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What Blood Pressure Goal in Type-2 Diabetes? Update 2011

P M Nilsson

Abstract: Hypertension in diabetes is a well-known risk factor for cardiovascular diseases that should be taken seriously. Observational studies have shown a more or less linear relationship between systolic blood pressure levels and risk, but this does not correspond with the outcome results of intervention trials to lower blood pressure. In fact, tight blood pressure control has only been shown to be of general benefit in the range of 130–135 mmHg systolic blood pressure, but not below except for stroke prevention. On the other hand, there might even exist an increased risk for coronary heart disease events and cardiovascular mortality at lower ranges based on data from observational studies. This fact, in combination with the increased costs and risk of serious adverse events, cautions clinicians not to lower systolic blood pressure too much in susceptible patients with longer diabetes duration, more comorbidities, and in older age groups. However, we should not lose sight of the challenge that still around half of all patients with type-2 diabetes are not even below the desired minimum goal of 140 mmHg systolic blood pressure. This calls for improved actions to control blood pressure as part of a general strategy to counteract all cardiovascular risk factors in patients with type-2 diabetes. The higher the risk, the more ambitious should be the approach to screen, detect, treat, and monitor these risk factors.

Key words: blood pressure, diabetes, guideline, hypertension, meta-analysis

Kurzfassung: Welcher Blutdruckzielwert ist bei Diabetes mellitus Typ 2 anzustreben? Update 2011. Arterieller Hochdruck ist bei Diabetes ein allseits bekannter Risikofaktor für kardiovaskuläre Erkrankungen und sollte sehr ernst genommen werden. Beobachtungsstudien haben eine mehr oder weniger lineare Beziehung zwischen systolischem Blutdruckniveau und Risiko gezeigt, doch die Ergebnisse von Interventionsstudien zur Senkung des Blutdrucks entsprechen nicht diesen Beobachtungen. Tatsächlich hat eine strikte Blutdruckkontrolle nur bis zu einem Bereich von 130–135 mmHg systolisch einen generellen Nutzen gezeigt, nicht jedoch darunter, ausgenommen für die Vorbeugung gegen Schlaganfall. Andererseits weisen Daten von Beobachtungsstudien darauf hin, dass bei tieferen Druckwerten sogar ein erhöhtes Risiko für koronare Ereignisse und kardiovaskuläre Mortalität bestehen könnte. Dieser Umstand, zusammen mit vermehrten Kosten und erhöhtem Risiko für ernste Nebenwirkungen, sollte Kliniker zurückhalten, bei gefährdeten Patienten mit langer Diabetesdauer, vielen Komorbiditäten und höherem Alter den Blutdruck zu tief zu senken. Wir sollten indessen nicht die Herausforderung übersehen, dass immer noch etwa die Hälfte der Typ-2-Diabetes-Patienten nicht einmal das Minimalziel von 140 mmHg systolisch erreicht. Das ruft nach besseren Strategien der Blutdruckkontrolle als Teil des generellen Managements, bei Typ-2-Diabetikern alle kardiovaskulären Risikofaktoren zu bekämpfen. Je höher das Risiko ist, umso ambitionierter sollten Screening, Entdeckung, Behandlung und Monitoring dieser Risikofaktoren erfolgen. **J Hypertonie 2011; 15 (4): 9–14.**

Schlüsselwörter: Blutdruck, Diabetes, Leitlinie, Hypertonie, Metaanalyse

Introduction

In 1921, the Austrian physician, Karl Hitzenberger (Figure 1), was one of the first to describe the association between elevated blood pressure (BP) and disturbances of glucose metabolism in the finding of hyperglycemia in patients with hypertension based on observations in his clinic in Vienna [1]. This skillful observation has thereafter been repeatedly confirmed in numerous studies describing patients with established type-2 diabetes or in various states of pre-diabetes, or the so-called metabolic syndrome, as reviewed [2]. Patients with type-2 diabetes run an increased cardiovascular risk [3] not only due to hyperglycemia, but to a cluster of other risk factors, most notably dyslipidemia, hypertension, impaired fibrinolysis, and risk of thrombosis. These risk factors should all be addressed by a strategy to reduce modifiable risk factor levels by lifestyle intervention and appropriate drug therapy, as documented in the Steno-2 study [4].

