Hypertension in the elderly

Classes of antihypertensive agent:

ACE inhibitors (angiotensin converting enzyme inhibitors) (perindopril, ramipril, captopril, enalapril, lisinopril, trandolapril, quinapril)
Alpha blockers (doxazosin)
Alpha receptor agonists (clonidine, methyldopa, guanfacine)
ARBs (angiotensin receptor blocker) (candesartan, irbesartan, olmesartan, losartan, valsartan, telmisartan)
Beta blocker (acebutolol, atenolol, sotalol, betaxolol, bisoprolol, carvedilol, nadolol, propranolol, metoprolol, pindolol, timolol, labetalol
CCBs (Calcium Channel Blockers)
1. Dihydropyridine (nifedipine, amlodipine, nicardipine, clevidipine, isradipine, felodipine, nimopidine, nisoldipine)
2. Non-dihydropyridine (verapamil, diltiazem,
Diuretics
1. Loop (furosemide, ethacrynic acid, torsemide, bumetanide
2. Thiazide (hydrochlorothiazide, metolazone, methyclothiazide, indapamide, chlorothiazide, chlorthalidone)
3. Potassium-sparing (spironolactone, amiloride, triamterene)
4. Other (acetazolamide, parnabrom, methazolamide,
Other (reserpine, fenoldopam, phentolamine, aliskiren)

Treatment with antihypertensive agents is beneficial, even in the very elderly

“Results from HYVET (Hypertension in the Very Elderly Trial) showed that, at 2-year follow-up, antihypertensive drug therapy with indapamide, plus perindopril if needed, reduced fatal or nonfatal stroke by 30%, fatal stroke by 39%, all-cause mortality by 21%, cardiovascular death by 23%, and heart failure by 64%. These results indicate that hypertensive patients aged 80 years and older should be treated with antihypertensive drugs.” {Aronow, 2008, Nat Clin Pract Cardiovasc Med, 5, 514-5}
Treatment of persons over 80 who had sustained systolic BP of 160 mm Hg or higher to a target BP of 150/80 mm Hg led to significant reductions in strokes, death, and heart failure {Beckett et al., 2008, N Engl J Med, 358, 1887-98}
In the Syst-Eur trial, patients over 60 with isolated systolic hypertension (blood pressure when seated of 160-219 mm Hg systolic and below 95 mm Hg diastolic) were treated with up to three drugs to reduce systolic BP by at least 20 mm Hg to reach a value below 150 mm Hg. Active treatment reduced incidence of dementia by 50%, compared to placebo, during a median followup by ITT. In the active treatment group, BP decreased by 8.3 mm Hg systolic and 3.8 mm Hg diastolic. On average, MMSE scores did not change in either group. {Forette et al., 1998, Lancet, 352, 1347-51}

However, overall mortality is not improved

A meta-analysis of outcomes of treatment with antihypertensive drugs for patients aged 80 and over found that treatment prevented strokes and heart failure, but did not reduce mortality {Gueyffier et al., 1999, Lancet, 353, 793-6}

Mortality may be higher with low as well as high BP

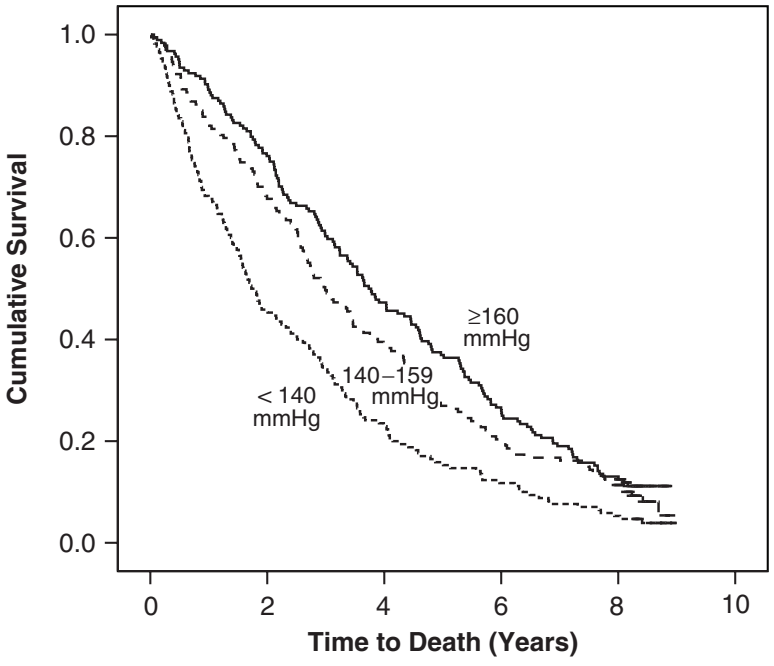
"In the oldest old, high blood pressure is not a risk factor for mortality, irrespective of a history of hypertension. Blood pressure values below 140/70 mmHg are associated with excess mortality." {van Bemmel et al., 2006, J Hypertens, 24, 287-92}

"A recent study of elderly veterans {Oates et al., 2007, J Am Geriatr Soc, 55, 383-8} found a higher mortality rate among patients aged >80 years with lower BP, raising concern about the advisability of aggressive BP targets in the oldest-old, although the cohort design may have led to unmeasured confounders that influenced the result." {Bushnell and Colon-Emeric, 2009, Drugs Aging, 26, 209-30}

"In men aged 75 and over low diastolic blood pressure was associated with the greatest all cause (p=0.04) and cardiovascular (p=0.02) mortality and higher diastolic blood pressure predicted survival." {Langer et al., 1989, BMJ, 298, 1356-7}

"In a cohort of very old, hypertensive veterans, in subjects with controlled BPs, subjects with lower BP levels had a lower 5-year survival than those with higher BPs. This suggests that clinicians should use caution in their approach to BP lowering in this age group." {Oates et al., 2007, J Am Geriatr Soc, 55, 383-8}. The article notes that most of these male vets were on antihypertensive medication.

