Published in final edited form as:
Curr Cardiovasc Risk Rep. 2013 June ; 7(3): 233–237. doi:10.1007/s12170-013-0301-5.

Type 2 diabetes in older people; the importance of blood pressure control

Ankur Jindal, MD,
Department of Internal Medicine, Division of Hospital Medicine, School of Medicine, Univeristy of Missouri, One Hospital Drive, Coulumbia, MO 65212

Adam Whaley-Connell, DO, and
Departments of Internal Medicine, Nephrology and Hypertension, Endocrinology and Metabolism, Harry S Truman Memorial Veterans Hospital, School of Medicine, University of Missouri, Columbia, MO

James R Sowers, MD
Professor of Medicine, and Medical Pharmacology and Physiology, Departments of Internal Medicine, Endocrinology and Metabolism, Harry S Truman Memorial Veterans Hospital, School of Medicine, University of Missouri, D109 Diabetes Center HSC, One Hospital Drive, Columbia, MO 65212, Phone: (573)884-0769, Fax: (573)884-5530

Ankur Jindal: jindala@health.missouri.edu; James R Sowers: sowersj@health.missouri.edu

Abstract

Diabetes and hypertension often coexist and their coexistence substantially promote cardiovascular disease (CVD) and chronic kidney disease. Control of blood pressure to a level of 140/90 mm Hg in people with diabetes can prevent or at least delay CVD and chronic kidney disease.. In the past many society treatment guidelines have stressed tight blood pressure control (=< 130/80) for people with diabetes. But recommendations for such tight blood pressure control have not been supported by recent large randomized control trials, especially in in elderly. Here we review the recent literature regarding the benefits of blood pressure control in elderly patients with diabetics. We further focus on evidence for specific levels of blood pressure treatment goals, in this population subset..

Keywords

Diabetes; Hypertension; Diabetes complications; Blood pressure control

Introduction

Data from the Centers for Disease Control and prevention (CDC) suggest that in 2010 26.9% of the United States (US) population aged 65 yrs. or older had diabetes. It was previously reported that up to 67% people aged 20 yrs. or older with self-reported diabetes had hypertension [1]. The elderly population with diabetes is a unique subset of our population with an unusually high prevalence of hypertension and high CVD risk. Indeed, in patients with hypertension and type 2 diabetes mellitus (T2DM), the risk for complications increases progressively with age. Data from Action in Diabetes and Vascular disease

Correspondence to: James R Sowers, sowersj@health.missouri.edu.

Disclosure
No potential conflicts of interest relevant to this article were reported.

(ADVANCE) trial suggest that in patients with T2DM and hypertension, the risk for a major macro-vascular or micro-vascular event increases by 24% for every 10 year increase in age [2]. Hypertension is an important and powerful modifiable risk factor of cardiovascular disease (CVD) in patients with diabetes [3]. Some studies suggest the adverse effects of hypertension and T2DM on CVD outcomes might be additive, but this is controversial [4]. For example, results from Multiple Risk Factor intervention Trial (MRFIT) and United Kingdom Prospective Diabetes Study (UKPDS) indicate that blood glucose and blood pressure might have additive effects on the CVD risk of complications in patients with T2DM [5].

Hypertension in diabetics is an area of research interest in this growing subset of our population. Ironically, treatment guidelines for blood pressure control in patients with T2DM still lack robust clinical trial data support. Data regarding management goals for hypertension in elderly diabetics is sparse and inconsistent. Review of data from some of the studies regarding management of hypertension in T2DM shows that even though it might not be the intent; the population cohorts studied had very high proportion of elderly [2,5–12]. This reflects the demographics and disease distribution in the general population and it helps formulate treatment plans for elderly diabetics.

Emerging data has raised new uncertainties regarding treatment goals for hypertension in elderly and elderly diabetics. With the changing demographics of the United States population, specifically aging of the population, there is an increased need for research focused specifically on this growing subset of the population: elderly diabetics with hypertension.

CVD benefits of treatment of hypertension in elderly diabetics

Many studies that contribute to our understanding of the CVD benefits of BP reduction have been conducted in elderly diabetics aged >60 years [2,10,11,13,14]. However, clinical trials have failed to consistently show benefits of blood pressure reduction in the very elderly (e.g. octogenarians), and data from some studies suggests that an inverse relation exists between blood pressure reduction and the risk of death in very elderly [14–17]. Though these findings appear counter intuitive, they have added to clinical outcome uncertainties. More recent studies show benefits of regular evaluation and early treatment of hypertension in those >60 years of age [10,11].