Figure 1. Professor Karl Hitzenberger. Reprinted with kind permission of the Archive of the University of Vienna, Signature 106.I.924.

Elevated blood pressure is of special importance as observational studies have revealed a more or less linear relationship between the height of systolic blood pressure and the risk of coronary heart disease and stroke [5], which has not always been found in intervention studies. The treatment of hypertension in type-2 diabetes is thus of great importance to avoid costly complications and human suffering. The evidence-base for recommending a treatment target for blood pressure control has expanded due to the publication of several new studies and meta-analyses during recent years, which will be summarized and commented upon in this overview.

Tighter BP control in hypertensive patients with type-2 diabetes (by use of several antihypertensive drug classes versus placebo) has been documented to reduce the risk of both micro- and macrovascular disease in the UKPDS [6, 7] as well as in several other intervention studies [8–11]. Most guidelines have so far advocated a treatment target of BP < 130/80 mmHg for patients with type-2 diabetes [12–14], even the 2011 version of the „Medical Treatment Standards“ from the American Diabetes Association (ADA), although with some comments on the need of individualizing the treatment [15].

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However, the recent reappraisal of European guidelines in 2009 from the European Society of Hypertension (ESH) recommends that patients with diabetes should lower their SBP well below 140 mmHg without mentioning a specific lowest target [16], because the lower BP goals (< 130/80 mmHg) recommended for patients with diabetes never really had been achieved in any single large trial and are even more rarely attained in medical practice. This ESH recommendation was also based on the results in some newer trials [17, 18] and *post-hoc* analyses of high-risk hypertensive patients [19, 20], as in the ONTARGET *post-hoc* analyses [21, 22] of high-risk patients (49 % with a previous CHD and 38 % with diabetes) demonstrating a J-shaped risk curve with a nadir of around 130 mmHg for in-treatment SBP and all cardiovascular outcomes except stroke. In the VADT study, a *post-hoc* analysis showed increased cardiovascular risk associated with a lowering of the diastolic blood pressure < 70 mmHg [23].

Evidence from Studies

A summary of the most important studies from recent years and their findings is presented below.

ACCORD-BP

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) BP trial [24] in 4733 high-risk patients with type-2 diabetes (34 % had previous CVD) analysed 2 randomly selected groups, one group assigned to intensive therapy targeting an SBP < 120 mmHg, and another group on standard therapy targeting an SBP < 140 mmHg. Mean SBP after one year was 119 mmHg and 134 mmHg, respectively, and mean follow-up was 4.7 years. The primary composite outcome was non-fatal myocardial infarction, non-fatal stroke, or death from cardiovascular causes. The study investigators found no significant difference between the 2 groups concerning the risk for the primary outcome or in risk for total mortality, with hazard ratios (HR) for intensive therapy of 0.88 (0.73–1.06; p = 0.2) and 1.07 (0.85–1.35; p = 0.5), respectively. However, the risk for the pre-specified secondary endpoint stroke was reduced with intensive therapy, HR 0.59 (0.39–0.89; p = 0.01). Serious adverse events attributed to antihypertensive treatment occurred more frequently (p < 0.001) in the intensive-therapy group – 77 of the 2362 participants (3.3 %) – compared to the standard therapy group – 30 of 2371 (1.3 %).