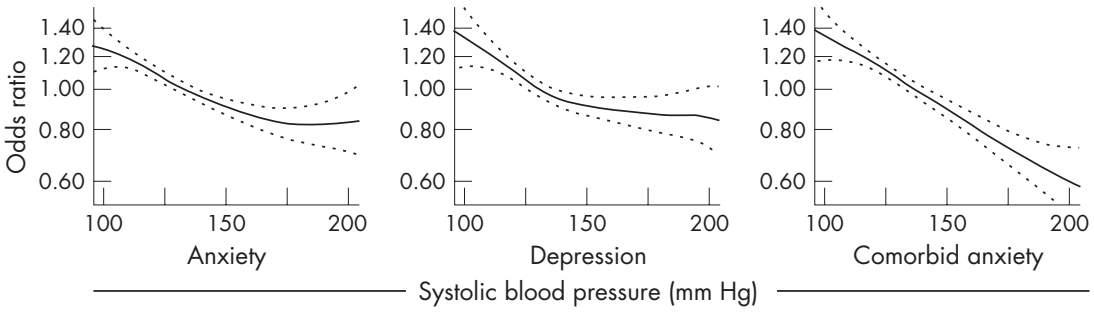
A study of BP and mortality in people aged 85 and older found that over 9 years of followup, low SBP was associated with risk of death after adjusting for age, sex, functional status, and coexisting diseases {Rastas et al., 2006, J Am Geriatr Soc, 54, 912-8}



Low BP and depression

"findings support the existence of a link between low blood pressure and higher levels of depressive symptomatology, and also a range of somatic and psychosocial symptoms." {Stroup-Benham et al., 2000, J Am Geriatr Soc, 48, 250-5}

A cross-sectional population-based study including 60,799 men and women aged 20-89 years who filled in the Hospital Anxiety and Depression Scale, showed that lower blood pressures were associated with higher levels of anxiety, depression, and comorbid anxiety and depression. Physical impairment, smoking, and angina influenced these associations marginally, whereas stroke, MI, use of antihypertensives, and BMI had no influence {Hildrum et al., 2007, J Epidemiol Community Health, 61, 53-8}.



Low BP and cognition

"Older people taking CCBs were significantly more likely than those using other agents to experience cognitive decline."

Characteristic	Unadjusted OR (and 95% CI)	Adjusted OR (and 95% CI)
β-Blocker (reference group)	1.00	1.00
ACE inhibitor	1.54 (0.50–4.74)	1.36 (0.41–4.55)
Diuretic or other antihypertensive	1.49 (0.55–4.00)	1.45 (0.51–4.14)
Nifedipine	1.51 (0.44–5.24)	1.94 (0.52–7.27)
Diltiazem or verapamil	2.60 (0.94–7.22)	3.72 (1.22–11.36)

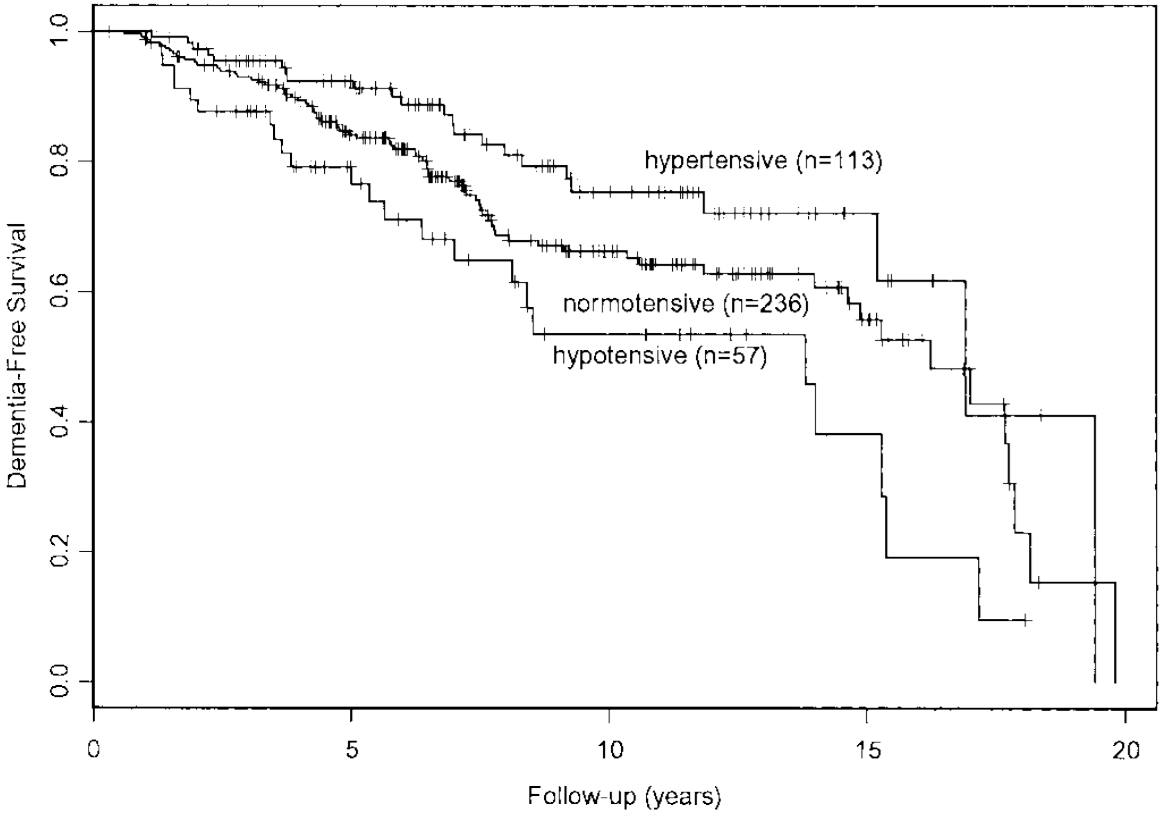
*Obtained from multivariate logistic regression model, adjusted for age, sex, use of other drugs, history of stroke or diabetes, cardiac symptoms and diastolic blood pressure.
†Defined as a decrease in 3MS score of 10 points or more.

{Maxwell et al., 1999, CMAJ, 161, 501-6}

A study of 385 individuals (2/3 female) average age 83, looked at systolic blood pressure (SBP) and MMSE scores over 4 years of followup. A medical history of arterial hypertension was associated with lower MMSE scores and a higher prevalence of dementia and cognitive decline at baseline. However, intact cognition through the