There is a growing body of literature that supports early intervention for management of hypertension in elderly with diabetes, especially in those >60. The literature is inconsistent regarding the target blood pressure parameters. Though the accumulating data points to treatment targets considerably more liberal than those, recommended in the treatment guidelines for adults with diabetes [3]. Data from Systolic hypertension in Europe (Syst-Eur) trial showed that active treatment of isolated systolic hypertension in elderly (older than 60 yrs.), decreased the incidence of stroke by 42% and all CVD complications by 26% [18]. An open label extension of Syst-Eur trial was performed to study the impact of immediate versus delayed treatment of systolic hypertension (target level 150 mmHg) in elderly. In this extension study, the mean age of participants was 69 years, and the data showed early treatment of hypertension in elderly decreased the rates of CVD complications, including stroke. The risk reduction for CVD events, including fatal and non-fatal strokes was greater in elderly with diabetes, than in those without diabetes. Relative risk reduction of 38% in total mortality, 51% in all CVD events, including a 60% reduction in strokes was noted in elderly diabetics with early treatment of hypertension, compared to that observed with delayed treatment. Unexpectedly, risk of death increased slightly in actively treated patients 80 years or older [10].

HYpertension in the Very Elderly Trial (HYVET) was designed to evaluate the benefits and risks of antihypertensive treatment in a subset of elderly population, subjects 80 years and older. Data from this trial showed that treatment of hypertension in elderly with a sustained systolic blood pressure greater than 160, using indapamide alone or in combination with perindopril, to achieve a target blood pressure of 150/80, was associated with decreased mortality from stroke and heart failure. The rate of stroke, heart failure and death from any cause were reduced by 30%, 64%, and 21% respectively with active treatment of hypertension [14]. A one year open label active treatment extension of HYVET was performed. During this extension study, the placebo group from HYVET was started on treatment for hypertension and was followed along with the active treatment group. The risk CVD events became comparable in the two groups, while the total and CVD mortality remained significantly higher in the group assigned to placebo in the original study. Data from this study underscores the importance of early intervention and sustained antihypertensive treatment in non-frail octogenarians with hypertension [11].

Systolic Hypertension in the Elderly Program (SHEP) Trial was designed to study the effects of diuretic based antihypertensive treatment in non-insulin dependent elderly diabetics with Isolated Systolic Hypertension (ISH). The mean age of the cohort was 71 yrs. and the goal SBP in the treatment arm was 140–160 depending on the baseline blood pressure. Analysis of the data showed that treatment of ISH based on SHEP protocol prevented cardiovascular event in 101/1000 and 51/1000 diabetic and non-diabetic participants respectively. Absolute risk reduction for cardiovascular disease (fatal and nonfatal stroke and coronary heart disease) was seen in diabetic as well as non-diabetic elderly, though the reduction was twice as great in diabetics [8]. Diuretic use is known to be associated with an increased occurrence of diabetes. It is unclear if increased incidence of diabetes associated with diuretic use diminishes the cardiovascular benefits of blood pressure control overtime. A follow up study of SHEP participants was designed to answer this question. It was found that the incidence of diabetes was higher in the group actively treated with diuretics, though the diabetes diagnosed during diuretic therapy was comparatively mild. The data showed that development of diabetes during the trial was associated with increased CV and total mortality, in participants on placebo, but not in participants on diuretic therapy. Strong association between chlorthalidone therapy and lower long term CVD and total mortality was also demonstrated in this study [13].

The ADVANCE Trial was designed to answer many critical questions about management of CVD risk factors in diabetes. Data was also collected and analyzed to evaluate the safety and efficacy of blood pressure treatment in elderly with T2DM and the results confirmed that treatment of hypertension, using perindopril and indapamide, in elderly with T2DM is safe and well tolerated. The treatment reduced risk for macro-vascular disease, death and renal events in all studied age groups, but the absolute benefits were progressively greater in older people [2].

Data from the United Kingdom Prospective Study (UKPDS) showed that both macro vascular and micro vascular outcomes improved significantly with more tight blood pressure control, in diabetic patients. Risk of deterioration of visual acuity, retinopathy and development of albuminuria was decreased with sustained treatment of hypertension to achieve relatively tight blood pressure control (goal of 140/90 mm HG [19].