INVEST

The International Verapamil-Trandolapril Study (INVEST) was a randomized controlled trial in 22,500 patients with hypertension and coronary heart disease (CHD), with the objective to compare the effects of treatment with verapamil – trandolapril or atenolol – hydrochlorothiazide on the risk for CVD. The primary outcome was first occurrence of all-cause mortality, non-fatal myocardial infarction, or stroke, mean follow-up was 2.7 years. A *post-hoc* observational subgroup follow-up analysis of 6400 hypertensive patients with diabetes and CHD has been presented [25], showing a higher risk for the primary endpoint with an SBP ≥ 140 mmHg (outcome rate 19.8 %, adjusted HR 1.46 [1.25–1.71; p < 0.001]), and a similar risk with an SBP < 130 mmHg (outcome rate 12.7 %, adjusted HR 1.11 [0.93–1.32; p = 0.2]), compared to usual control 130–139 mmHg as reference (outcome rate 12.6 %).

NDR-BP

This observational study from the Swedish National Diabetes Register (NDR) of 12,677 patients with type-2 diabetes treated with antihypertensive drugs [26] analysed the effect of SBP levels on risks for fatal/non-fatal CHD, stroke, and CVD, when followed for 5 years from 2002–2007 after exclusion of patients with a history of heart failure. Risk curves of CHD and stroke increased progressively with higher baseline or updated mean SBP across 110–180 mmHg in a Cox regression model, and no J-shaped risk curves were seen at low SBP levels in all patients, or in 2 subgroups without (n = 10,304) or with (n = 2373) a history of CVD. With an updated mean SBP 110–129 mmHg (mean 123 mmHg) as reference, SBP ≥ 140 mmHg (mean 152 mmHg) showed an adjusted HR 1.37 (1.12–1.68) for CHD, 1.86 (1.34–2.59) for stroke and 1.44 (1.21–1.72) for CVD (p = 0.003– < 0.001), while an SBP 130–139 mmHg (mean 135 mmHg) showed a non-significant risk increase for these outcomes. Furthermore, a with baseline SBP 110–129 mmHg, a further SBP reduction from baseline to follow-up was associated with an increase in risks for CHD and CVD, adjusted HR 1.7 (p = 0.002) compared to no further SBP reduction, although this was not seen for stroke. However, with a baseline SBP of ≥ 130 mmHg, strong benefits of further SBP reduction were seen with considerable risk reductions for CHD, stroke, and CVD, adjusted HR 0.5–0.7 (p = 0.02– < 0.001). Similar results have been reported in the ONTARGET *post-hoc* analysis in patients on antihypertensive treatment (38 % with diabetes) with a baseline SBP < 130 mmHg [21, 22], in which cardiovascular mortality was increased with a further SBP reduction from baseline to follow-up (p < 0.001).

The NDR-BP results [26] are in accordance with both ACCORD-BP [24] and the *post-hoc* INVEST [25] studies showing strong benefits in CVD risk with an SBP < 140 mmHg, although no obvious difference in benefits between lower intervals in the SBP range 110–139 mmHg, though it must be taken into account that NDR-BP is an observational study. Thus, these recent studies support the reappraisal of the European guidelines aiming for an SBP well below 140 mmHg [16]. In a further analysis from the NDR study, different statistical methods were applied to illustrate the same data [27, 28]. The conclusion was that some spline statistics (graphs) are maybe not so accurate as to show the data by defined blood pressure intervals because the uncertainty at both ends of the spline curve makes it less reliable and can even be interpreted as an exaggerated graphical illustration, as used in the *post-hoc* analysis of attained blood pressure levels and coronary risk in the Treatment to New Targets (TNT) statin intervention trial [20, 29].

ADVANCE

The Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial [11] was a randomised controlled trial in 11,140 patients with type-2 diabetes, analysing the effect of treatment with a fixed combination of an ACE inhibitor (perindopril) and a thiazide (indapamide) compared to placebo, for the effect on micro- and macrovascular complications, with a mean follow-up of 4.3 years. The SBP was reduced to < 135 mmHg in drug-treated patients, compared with patients on placebo in whom

the SBP remained at approximately 140 mmHg. The primary endpoint was a composite of major macro- and microvascular events, defined as death from cardiovascular disease, non-fatal stroke, or myocardial infarction, and new or worsening renal or diabetic eye disease. The relative risk of the primary endpoint was reduced by 9 %, HR 0.91 (0.83–1.00; p = 0.04). The separate reductions in macro- and microvascular events were similar but not independently significant, while HR for fatal CVD and total mortality were significant, 0.82 (0.68–0.98; p = 0.03) and 0.86 (0.75–0.98; p = 0.03), respectively.