observation period was associated with higher baseline SBP. This relationship also remained when the frailty of aging subjects, indicated by remaining time to death, was taken into account. Conclusions: Lower SBP in the oldest old is associated with an increased risk of cognitive impairment even after adjustment for compromised vitality. {Nilsson et al., 2007, Aging Clin Exp Res, 19, 41-7}
In a study of Nigerian elderly hypertensive patients, diastolic blood pressure was found to correlate negatively with cognitive performance {Imarhiagbe et al., 2005, Afr J Med Med Sci, 34, 269-73}
The findings in the hypertension/cognition debate have been reviewed {Birns and Kalra, 2009, J Hum Hypertens, 23, 86-96}, who provide an explanation for the physiology involved, and conclude: “The results of cross-sectional studies investigating the relationship between BP and cognition showed conflicting relationships with positive, negative and J- and U-shaped associations. The majority of longitudinal studies demonstrated elevated BP to be associated with cognitive decline and a small number of randomized controlled trials demonstrated heterogeneous effects of BP lowering on cognitive function. The same researchers also reviewed 16 randomized, controlled trials involving a total of 19,501 subjects, which looked at the effects on cognition of blood pressure reduction {Birns et al., 2006, J Hypertens, 24, 1907-14}. “Modest reductions in blood pressure (< 5/3 mmHg) in 13,860 subjects were associated with improvements in Mini Mental State Examination score [weighted mean difference (WMD) = 0.19; 95% confidence interval (CI) = 0.19–0.19] and performance on immediate (WMD = 0.62; 95% CI = 0.21–1.02) and delayed (WMD = 0.67; 95% CI = 0.23–1.11) logical memory tasks. However, studies in 2380 subjects that included tests of perceptual processing and learning capacity (trail making test-A, paired associated learning test) showed impaired performance (WMD = -1.12 s; 95% CI = -1.22 to -1.02 and WMD = -0.04; 95% CI = -0.04 to -0.04) on these tests.
BACKGROUND: The role of blood pressure (BP) as a risk factor for dementia is complex and may be age dependent. In very old individuals, low BP might increase risk for dementia, perhaps by reducing cerebral perfusion pressure. METHODS: The association between BP and dementia was examined in the Bronx Aging Study, a prospective study of 488 community-dwelling elderly individuals over age 75, dementia-free at baseline (1980 to 1983) and followed at 12- to 18-month intervals. Subjects with baseline BP and with at least one follow-up visit were included (n = 406). Incident dementia was diagnosed using the criteria of the Diagnostic and Statistical Manual of Mental Disorders (3rd rev. ed.). RESULTS: Over 21 years (median 6.7 years), 122 subjects developed dementia (65 Alzheimer's disease [AD], 28 vascular dementia, 29 other dementias). Relative risk of dementia increased for each 10-mm Hg decrement in diastolic (hazard ratio [HR] 1.20, 95% CI 1.03 to 1.40) and mean arterial (HR 1.16, 95% CI 1.02 to 1.32) pressure, adjusted for age, sex, and education. Low diastolic BP significantly influenced risk of developing AD but not vascular dementia. Upon examination of groups defined by BP, mildly to moderately raised systolic BP (140 to 179 mm Hg) was associated with reduced risk for AD (HR vs normal systolic BP group 0.55, 95% CI 0.32 to 0.96), whereas low diastolic BP (<or=70 mm Hg) was associated with increased risk of AD (HR vs normal diastolic BP group 1.91, 95% CI 1.05 to 3.48). Subjects with persistent low BP over 2 years had higher risk of developing dementia (HR 2.19, 95% CI 1.27 to 3.77). CONCLUSIONS: Low diastolic pressure is associated

with higher risk of dementia in elderly individuals over age 75. Dementia risk was higher in subjects with persistently low BP.



{Kennelly and Collins, 2012, J Alzheimers Dis, 32, 609-21} review the various studies looking at BP and the development of dementia:

Vascular risk factors are implicated in the pathogenesis of Alzheimer's disease (AD). There is an age-dependent relationship between blood pressure and the risk of AD. Given the potential temporal lag that can exist between the two conditions, longitudinal population studies offer the best opportunity to identify a causal relationship. Midlife hypertension increases the risk for AD, yet later-life hypertension does not appear to confer the same risk and may in fact be protective. Low diastolic blood pressure, especially in later-life, is associated with an increased risk of AD. Orthostatic hypotension and other neurocardiovascular syndromes may increase the risk for cognitive impairment and AD. Several physiopathological mechanisms may contribute to this increased risk. Dynamic blood pressure changes and impaired cerebrovascular autoregulation may result in cerebral hypoperfusion. Hypertensive patients also develop cerebral infarcts, resulting in diminished perfusion. Subsequent hypoxia driven pathways result in increased cerebral amyloid-beta and phosphorylated tau protein accumulation. Treatment of elevated blood pressure with antihypertensive medications attenuates the risk of AD attributable to elevated midlife hypertension. Certain antihypertensive compounds have neuroprotective properties that may reduce the risk of AD, independent of their effects on blood pressure.

“A decline in blood pressure is common at ages above 75 years. In this study, the decline in blood pressure started earlier and was greater in subjects who developed dementia, especially in those developing Alzheimer’s disease, and in those with white-

matter lesions, than in non-demented subjects." {Skoog et al., 1996, Lancet, 347, 1141-5}
"Thus subsequent episodes of hypotension (eg, induced by drugs or cardiac failure) may lead to hypoperfusion and ischaemia in vulnerable areas,3,4,7 such as in the deep white matter, supplied by long penetrating end-arteries with few collaterals.3,4" {Skoog et al., 1996, Lancet, 347, 1141-5}
The Systolic Hypertension in the Elderly Program failed to find any effect of treatment (primarily with chlorthalidone) vs placebo in either the evolution of cognitive function or the incidence of dementia over an average observation period of 5 years, as reported in {Birkenhager et al., 2001, Arch Intern Med, 161, 152-6}. In the Medical Research Council trial of treatment in older patients with hypertension randomized to a diuretic, beta-blocker, or placebo, over a period of 54 months, no significant difference in psychometric test scores were detected between active treatment and placebo groups. However, in the Syst-Eur trial, treatment with nitrendipine as the primary drug showed a reduction in the rate of dementia by 50% compared to placebo, over a 2-year treatment period, based on an intention-to-treat analysis. Both of these were reported on in {Birkenhager et al., 2001, Arch Intern Med, 161, 152-6}. I note that an intent-to-treat analysis is problematic when dealing with illnesses which have a downhill course, as the arm with more dropouts will show better results.
In the HYVET trial, there was no analysis to determine if the improvements in mortality, etc., were actually related to blood pressure lowering. Note that after two years, less than 50% of patients had their blood pressures lowered to the target of 150/80 {Beckett et al., 2008, N Engl J Med, 358, 1887-98}. Thus it may be that the medication itself provided a benefit independent of blood pressure lowering. This is certainly true for the risk of cardiac failure with a diuretic.
A recent Australian study looking at the longitudinal effect of BP on cognitive function showed that over 5 years, AD patients with both low and high diastolic BP or low and high pulse pressure had more rapid decline in CAMCOG (Cambridge Cognitive Assessment) scores compared to patients with midrange pressures {Razay et al., 2009, Dement Geriatr Cogn Disord, 28, 70-4}.

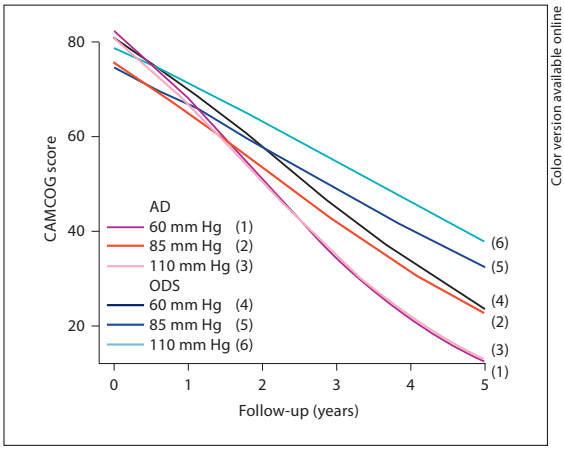


Fig. 1. The longitudinal change in CAMCOG scores at 3 levels of diastolic BP (60, 85 and 110 mm Hg) through follow-up in AD and ODS.

