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Chinese expert consensus on the management of hypertension in the very elderly

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1 Introduction

Population aging has become a major challenge for the healthcare in China. More than 23 million Chinese are currently ≥ 80 years, with an annual increase of 5%. The Chinese population of 80 years or older is expected to reach 30.67 million by 2020 and 74 million by 2040.

Hypertension is the most important risk factor for cardiovascular disease. It was estimated that two million people died from complications of hypertension each year in China. Furthermore, 71% of stoke related death and 53% of coronary artery disease (CAD) related deaths are associated with hypertension.

The prevalence of hypertension rises up along with aging,[1] and studies indicated that 70%–90% of persons ≥ 80 years have hypertension.[2,3] Thus, hypertension is a major public health problem in the very elderly population. The Chinese Society of Geriatric Hypertension and Chinese Geriatrics Society develop this expert consensus to inform and guide clinical management of hypertension in the very elderly population (persons ≥ 80 years), especially in areas where rigorous evidence may not be available or evidence to date is not widely applied to clinical practice.

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2 The diagnosis of hypertension in the very elderly

2.1 Diagnosis

Diagnosis of hypertension should be based on at least three different blood pressure (BP) measurements, taken on ≥ 2 separate office visits, with a mean systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg on at least two occasions. Isolated systolic hypertension (ISH) is defined as a SBP of at least 140 mmHg and a DBP of less than 90 mmHg.

Diagnosis of hypertension in the elderly should be based on BP measurements in the clinic office, but out-of- office BP measurements (including home self BP monitoring and the 24-h ambulatory BP monitoring) may help to improve the accuracy of diagnosis.

2.2 Measurement of BP

BP should be measured in the sitting position with the back supported, feet on the floor, arm supported in the horizontal position, and the BP cuff at heart level. In the initial evaluation, BP should be measured in both arms which is helpful to detect coarctation of the aorta and occlusion of the upper limb arteries.[4]

In most cases, diastolic BP is defined as the onset of phase V of Korotkoff sound in auscultation. If the sound is still heard when the cuff pressure has reduced to 0, phase IV of the Korotkoff sound is used to define DBP.

The standing BP should be monitored before and during the course of medication or treatment alteration to monitor for orthostatic hypotension-defined as a reduction in SBP of ≥ 20 mmHg or in DBP of ≥ 10 mmHg within 3 min of standing.

If dizziness is associated with meals, postprandial BP or 24-h ambulatory BP should be measured.

A qualified sphygmomanometer including desktop mercury sphygmomanometer, electronic sphygmomanometer, or ambulatory BP monitoring is recommended and regularly calibrating is needed. Measurement error may occur when using automatic electronic sphygmomanometer in patients with arrhythmias, such as atrial fibrillation, and need to be carefully monitored.

Home BP self-monitoring and 24-hour ambulatory BP monitoring is helpful to detect orthostatic hypotension, white coat hypertension and masked hypertension.[5,6]

Validated, standardized, arm-type full-automatic sphygmomanometer is preferred in family self-monitoring BP. Patient or family member training of self BP measurement is recommended. For home BP monitoring, the cut-off value for definition of hypertension is 135/85 mmHg. Diet, smoking, anxiety, depression, fatigue, bladder filling, excessive cold, overheating, and limb movement disorders, such as Parkinson's disease, will affect the accuracy of BP measurement.

Subgroup analysis from Hypertension in the Very Elderly Trial (HYVET) indicated that difference of ambulatory BP and clinic BP in the elderly was greater in octogenarians than in those under the age of 80. Therefore, reference value of 24-hour ambulatory BP of the very elderly is needed to be further studied.[7]

3 Characteristics of hypertension in the very elderly

The clinical characteristics in the very elderly patients with hypertension are different from those below 80 years old: they typically have worse arteriosclerosis and decreased vascular elasticity, and have higher prevalence of left ventricular hypertrophy, diastolic dysfunction, decreased baroreceptor sensitivity, renal dysfunction, reduced ability of water and electrolyte metabolism, increased insulin resistance, abnormal glucose metabolism and endocrine dysfunction.[8–13]

3.1 Isolated elevation in systolic BP

The proportion of ISH increased with age and accounts more than 90.0% in the very elderly with hypertension.[2] Compared with DBP, SBP is a stronger predictor of target organ damage and cardiovascular events in older patients. Therefore, reaching target level of SBP should be more emphasized in the antihypertensive treatment of the very elderly patients.