The ADVANCE trial also demonstrated a reduced risk of 18 % (95-% CI: 1–32 %; p = 0.04) for total mortality with a combination of antihypertensive drug treatment and intensive glucose control compared to placebo BP treatment and standard glucose control [30]. The SBP was reduced < 140 mmHg in the combined treatment group, with a difference in an SBP of 7 mmHg and in HbA_{1c} of 0.6 %. Combination treatment reduced the risks of new or worsening nephropathy by 33 % (12–50 %; p = 0.005), new onset of macroalbuminuria by 54 % (35–68 %; p < 0.001), new onset of microalbuminuria by 26 % (17–34 %), and total mortality by 18 % (1–32 %; p = 0.04) [30].

The effects of BP and glucose control were found to be additive in the ADVANCE trial, with no interaction between them. Similar findings of such additive combined effects have also been reported in observational data from UKPDS, the Swedish NDR, the Multiple Risk Factor Intervention Trial [3], and the Diabetes Intervention Study [31]. The UKPDS 75 publication [32] analysed outcome incidences in an adjusted Poisson model in 4320 newly detected patients with type-2 diabetes followed for 10 years, and found that those in the highest HbA_{1c} and the SBP categories (≥ 8 % and ≥ 150 mmHg), compared to those in the lowest category (< 6.0 % and < 130 mmHg), had a relative risk (RR) of 4.1 for fatal/non-fatal myocardial infarction (MI), 12.8 for stroke, and 16.3 for microvascular disease (retinopathy or renal failure). The NDR study [33] found that 2593 patients with type-2 diabetes on tight combined control (median HbA_{1c} and BP 6.5 % and 130/80 mmHg), compared with 2160 patients on adverse control (median 8.1 % and 155/85 mmHg), had significantly reduced risks of fatal/non-fatal CHD and stroke when followed for a mean 5.7 years, adjusted hazard ratio 0.69 (0.55–0.86; p < 0.001) and 0.62 (0.45–0.84; p < 0.001), respectively. Baseline lower BMI and absence of microalbuminuria were associated with tight control. These findings in ADVANCE, UKPDS, and NDR jointly call for a multifactorial approach to improve HbA_{1c}, BP, and other risk factors, as has been proposed in the so-called Steno-2 model [4].

Two New Meta-Analyses from 2011

It is customary to try to collect the evidence for performing a meta-analysis if a controversy exists in clinical science in order to look for results based on the bulk of evidence available. In May 2011, a new meta-analysis was published to investigate the appropriate blood pressure goal in patients with type-2 diabetes, based on extensive searches via PubMed and other databases until October 2010 [34]. Studies were included based on patients with type-2 diabetes mellitus or impaired fasting glucose/impaired glucose tolerance that enrolled at least 100 patients with an achieved SBP of ≤ 135 mmHg in the intensive blood pressure control group and ≤ 140 mmHg in the standard blood pressure control group, had a follow-up of at least one year, and evaluated macro- or microvascular events. Finally, the authors were able to identify 13 randomized clinical trials enrolling 37,736 participants. Intensive blood pressure control was associated with a 10-% reduction in all-cause mortality, odds ratio (OR) 0.90 (95-% CI: 0.83–0.98), a 17-% reduction in stroke, and a 20-% increase in serious adverse effects, but with similar outcomes for other macro- and microvascular (cardiac, renal, and retinal) events compared with standard blood pressure control. The results were similar in a sensitivity analysis using a so-called Bayesian random effects model. More intensive blood pressure control (≤ 130 mmHg) was associated with a greater reduction in stroke, but did not reduce other events.