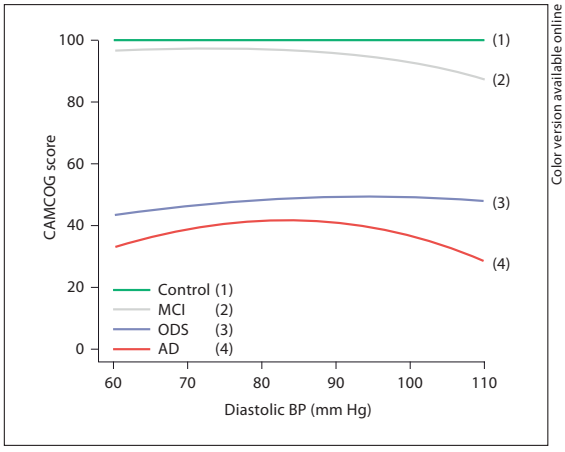
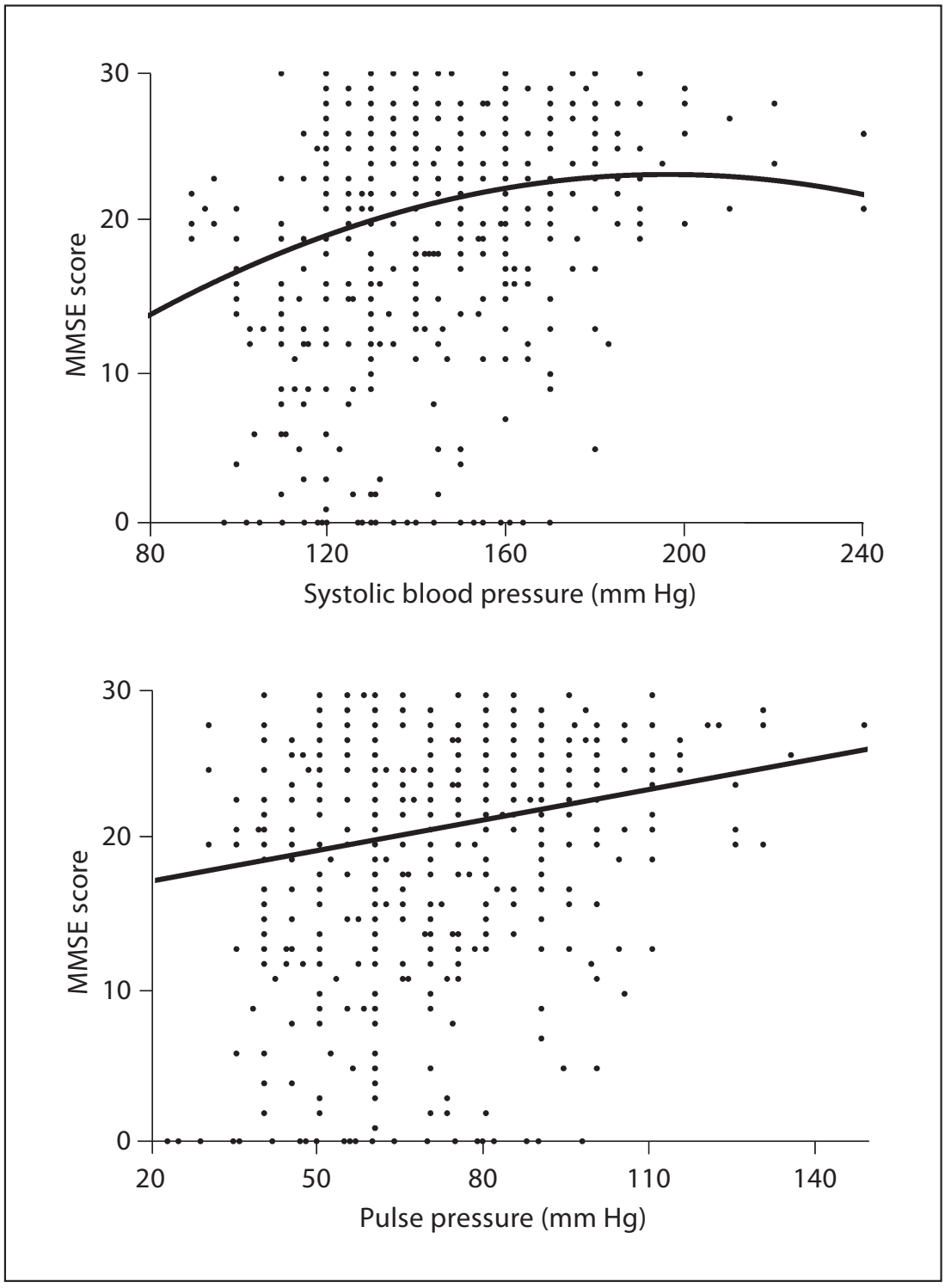


Fig. 2. CAMCOG scores according to the levels of diastolic BP in each diagnostic category after 3 years.

A cross-sectional study of 575 individuals aged 85, 90 or 95 years and above and living in northern Sweden or Finland, showed that MMSE scores were lower for individuals with both high and low SBP. The relationship was linear for PP and MMSE scores, with higher PP predicting better cognition {Molander et al., 2010, Dement Geriatr Cogn