Renal hemodynamics and benefits of blood pressure treatment

The cerebral and renal microcirculations share some similarities. The renal vasculature is a low resistance system, thereby exposing the nephron to the detrimental effects of high upstream pressures. With aging, there is progressive stiffening of aorta leading to increased

pulse pressure, which is directly transferred to kidney arteries as renal vasculature is a low resistance system, and lacks the protection conferred by increased resistance in larger arteries. This exposes the small arteries in kidney to higher circumferential and longitudinal stress. The ability of renal vasculature to withstand such increased stress is compromised in people with diabetes, thus putting them at risk for renal micro-vascular disease [20]. Micro-vascular renal disease can lead to chronic hypoxia, which can further lead to renal interstitial injury and dysfunction [21]. Investigators have studied the effects of American Diabetes Association (ADA) recommended tight glycemic, blood pressure and cholesterol control on progression of diabetic nephropathy in subjects with T2DM and micro albuminuria. They found that intensive blood pressure and glycemic control was associated with remission of micro albuminuria, and such remission was achieved in 35.8% of the 587 studied subjects [22]. Remission of nephropathy in subjects with T1DM or T2DM, with tight blood pressure or glucose control has been reported by many researchers in the recent past [12,22–25]. A longitudinal cohort study was conducted, which enrolled persons with T2DM and normo-albuminuria. During this study a mean SBP 129.3 mm Hg was achieved in these subjects and a strong association was noted between SBP and development of microalbuminuria, leading to the conclusion that new onset microalbuminuria can be delayed with intensive blood pressure management in patients with T2DM [12]. Data from Action to Control Cardiovascular Risk in Diabetes (ACCORD) and ADVANCE trials suggest potential renal benefits of intensive blood pressure control (SBP<120 mm HG), even though such intensive control did not reduce major CVD events compared to less intensive control [22].

Blood pressure goals

Multiple trials and observational studies have shown associations between blood pressure and incidence of cardiovascular and renal adverse events and progression of CKD [23]. Randomized trials do not support the strategy to lower systolic blood pressure below 140 mm Hg in patients with T2DM.

The UKPDS 38 study reported a risk reduction of 32% for death related to diabetes, 44% for stroke, and 37% for microvascular disease in patients with T2DM and hypertension, when tight BP control was achieved compared to less tight control. Over 9 yrs., mean BP of 144/82 was achieved in the tight control group, compared to a mean BP of 154/87 in the less tight control group. The mean age of the participants was 56.4 yrs.(SD 8.1) [19]. Based on a meta-analysis of 31 intervention trials involving 73913 participants with diabetes, investigators concluded that there is progressive reduction in the risk of stroke with progressive reduction in blood pressure in diabetics, though they were unable to find similar relation between blood pressure reduction and risk for myocardial infarction [26]. They further observed that there was a 13% reduction in the risk of stroke with every 5 mmHg reduction in SBP or 2 mm HG reduction in Diastolic Blood Pressure (DBP) [26] Another investigative group performed a meta-analysis and found that intensive blood pressure control (SBP <130 mm HG), compared to standard control SBP < 140 mm Hg might have cerebrovascular benefits in certain high risk groups such as those with diabetes, but the benefit of such aggressive treatment approach for cardiac, renal and retinal outcomes is uncertain [7]. The authors also noted that more intensive blood pressure targets were associated with increased risk of serious adverse events which could necessitate hospitalization or cause permanent disability.

Compared to the blood pressure targets in the trials mentioned previously, lower blood pressure targets were studied in ACCORD BP trial. A total of 4733 participants with a mean age of 62.2 (SD 6.9) were enrolled and assigned to intensive therapy or standard therapy for SBP goals of <120 or <140 respectively. The mean SBP achieved in the 2 groups was 119.3 and 133.5 respectively. Significant benefit in terms of cardiovascular outcome or death from

any cause was not noted with intensive SBP control, though some reduction in rate of total and non-fatal stroke was noted. Small decrease in the rate of strokes with intensive blood pressure control was at a cost of significant increase in serious adverse events, hypokalemia, acute renal failure and episodes of syncope [6].

A post hoc analysis of a cohort of patients with diabetes in the International VerapamilSR-Trandolapril Study (INVEST) led to similar conclusions. It was found that CVD outcomes were not better with tight blood pressure control (SBP <130 mm Hg) compared to usual blood pressure control (SBP of 130–140 mm Hg). These researchers also observed that there was a greater risk for all-cause mortality in tight blood pressure control group [9]. Data from post-trial monitoring of a cohort of UKPDS blood pressure intervention trial suggests that sustained good blood pressure control is required to maintain the outcome benefits achieved with tight blood pressure control. Loss of the intensive blood pressure control was associated with loss of outcome benefits (relative risk reduction for stroke, micro vascular disease, diabetes related death, myocardial infarction) observed in the group assigned to intensive blood pressure therapy [5].