Meta-regression analysis showed continued risk reduction for stroke to an SBP of < 120 mmHg. However, at levels of < 130 mmHg, there was also a 40-% increase in SAEs with no benefit for other outcomes.

The authors concluded that in patients with type-2 diabetes mellitus/impaired fasting glucose/impaired glucose tolerance, an SBP treatment goal of 130–135 mmHg is acceptable [34].

However, with more aggressive goals (< 130 mmHg), they observed target organ heterogeneity in that the risk of stroke continued to fall, but there was no benefit regarding the risk of other macro- or microvascular (cardiac, renal, and retinal) events, and the risk of SAEs even increased. These facts underscore the importance of a balanced approach to blood pressure control in patients with type-2 diabetes.

In a second recent meta-analysis, estimates of the effects of blood pressure reduction on the risks of myocardial infarction and stroke in diabetic patients were investigated [35]. A number of 73,913 patients with diabetes (295,652 patient years of exposure) were included, randomized in 31 intervention trials. Abstract-retrieved data were used. Overall, experimental treatment reduced the risk of stroke by 9 % (p = 0.006), and that of myocardial infarction by 11 % (p = 0.002). Allocation to more-tight, compared with less-tight, blood pressure control reduced the risk of stroke by 31 %, relative risk (RR) 0.61 (95-% CI: 0.48–0.79), whereas the reduction in the risk of myocardial infarction approached, but did not achieve, significance, odds ratio (OR) 0.87 (95-% CI: 0.74–1.02). In a meta-regression analysis, the risk of stroke decreased by 13 % (95-% CI: 0.05–0.20; p = 0.002) for each 5-mmHg reduction in SBP, and by 11.5 % (95-% CI: 0.05–0.17; p < 0.001) for each 2-mmHg reduction in diastolic blood pressure (DBP).

In contrast, the risk of myocardial infarction did not show any association with the extent of blood pressure reduction (p > 0.20). It was concluded by Reboldi et al that in patients with diabetes protection from stroke increases with the magnitude of blood pressure reduction, but this relation was not seen for myocardial infarction.

The 2 new meta-analyses [34, 35] taken together thus suggest that even if stroke is prevented by lower attained blood pressure levels, this does not involve myocardial infarction or prevention of cardiovascular mortality. As there is a price to be paid regarding increased costs and risk of serious adverse events, it is recommendable to go for a flexible blood pressure goal taking into account significant background factors in each patient for individual evaluation. This often leads to the aiming of a systolic blood pressure goal in the range of 130–135 mmHg in most patients, somewhat higher than recommended in most current guidelines. The inevitable conclusion thus has to be that these guidelines do not reflect the summary of available evidence at present.

Discussion

Even if observational studies show a linear relationship between increasing systolic blood pressure levels and risk of ischemic heart disease [5], this does not mean that a reduction of blood pressure by treatment will show the expected benefits (Table 1). On the contrary, there might even exist a risk of increased risk in some susceptible elderly patients with longer diabetes duration and a number of comorbidities. This should, however, not preclude clinicians from realising that still a very large number of patients with diabetes have not reached an acceptable blood pressure control of < 140 mmHg systolic blood pressure. A high BP ≥ 140/90 mmHg was reported in 29 % of patients with type-1 diabetes and in 46 % of patients with type-2 diabetes in the national register [36]. The frequency was 40 % in a representative sample of patients with diabetes (mean age 59 years, 54 % on oral agents alone, and 17 % on insulin alone) in NHANES 1999–2000 [37]. In a recent report on trends from the NDR, it was shown that even if blood pressure control improved from 2005–2009, still almost half of all patients with established type-2 diabetes is not <140/90 mmHg [38]. This underlines that strong efforts should be carried out in order to reduce this category of patients in poor control.