Disord, 29, 335-41}



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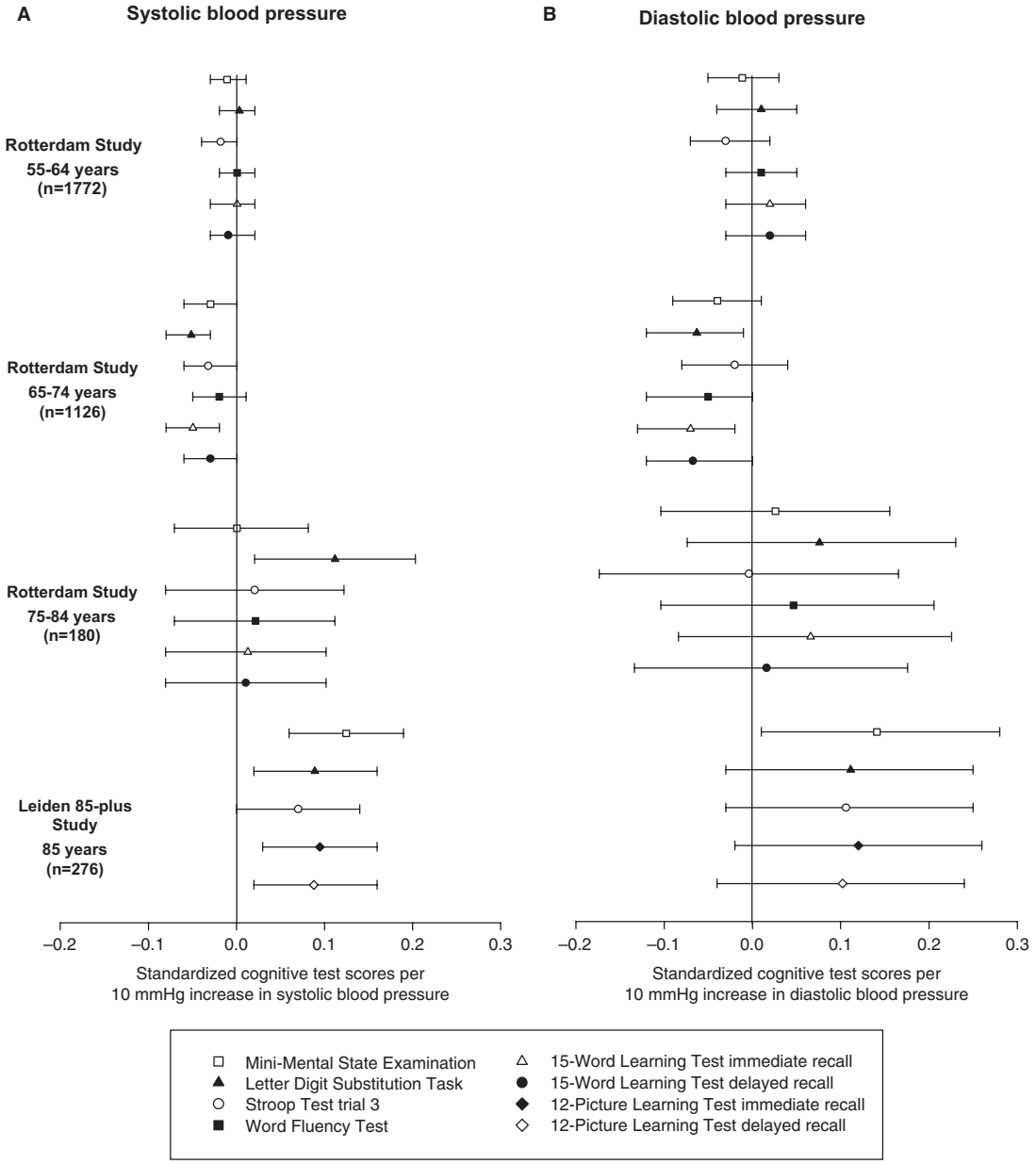
Sometimes higher BP predicts better cognition

In the elderly, age may play an important role in determining whether an elevated blood pressure predisposes to cognitive impairment. Two prospective population-based cohort

studies in the Netherlands, together looking at 3078 men and women, assessed cognitive function at the end of followup, and looked at the association to baseline BP {Euser et al., 2009, J Am Geriatr Soc, 57, 1232-7}.



The graph shows that under-65s, BP and later cognition were not associated; for persons aged 65-74, higher baseline BP was related to worse cognition 11 years later; for those 75 and older, higher BP was related to improved cognition later on, and this effect was stronger for those older than 85.

A cross-sectional study in 327 geriatric outpatients with probable Alzheimer's diagnoses found that higher systolic blood pressure and pulse pressure were associated with better cognitive test performance on the MMSE {van Bruchem-Visser et al., 2009, Dement Geriatr Cogn Disord, 28, 320-4}.

“At old age, mild hypertension may increase cognitive performance” {Anson and Paran, 2005, Am J Ther, 12, 359-65}

“The lower the better”

A large meta-analysis concluded that everyone at significant risk of cardiovascular disease would benefit from blood pressure lowering, irrespective of pretreatment blood pressure. So, no more need to monitor blood pressure! {Law et al., 2009, BMJ, 338, b1665}. However, does such a meta-analysis suffer because negative trials are less likely to be included? Also, “As the reduction in blood pressure was not reported in most trials in people with a history of CHD, we estimated the average reduction from the average pretreatment blood pressure and the average drug dose, using results from a meta-analysis.” Why would blood pressure lowering studies not report reductions in blood pressure? The authors apparently have suggested a “polypill” which could combine inexpensive generic medications, but then obtained a patent on the polypill, according to a commenter.

The above study also suggests that “the lower the better” in terms of blood pressure. This contradicts a Cochrane Collaboration meta-analysis which concluded there is no additional benefit to BP reductions <140-160/90-100 mm Hg {Arguedas et al., 2009, Cochrane Database Syst Rev, CD004349}. Other commenters to the Law paper also point out that thiazide diuretics have a much better effect on heart failure than other classes of antihypertensives.

The very old may have different risk profiles

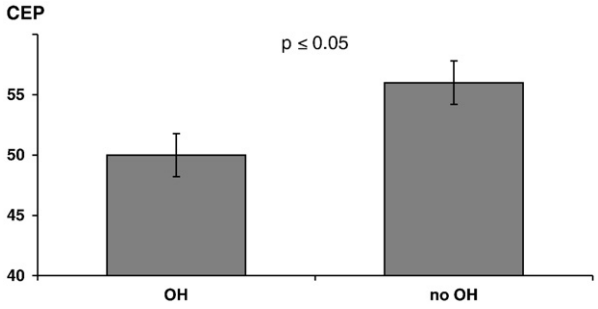
There is evidence that in the very old, the risk factor profiles for dementia and cognitive decline are different than for younger patients. For example, in the 3336 hypertensive participants in the HYVET trial for whom longitudinal cognitive data was available, heart failure, diabetes, atrial fibrillation, prior stroke, glucose, or hemoglobin levels were unrelated to dementia and cognitive decline, while higher creatinine, higher total and lower high- density lipoprotein cholesterol were associated with lower risk of cognitive decline {Peters et al., 2009, J Hypertens, 27, 2055-62}.

A recent review {Novak and Hajjar, 2010, Nat Rev Cardiol, 7, 686-98} of the relationship between cognition and blood pressure made the following key points:

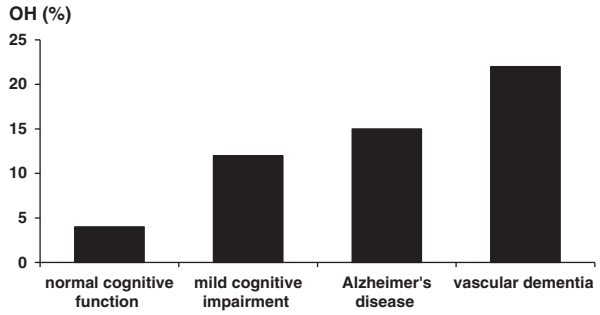
- Hypertension and hypotension affect neurovascular coupling, leading to a decrease in perfusion, oxygenation, and vascular reserve capacity, and are associated with microvascular disease, stroke, cognitive function decline, and dementia
- Risk factors for vascular disease accelerate age-related decline in perfusion and brain tissue volumes and have additive effects in worsening cognitive outcomes late in life
- Hypertension and other vascular risk factors are linked to poorer performance in executive function and attention tests than in memory or language scores
- Results of antihypertensive treatment in trials for prevention of dementia in the elderly remain inconclusive, but some studies indicate that single-drug or combined antihypertensive therapies have protective effects on cognition
- More research is needed to determine which blood pressure values should be targeted to optimize perfusion and to prevent cognitive decline in the elderly

Orthostatic Hypotension

A study of 495 consecutive elderly outpatients attending a memory centre looked at the relationship between cognitive status and orthostatic hypotension, using a validated comprehensive battery of neuropsychological tests, the cognitive efficiency profile (CEP) assessing the main cognitive areas {Mehrabian et al., 2010, J Neurol Sci, 299, 45-8}. After adjusting for age, education level, SBP, DBP, weight, and antihypertensive drugs, OH patients (14%) had worse cognitive scores. Note that the vertical axis does not go down to zero.