Conclusion

The importance of early detection and appropriate management of blood pressure in elderly patients with diabetes cannot be over emphasized. Studies clearly demonstrate the benefits of blood pressure reduction in elderly diabetics, though target blood pressure parameters are open to debate. The available data regarding target blood pressure parameters in elderly diabetics is inconsistent, and there are significant variations depending on the outcomes studied. Regardless, it might be safe to say that the SBP target should be less than 140 mm HG. Whether the risk benefit ratio of further lowering of the SBP, is acceptable, is questionable. Some studies suggest cerebrovascular and possibly renal benefits of lower SBP targets. Data from a met- analysis of prospective studies involving a total of 1 million participants, 12.7 million person years at risk, suggests that blood pressures greater than 115/75 mm Hg have a strong direct relation to CVD mortality [27].

One of the limitation of studies of treatment of hypertension in elderly patients with hypertension is that the follow up period in these studies might not be long enough to bring forth the desirable effects of more strict blood pressure parameters. Available data indicates that one level might not fit all. At least till we have comprehensive data, to allow more definitive and evidence based recommendations, management decisions should to be tailored, in accordance with patient risk factors and attributes.

Acknowledgments

This research was supported by the NIH (R01 HL73101-01A1 and R01 HL107910-01 to JRS), the Veterans Affairs Merit System 0019 (JRS). The authors would like to thank Brenda Hunter for her assistance in editing the manuscript.

bibliography

1. Centers for disease control and prevention. National diabetes fact sheet: National estimates and general information on diabetes and prediabetes in united states 2011. National diabetes fact sheet. 2011
2. Ninomiya T, Zoungas S, Neal B, Woodward M, Patel A, Perkovic V, Cass A, Cooper M, Grobbee D, Hamet P, Harrap S, et al. Efficacy and safety of routine blood pressure lowering in older patients with diabetes: Results from the advance trial. Journal of hypertension. 2010; 28(6):1141–1149. [PubMed: 20486273]

3. Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR, Holman RR. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United kingdom prospective diabetes study (ukpds: 23). Bmj. 1998; 316(7134):823–828. [PubMed: 9549452]

4. Kengne AP, Patel A, Barzi F, Jamrozik K, Lam TH, Ueshima H, Gu DF, Suh I, Woodward M. Systolic blood pressure, diabetes and the risk of cardiovascular diseases in the asia-pacific region. Journal of hypertension. 2007; 25(6):1205–1213. [PubMed: 17563533]

5. Holman RR, Paul SK, Bethel MA, Neil HA, Matthews DR. Long-term follow-up after tight control of blood pressure in type 2 diabetes. The New England journal of medicine. 2008; 359(15):1565–1576. [PubMed: 18784091]

6*. Cushman WC, Evans GW, Byington RP, Goff DC Jr, Grimm RH Jr, Cutler JA, Simons-Morton DG, Basile JN, Corson MA, Probstfield JL, Katz L, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. The New England journal of medicine. 2010; 362(17):1575–1585. This study showed that targeting SBP 120 compared to SBP 140 in patients with T2DM, diidnot improve cardiovascular outcome. [PubMed: 20228401]

7. Bangalore S, Kumar S, Lobach I, Messerli FH. Blood pressure targets in subjects with type 2 diabetes mellitus/impaired fasting glucose: Observations from traditional and bayesian random-effects meta-analyses of randomized trials. Circulation. 2011; 123(24):2799–2810. [PubMed: 21632497]

8. Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, Camel G, Davis BR, Frost PH, Gonzalez N, Guthrie G, et al. Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. Systolic hypertension in the elderly program cooperative research group. JAMA : the journal of the American Medical Association. 1996; 276(23):1886–1892. [PubMed: 8968014]

9. Cooper-DeHoff RM, Gong Y, Handberg EM, Bavry AA, Denardo SJ, Bakris GL, Pepine CJ. Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease. JAMA : the journal of the American Medical Association. 2010; 304(1): 61–68. [PubMed: 20606150]

10. Staessen JA, Thijisq L, Fagard R, Celis H, Birkenhager WH, Bulpitt CJ, de Leeuw PW, Fletcher AE, Forette F, Leonetti G, McCormack P, et al. Effects of immediate versus delayed antihypertensive therapy on outcome in the systolic hypertension in europe trial. Journal of hypertension. 2004; 22(4):847–857. [PubMed: 15126928]

11*. Beckett N, Peters R, Tuomilehto J, Swift C, Sever P, Potter J, McCormack T, Forette F, Gil-Extremera B, Dumitrascu D, Staessen JA, et al. Immediate and late benefits of treating very elderly people with hypertension: Results from active treatment extension to hypertension in the very elderly randomised controlled trial. Bmj. 2011; 4(344) Data from this study highlight the importance of early intervention and sustained antihypertensive treatment in very elderly.