The ESH statement [16] of an SBP treatment target in patients with type-2 diabetes far below 140 mmHg points to the value of not recommending a specific lowest SBP target which is as yet unproven. ACCORD-BP [24] had a mean SBP of 119 mmHg in those on intensive treatment targeting SBP below 120 mmHg, and ADVANCE [11] had a mean SBP < 135 mmHg with intensive drug treatment. Furthermore, the INVEST *post-hoc* analysis also reported that a subgroup with very tight control of SBP < 110 mmHg had an increased risk of total mortality, HR 2.18 (1.17–4.09; p = 0.02), compared to SBP 125–129 mmHg, adjusting for but not excluding previous heart failure [25]. NDR-BP found an increased risk of CHD, but not of stroke, with a further SBP reduction during follow-up below baseline 110–129 mmHg, excluding previous heart failure [26]. Increased risks of MI, CVD, total mortality, but not of stroke, with very tight SBP control < 110–120 mmHg was recently reported in the *post-hoc* observational analysis of the Treating to New Targets (TNT) trial of 10,003 patients with a history of CHD in the general population [29], a phenomenon that could also be influenced by reversed causality as previous heart failure was adjusted for but only excluded for an ejection fraction < 30 %. A useful clinical approach may be an individualized lowest target well below 140 mmHg, taking into account individual clinical factors and comorbidities of importance. The presence of a history of CVD might be one of these factors, even if NDR-BP [26] showed no sign of a J-shaped risk curve at the lowest SBP levels down to 110 mmHg in 2373 patients with a history of CVD after exclusion of patients with heart failure. It can also be argued that a lower SBP target might be of value in patients ex-

Table 1. Summary of results from recent intervention trials, observational studies, and meta-analyses in patients with combination of type-2 diabetes and hypertension.

Study [Reference]	Participants	Design	Major outcomes
ADVANCE-BP [11]	11,140	RCT	Reduced major micro- and macrovascular events and mortality with SBP < 135 versus ~ 140 mmHg
ACCORD-BP [24]	4733	RCT	No difference in risk of fatal/non-fatal CVD between SBP < 120 and < 140 mmHg
INVEST [25]	6400	*Post-hoc* observational analysis of RCT	No difference in risk of total mortality, non-fatal myocardial infarction, or stroke between SBP < 130 and 130–139 mmHg, but increased risk of total mortality with SBP < 110 versus 125–129 mmHg
ONTARGET-DM [22]	9300	*Post-hoc* observational analysis of RCT	Increased cardiovascular mortality with SBP < 125 mmHg compared to SBP < 130 mmHg
VADT [23]	1791	*Post-hoc* observational analysis of RCT	Increased risk with DBP ≥ 70 mmHg even if SBP was within range recommended by guidelines
NDR-BP [26]	12,677	Observational national study	No difference in risk of fatal/non-fatal CVD between SBP 110–129 and 130–139 mmHg, but increased risk with baseline SBP 110–129 mmHg and further SBP reduction from baseline to follow-up
Meta-analysis I [34]	37,736	Meta-analysis of 13 RCT with DM2 or IFG patients	More intensive SBP control ≤ 130 mmHg was associated with greater reduction of stroke but not with other outcomes. Recommended goal: SBP 130–135 mmHg.
Meta-analysis II [35]	73,913	Meta-analysis of 31 RCT with DM2 patients	Protection of stroke increases with SBP reduction but this was not seen for myocardial infarction

RCT: randomized controlled trial; SBP: systolic blood pressure; CVD: cardiovascular disease; DM2: type-2 diabetes; IFG: impaired fasting glucose

pected to have a higher risk of future stroke than CHD, as ACCORD-BP found a significant risk reduction of 41 % (p = 0.01) for the pre-specified secondary endpoint stroke with intensive therapy aiming at an SBP < 120 mmHg [24]. This could apply to some populations at high risk for stroke, e g, in East Asian countries such as China and Japan.