There was a significant relationship between OH and cognitive status.



In a study of 2321 community-living elderly Chinese, free of cardiovascular disease and stroke, mean age 65.5 years, 16.6% had OH. Overall, OH was unrelated to cognitive impairment, as determined by MMSE score <24. However, in hypotensives, OH increased the odds of cognitive impairment by 4.1 times, while hypertensives with OH had 0.48 the risk of cognitive impairment compared to hypertensives without OH {Yap et al., 2008, Dement Geriatr Cogn Disord, 26, 239-46}.

Orthostatic hypotension patients had deficits in cerebral perfusion in the bilateral frontal areas but not in other areas of the brain, compared to controls without orthostatic hypotension, in a small study using SPECT {Hayashida et al., 1996, J Nucl Med, 37, 1-4}.

Constitutional or Chronic Hypotension

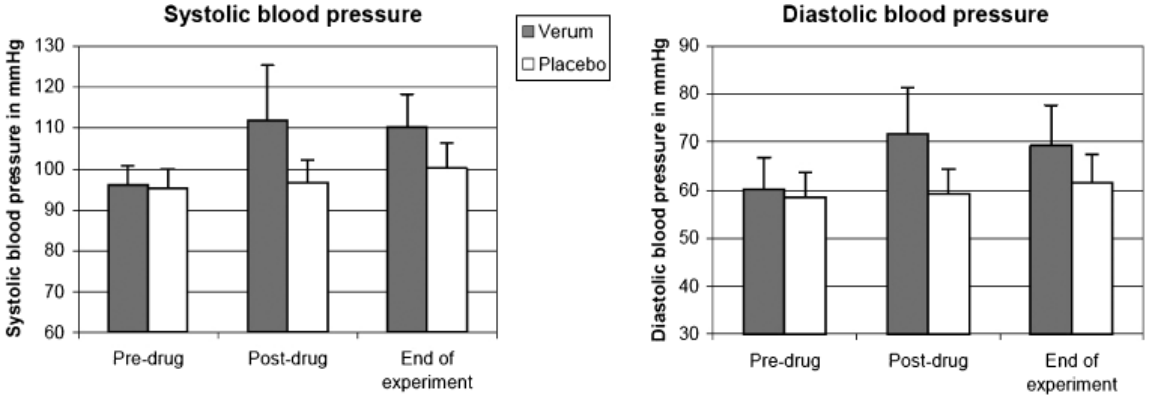
Constitutional hypotension, defined by the WHO as SBP < 110 in males or < 100 in females, regardless of DBP, affects perhaps 3% of the population. “Chronically low blood pressure is accompanied by a variety of complaints including fatigue, reduced drive, faintness, dizziness, headaches, palpitations, and increased pain sensitivity [1–4]. In addition, hypotensive individuals report cognitive impairment, above all deficits in attention and memory.” {Duschek and Schandry, 2007, Clin Auton Res, 17, 69-76}. The

table below summarizes studies on cognitive performance in hypotension.

Table 1 Studies on cognitive performance in hypotension (SBP, systolic blood pressure; DBP, diastolic blood pressure)

Authors	Main focus	Samples	Assessment instruments	Main results
Richter-Heinrich et al. [18]	Attentional performance in hypotension and hypertension	30 hypotensives (SBP < 106 mmHg); 40 hypertensives (SBP > 140 mmHg); 31 normotensive controls; age 16–40 years	Konzentrations-Verlaufs-Test (course of concentration test) [25]	Reduced attentional performance in the case of both lowered and elevated blood pressure
Stegagno et al. [26]	Attentional, memory and arithmetic performance in hypotension	17 female hypotensives (SBP < 100 mmHg); 19 normotensive controls; mean age 23 years	Reaction times to acoustic stimuli; digit span [27]; recall of word lists [28]; serial subtractions	Prolonged reaction times, poorer performance on the verbal memory and arithmetic tasks in hypotension, no effect for digit span
Costa et al. [29]	Attentional and memory performance in hypotension	26 female hypotensives (SBP < 105, DBP < 65 mmHg), 22 normotensive controls; mean age 29 years	Aufmerksamkeits-Belastungs-Test (attentional strain test) [30]; Zahlen-Verbindungs-Test (trail making test) [31]; recall of word lists [28]	Poorer attentional and memory performance on each of the three tests in hypotension
Morris et al. [32]	Relationship between blood pressure and cognitive performance in elderly persons	Representative population sample covering the total spectrum of blood pressure (n = 5,816; age over 64 years)	East Boston Memory Test [33]; Symbol Digit Modalities Test [34]; Mini-Mental State Examination [35]	Weak U-shaped relationship between blood pressure and cognitive performance
Weisz et al. [22]	Attentional performance in hypotension	25 female hypotensives (mean SBP = 102 mmHg); 25 normotensive controls; age 19–44 years	Attentional and Cognitive Efficiency Battery [36]	Reduced performance on a subtest assessing cognitive flexibility in hypotension
Duschek et al. [37]	Attentional performance in moderate hypotension	26 borderline hypotensives (mean SBP = 112 mmHg); 29 normotensive controls; mean age 26 years	Reaction times to acoustic stimuli; Aufmerksamkeits-Belastungs-Test (attentional strain test) [30]; Zahlen-Verbindungs-Test (trail making test) [31]	Prolonged reaction times and poorer performance on the "Aufmerksamkeits-Belastungs-Test" in moderate hypotension, no effects for the "Zahlen-Verbindungs-Test"
Duschek et al. [38]	Attentional and working memory performance in hypotension with motor performance and mood controlled	40 hypotensives (SBP < 105 mmHg in women, SBP < 110 mmHg in men); 40 normotensive controls; age 19–45 years	Testbatterie zur Aufmerksamkeitsprüfung (battery for the assessment of attention) [39]; Motorische Leistungsserie (motor performance series) [40]; Befindlichkeitsskala (mood scale) [41]	Poorer performance on six tests assessing tonic and phasic alertness, selective, divided and sustained attention as well as working memory in hypotensives with fine motor performance and mood controlled

A study of the effects of a sympathomimetic drug, midodrine, in 50 hypotensive individuals in a randomized, placebo-controlled, double-blind design, showed that midrodine led to an increase in blood flow velocities as well as enhanced attentional performance {Duschek et al., 2007, Psychophysiology, 44, 145-53}.