12. Tu ST, Chang SJ, Chen JF, Tien KJ, Hsiao JY, Chen HC, Hsieh MC. Prevention of diabetic nephropathy by tight target control in an asian population with type 2 diabetes mellitus: A 4- year prospective analysis. Archives of internal medicine. 2010; 170(2):155–161. [PubMed: 20101010]

13. Kostis JB, Wilson AC, Freudenberger RS, Cosgrove NM, Pressel SL, Davis BR. Long-term effect of diuretic-based therapy on fatal outcomes in subjects with isolated systolic hypertension with and without diabetes. Am J Cardiol. 2005; 95(1):29–35. [PubMed: 15619390]

14*. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, et al. Treatment of hypertension in patients 80 years of age or older. The New England journal of medicine. 2008; 358(18):1887–1898. This study stresses that treatmetn of hypertension in people > 80 years is benificial. [PubMed: 18378519]

15. Rastas S, Pirttila T, Viramo P, Verkkoniemi A, Halonen P, Juva K, Niinisto L, Mattila K, Lansimies E, Sulkava R. Association between blood pressure and survival over 9 years in a general population aged 85 and older. J Am Geriatr Soc. 2006; 54(6):912–918. [PubMed: 16776785]

16. van Bemmel T, Woittiez K, Blauw GJ, van der Sman-de Beer F, Dekker FW, Westendorp RG, Gussekloo J. Prospective study of the effect of blood pressure on renal function in old age: The leiden 85-plus study. J Am Soc Nephrol. 2006; 17(9):2561–2566. [PubMed: 16914542]

17. Oates DJ, Berlowitz DR, Glickman ME, Silliman RA, Borzecki AM. Blood pressure and survival in the oldest old. J Am Geriatr Soc. 2007; 55(3):383–388. [PubMed: 17341240]

18. Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhager WH, Bulpitt CJ, de Leeuw PW, Dollery CT, Fletcher AE, Forette F, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The systolic hypertension in europe (syst-eur) trial investigators. Lancet. 1997; 350(9080):757–764. [PubMed: 9297994]

19. Uk prospective diabetes study group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: Ukpds 38. Bmj. 1998; 317(7160):703–713. [PubMed: 9732337]

20. O'Rourke MF, Safar ME. Relationship between aortic stiffening and microvascular disease in brain and kidney: Cause and logic of therapy. Hypertension. 2005; 46(1):200–204. [PubMed: 15911742]

21. Uzu T, Kida Y, Shirahashi N, Harada T, Yamauchi A, Nomura M, Isshiki K, Araki S, Sugimoto T, Koya D, Haneda M, et al. Cerebral microvascular disease predicts renal failure in type 2 diabetes. J Am Soc Nephrol. 2010; 21(3):520–526. [PubMed: 20110380]

22*. Hsieh MC, Hsieh YT, Cho TJ, Chen JF, Lin SD, Chen HC, Tu ST. Remission of diabetic nephropathy in type 2 diabetic asian population: Role of tight glucose and blood pressure control. Eur J Clin Invest. 2011; 41(8):870–878. This study indicates that there is a potential for remission of diabetic nephropathy with tight blood pressure and glycemic control. [PubMed: 21299554]

23. Uzu T, Kida Y, Yamauchi A, Kume S, Isshiki K, Araki S, Koya D, Haneda M, Kashiwagi A, Maegawa H, Kikkawa R. The effects of blood pressure control levels on the renoprotection of type 2 diabetic patients without overt proteinuria. J Am Soc Hypertens. 2012; 6(2):124–131. [PubMed: 22197317]

24. Gaede P, Tarnow L, Vedel P, Parving HH, Pedersen O. Remission to normoalbuminuria during multifactorial treatment preserves kidney function in patients with type 2 diabetes and microalbuminuria. Nephrol Dial Transplant. 2004; 19(11):2784–2788. [PubMed: 15328385]

25. de Galan BE, Perkovic V, Ninomiya T, Pillai A, Patel A, Cass A, Neal B, Poulter N, Harrap S, Mogensen CE, Cooper M, et al. Lowering blood pressure reduces renal events in type 2 diabetes. J Am Soc Nephrol. 2009; 20(4):883–892. [PubMed: 19225038]

26. Reboldi G, Gentile G, Angeli F, Ambrosio G, Mancia G, Verdecchia P. Effects of intensive blood pressure reduction on myocardial infarction and stroke in diabetes: A meta-analysis in 73,913 patients. Journal of hypertension. 2011; 29(7):1253–1269. [PubMed: 21505352]

27. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002; 360(9349):1903–1913. [PubMed: 12493255]