Combination of Blood Pressure and Glycemic Control

The ADVANCE, UKPDS 75, and NDR data on combined intensified treatment of both SBP and HbA_{1c} underline the importance of a multifactorial approach in order to reduce risks of macro- and microvascular complications, as demonstrated in the Steno-2 study as well [4]. The fact that reductions of both SBP and HbA_{1c} seem to have additive effects on these endpoints points to the need to obtain an HbA_{1c} target of < 7 % generally, although individualised based on e g, comorbid conditions, adults with limited life expectancy, and severe hypoglycemia in patients with advanced disease. The DCCT/EDIC observational study [39] and a recent observational NDR study [36] of patients with type-1 diabetes have demonstrated significant risk reductions of 40 % for fatal/non-fatal CVD and CHD, when groups of baseline HbA_{1c} mean ~ 7 % were compared with groups of HbA_{1c} mean 9 %. The role of intensified glycemic control in type-2 diabetes has been a subject of debate, although the benefits on microvascular complications are well-established for treatment of both type-1 and type-2 diabetes.

Antihypertensive drug treatment has been re-evaluated in recent guidelines [16]. In 2005, a large meta-analysis of available trials [10] showed that in diabetes all major antihypertensive drug classes protect against cardiovascular complications, probably because of the protective effect of BP lowering *per se*. Combination treatment is commonly needed to effectively lower BP. An agent that blocks the renin-angiotensin system should always be included because of the evidence of its superior protective effect against initiation or progression of nephropathy. A diuretic can be added in those with an estimated glomerular filtration rate (GFR) of ≥ 30 ml/min/1.73 m^2, if needed, or a loop diuretic for those with GFR < 30 ml/min/1.73 m^2. The ADVANCE trial used a fixed combination of an ACE inhibitor and a diuretic often on top of pre-existing antihypertensive drugs to produce some further BP reduction [11]. This resulted in benefits on the combined major macro- and microvascular endpoints and mortality. However, ACCOMPLISH [40], including 60 % of diabetic patients among 11,000 individuals, has reported superiority of an ACE inhibitor combined with a calcium antagonist, compared to the combination of an ACE inhibitor and a diuretic, with a relative risk reduction of 20 % (p < 0.001) for the primary endpoint fatal/non-fatal CVD.

The results from recent randomised clinical trials and observational studies support a systolic blood pressure goal in type-2 diabetes well below 140 mmHg, and < 135 mmHg based on data from ADVANCE [27]. This corresponds well with findings from recent meta-analyses [34, 35] stating a goal of 130–135 mmHg for systolic blood pressure [34]. In populations at high risk for stroke, the blood pressure goal could be even lower, although taking into account the increased risks of CHD and total mortality seen with a very tight SBP control < 110 mmHg. In addition, there are benefits with combined blood pressure and glycemic control [41]. In patients with chronic kidney disease, similar conclusions have been drawn, indicating that tight blood pressure control is only of proven benefit in patients with overt albuminuria > 500 mg/day [42]. Future studies could hopefully include a randomized design to compare all 3 systolic blood pressure goals 140, 130, and 120 mmHg. The prediction, however, is that we will have to wait for such studies and therefore the view expressed in this review reflects the current evidence that we will have to live with for a number of years to come.

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Conflict of Interest

None.

Relevanz für die Praxis

Vorrangiges Ziel bei Typ-2-Diabetikern mit Hypertonie sollte es sein, bei möglichst allen Patienten den systolischen Blutdruck dauerhaft auf < 140 mmHg, am besten auf etwa 130–135 mmHg zu senken. Für eine stärkere Blutdrucksenkung (< 130 mmHg) ist kein Nutzen für das kardiovaskuläre Risiko belegt; der bewiesene Benefit für das Schlaganfallrisiko wird durch vermehrte Nebenwirkungen und möglicherweise eine erhöhte kardiovaskuläre Morbidität und Mortalität erkauft.

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