Frontal Lobes

Frontal lobes have a basal metabolic rate 20% higher than other brain areas {Moretti et al., 2008, Vasc Health Risk Manag, 4, 395-402}. This suggests that frontal lobe function is more vulnerable to hypoperfusion than other brain areas. This contention is supported by a study which compared regional cerebral blood flow determined by SPECT in two groups of AD patients. One group had scored high on the Kana Pick-out Test (KPT) (indicating good frontal lobe function) while the other group had scored low. The low-scoring patients showed significant hypoperfusion in the subgenual cingulate gyrus {Kishimoto et al., 2011, Int Psychogeriatr, 23, 546-53}, a prefrontal region in which tissue loss is associated with disinhibition in frontotemporal dementia and in which lesions lead to impaired decision-making.

Another study of cerebral blood flow, this time using magnetic resonance angiography, suggested that a combination of high volume of white matter lesions together with lower

CBF may impair executive functioning, but not memory {Appelman et al., 2010, Dement Geriatr Cogn Disord, 29, 240-7}.
In patients with mild cognitive impairment, those with executive dysfunction showed hypoperfusion in several areas including bilateral middle frontal cortex, which was not the case for amnestic MCI patients {Chao et al., 2009, Alzheimer Dis Assoc Disord, 23, 245-52}.

Is the beneficial effect of antihypertensive treatment due to BP decrease or to other factors?

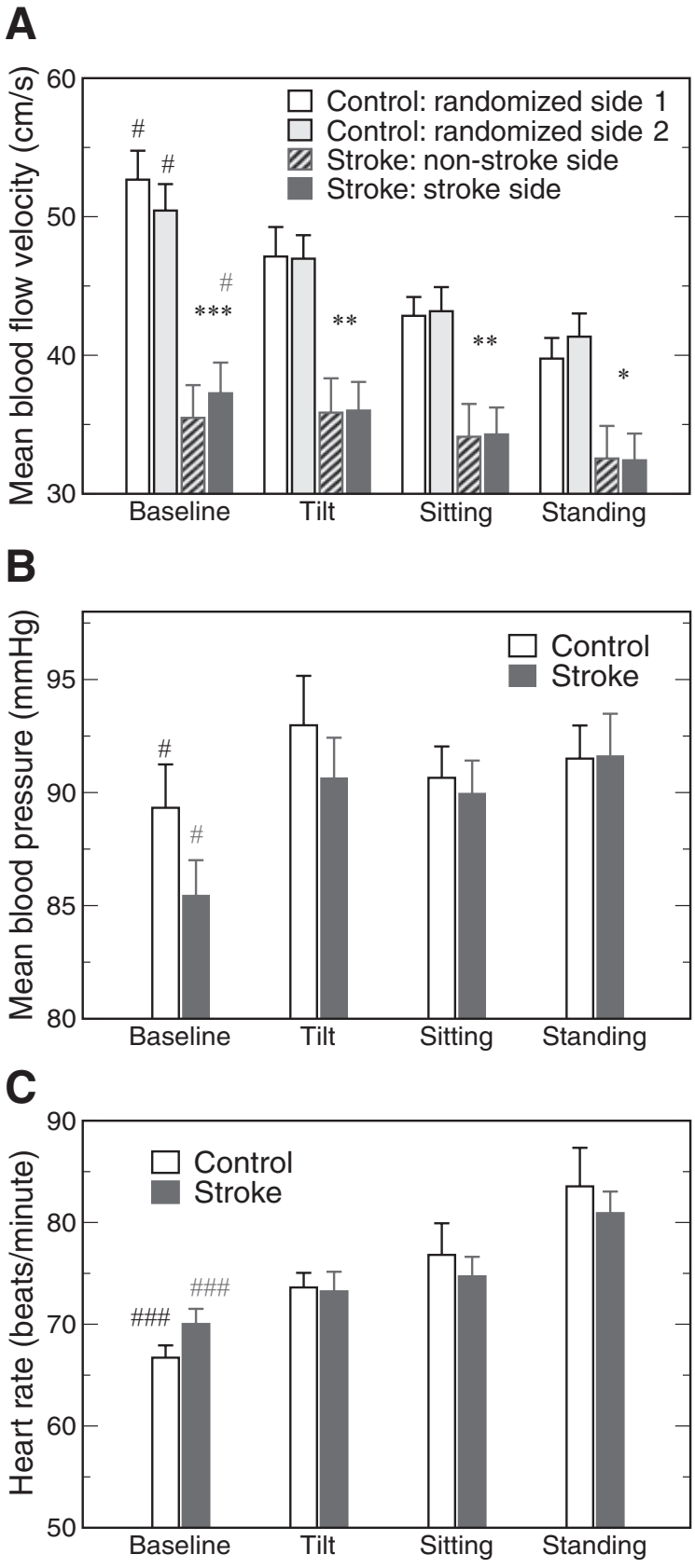
Various researchers have suggested (for example, {Boissel et al., 2005, Fundam Clin Pharmacol, 19, 579-84; Ruland and Gorelick, 2003, Curr Neurol Neurosci Rep, 3, 21-6} that the risk reduction effects of antihypertensive drugs or lipid-lowering drugs is at least partially due to what are called pleiotropic effects (ie multiple influences). Boissel et al used the INDIANA database of individual records of about 29,000 patients in 5 different antihypertensive studies, to look at the the extent to which risk reduction for coronary events or for stroke could be attributed to lowering of systolic BP. They concluded that results are inconclusive for coronary events, and for stroke BP lowering explains only 49% of the risk reduction from treatment. Their discussion goes into detail on how other attempts to link BP reduction to risk reduction have either failed or were reported incorrectly.
Another review {Turnbull, 2003, Lancet, 362, 1527-35} looked at 29 randomised trails involving over 162,000 patients, and demonstrated that greater reduction of risk for cardiovascular events was produced by regimens with lower blood pressure goals. It is unclear, however, if this simply reflects bigger doses, better compliance, or both. ACE inhibitors showed the best risk reduction but reduced blood pressure less.

