend metformin as first-line treatment, followed by addition of a second drug (often a sulfonylurea [SU]) if glycaemic control is not achieved and, when control is no longer sustained, triple therapy with two drugs added to metformin.
- 2 The aim of this systematic review with network meta-analysis was to establish the comparative effects of glucose-lowering strategies for T2D on mortality and cardiovascular (CV) events.
- 3 A total of 301 randomised clinical trials (1 417 367 patient-months) were included: 177 of drugs given as monotherapy; 109 of drugs added to metformin (dual therapy); and 29 of drugs added to metformin and SU (triple therapy).
- 4 Analyses found no significant differences in associations between any of nine drug classes as monotherapy, dual therapy or triple therapy with odds of CV or all-cause mortality in adults with T2D.
- 5 Metformin was associated with moderately lower HbA_{1c} levels compared with other drugs, including SUs, thiazolidinediones and dipeptidyl peptidase-4 inhibitors.
- 6 All drugs were estimated to be effective when added to metformin.
- 7 These findings are consistent with ADA recommendations for using metformin as initial treatment for people with T2D. Selection of additional therapies can be based on considerations for the individual.

Palmer SC, Mavridis D, Nicolucci A et al (2016) Comparison of clinical outcomes and adverse events associated with glucose-lowering drugs in patients with type 2 diabetes: a meta-analysis. *JAMA* **316**: 313–24

Diab Vasc Dis Res

Echocardiology and early myocardial impairment in T1D

Readability ★★★★
 Applicability to practice ★★★★
 WOW! Factor ★★★★

- 1 Cardiovascular disease (CVD) is the most common cause of mortality and morbidity in diabetes. The most common risk factor for CVD in T1D is the presence of albuminuria.
- 2 These investigators looked at myocardial function and time-related changes in myocardial function in relation to albuminuria in adults with T1D without known heart disease ($n=1093$) compared to healthy controls ($n=200$).
- 3 Conventional and tissue Doppler echocardiographic measurements were analysed in normoalbuminuria ($n=760$), microalbuminuria ($n=227$) and macroalbuminuria ($n=106$). Advanced echocardiography can detect early, sub-clinical changes.
- 4 In multivariable models, systolic velocity did not differ between individuals with T1D with normoalbuminuria and controls, but was impaired in those with microalbuminuria and macroalbuminuria.
- 5 Diastolic measurements were all significantly impaired in T1D compared with controls.
- 6 Premature myocardial impairment was detected in those with T1D compared to controls, and its severity increased with an increasing degree of albuminuria: 9.2, 17.3 and 41.4 years prematurely in normo-, micro- and macroalbuminuria, respectively.
- 7 The authors conclude that diastolic impairment in people with T1D may be the first marker of future myocardial disease and impaired systolic function.

Jensen MT, Sogaard P, Andersen HU et al (2016) Early myocardial impairment in type 1 diabetes patients without known heart disease assessed with tissue Doppler echocardiography: the Thousand & 1 study. *Diab Vasc Dis Res* **13**: 260–7

“Diastolic impairment in people with type 1 diabetes may be the first marker of future myocardial disease and impaired systolic function.”