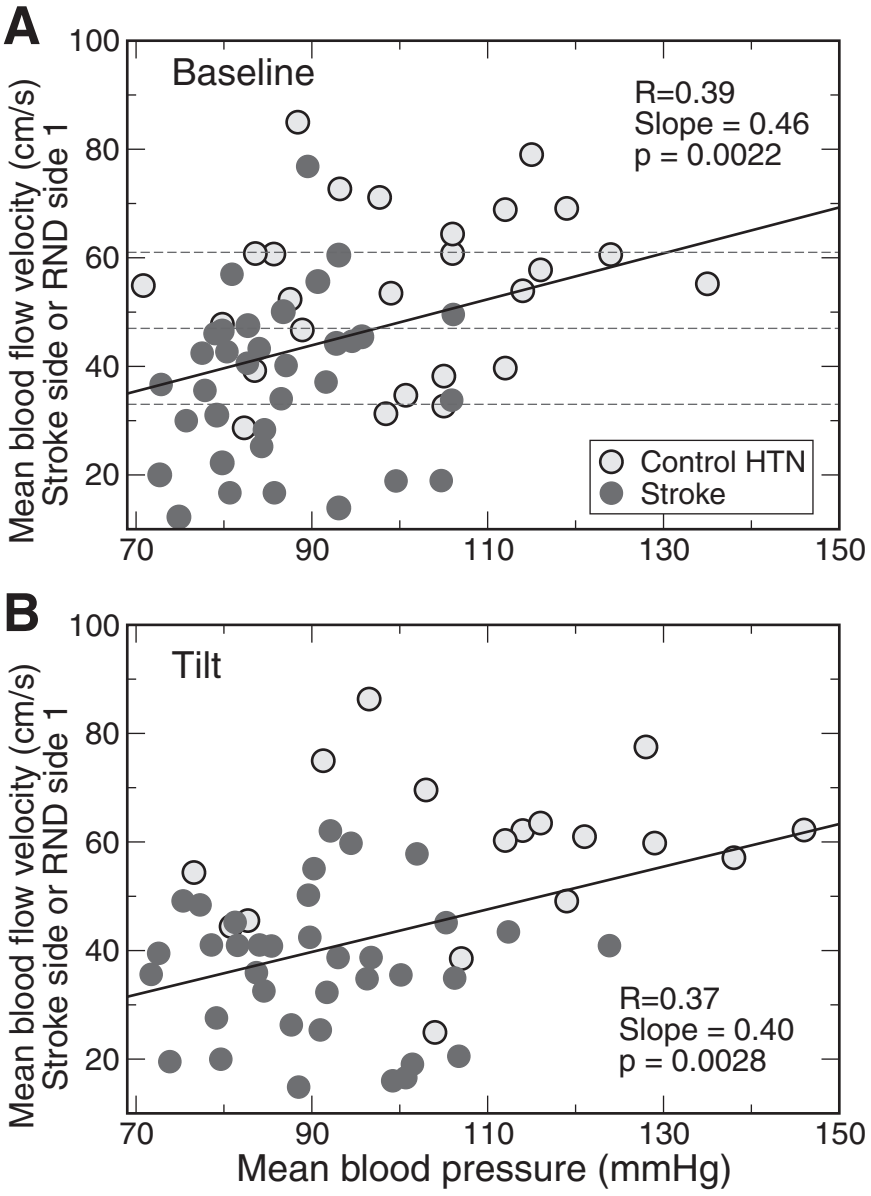
Overtreatment of HTN may cause hypoperfusion

“Antihypertensive treatment may increase the risk of myocardial infarction in elderly men with treated diastolic blood pressures < or = 90 mm Hg.” {Merlo et al., 1996, BMJ, 313, 457-61}
“Cognitively normal subjects with HTN (n=19) had decreased rCBF in the putamen, globus pallidus, bilaterally, and in the left hippocampus compared with normotensives (n=22). In addition, decreased rCBF was observed in the right and left anterior cingulate gyrus with extension to the subcallosal region, left posterior cingulate gyrus and medial precuneus, left lateral inferior and superior frontal, and inferior parietal, left orbitofrontal, and left superior temporal cortices. CONCLUSIONS: rCBF is affected in normal subjects with HTN, not only in the subcortical regions, but also in limbic and paralimbic structures. We hypothesize that the HTN creates a vulnerability state for the development of neurodegenerative disorders, especially Alzheimer disease.” {Dai et al., 2008, Stroke, 39, 349-54}
Adhering to clinical practice guidelines for chronic conditions may lead to undesirable effects when caring for elderly patients with several comorbidities {Boyd et al., 2005, JAMA, 294, 716-24}

Perfusion in HTN and stroke patients is dependent on BP

Cerebral blood flow velocities are lower in patient with stroke and daily activities such as standing can induce hypoperfusion


A
Mean blood flow velocity (cm/s)
60
50
40
30
Control: randomized side 1
Control: randomized side 2
Stroke: non-stroke side
Stroke: stroke side
#
#
#
***
**
**
*
Baseline
Tilt
Sitting
Standing
B
Mean blood pressure (mmHg)
95
90
85
80
Control
Stroke
#
#
Baseline
Tilt
Sitting
Standing
C
Heart rate (beats/minute)
90
80
70
60
50
Control
Stroke
###
###
Baseline
Tilt
Sitting
Standing



{Novak et al., 2010, Stroke, 41, 61-6}It should be noted that these reductions in BFV with sitting and standing are not due only to orthostatic hypotension which was present in only 23.3% of the stroke group and 31.3% of the control. The influence of BP on BFV is shown here

Miscellaneous

In the HYVET study, “Antihypertensive treatment in elderly patients does not statistically reduce incidence of dementia.” {Peters et al., 2008, Lancet Neurol, 7, 683-9}
The HYVET (Hypertension in the Very Elderly Trial) study:
Double-blind, randomized, placebo-controlled trial, 3845 hypertensive patients aged >= 80, with sustained systolic BP >= 160, randomized to a diuretic (indapamide slow

release 1.5 mg) or placebo. If the target BP of 150/80 was still exceeded, then an ACE inhibitor (perindopril 2 or 4 mg) or placebo was added.

Protocol

For elderly patients not on antihypertensive meds

Do not use BP measurements to adjust treatment

Measure BP only to determine whether HTN is present, as HTN is one of several risk factors for cardiovascular disease and dementia

If possible, use 24h ambulatory blood pressure monitoring to determine if high BP exists

If there are risk factors for cardiovascular disease and dementia, and blood pressure levels are adequate (ie greater than 140/90 in those > 85 years) treat with a so-called “antihypertensive”. Choose a medication based on its comparative efficacy in diminishing the risk of interest (ie stroke, MI, or dementia). Use a standard dose. If BP drops below 140/90, decrease the dose or switch to another agent.

For new elderly patients who are already taking antihypertensive meds

Unless it is clear from the history or the choice of medications being used that the medications are intended to treat or prevent heart failure, gradually taper and discontinue antihypertensive medications.

Once off medication, follow the protocol above for patients not on antihypertensive meds

If the meds are clearly being used to treat or prevent heart failure, aim for the lowest doses consistent with good management. Daily weights and corresponding adjustments of diuretic dosage can be useful. Consider using digitalis glycosides.

Possible consequences of low blood pressure

Inadequate perfusion of the brain, leading to cognitive impairment, behaviour problems (with frontal lobe hypoperfusion), TIA, stroke, dizziness, and falls.

Inadequate perfusion of coronary arteries, leading to angina or MI

Inadequate perfusion of kidneys, leading to kidney failure; inadequate diuresis which can increase risk of acute worsening in patients with heart failure.