3.2 Increase of pulse pressure

Pulse pressure increase with age and may reach up to 70–100 mmHg in the very elderly. Pulse pressure was positively correlated with total mortality and cardiovascular events, and increase in pulse pressure also indicates an increase in risk of dementia.[14] Unfortunately, drugs that decrease SBP only but do not reduce DBP are not presently available.

3.3 Abnormal circadian rhythm

BP normally decreases during the night—defined as 'dipping'. Abnormal circadian rhythm refers to drop of nocturnal BP less than 10% or more than 20%. In some patients, nocturnal BP is higher than daytime BP which contributes to an increased risk of target organ damage.

3.4 Large fluctuations of BP

The BP fluctuation increased with aging, and is associ-

ated with changes in mood, season, temperature, body position, diet and so on. These are some categories shown below.

Postural BP fluctuations: postural BP fluctuations include orthostatic hypotension and orthostatic hypertension. Orthostatic hypotension is often accompanied with some symptoms of hypoperfusion, such as dizziness, amaurosis, fatigue, nausea, blurred vision, cold sweats. The occurrence of orthostatic hypotension often leads to increase of adverse events, so the triggers, such as hypovolemia should be avoided. Orthostatic hypertension, defined as SBP elevation above 20 mmHg when position change from supine to upright, is more common in the elderly than in younger patients. Compared with hypertensive elderly patients with orthostatic hypotension, orthostatic hypertension patients are older, and with higher prevalence of left ventricular hypertrophy (LVH), CAD and asymptomatic cerebral vascular disease.

Morning hypertension: morning hypertension in elderly means that self measured BP within 1 h or ambulatory BP within 2 h after waking in the morning above 135/85 mmHg; or clinic BP during the time of 6: 00–10: 00 am greater than 140/90 mmHg.

Postprandial hypotension includes three conditions: (1) Postprandial SBP drops over 20 mmHg within 2 h than pre-prandial; (2) Pre-prandial SBP is above 100 mmHg, but postprandial SBP is below 90 mmHg; and (3) Postprandial SBP drops but do not meet the criteria mentioned above, but combined with cerebral ischemia symptoms after meal.

3.5 Pseudo hypertension

Pseudo hypertension is defined as SBP measured by cuff which is higher than invasive BP directly measured by artery puncture due to severe atherosclerosis, which leads to falsely elevated SBP. Pseudo hypertension occurs in 1.7% to 70% of the very elderly. Pseudo hypertension may contribute to excessive antihypertensive treatment, and result in hypotension which may cause falls, weakness, and other events. Therefore pseudo hypertension in the elderly warrants special consideration. For those very elderly patients with refractory hypertension, pseudo hypertension should be excluded.

3.6 White coat hypertension

Outpatient BP monitoring and 24-h ambulatory BP monitoring is helpful in making a definitive diagnosis.

3.7 Secondary hypertension

Renovascular and renal diseases, primary hyperaldosteronism, obstructive sleep apnea-hypopnea syndrome are common causes of secondary hypertension. In some situation, secondary hypertension is due to atherosclerosis. If BP is refractory to medical control, other causes of secondary hypertension should be considered, including evaluation of accuracy of diagnosis and rationality and compliance of the treatment, the affective factors, such as sleep disorder, and medication that could influence BP.

3.8 Multiple risk factors, concomitant disease, and target organ damage

Recent studies of Chinese very elderly patients with hypertension showed that their prevalence of diabetes was 39.8%; hyperlipidemia was 51.6%; CAD was 52.7%; renal dysfunction was 19.9%; and cerebrovascular disease was 48.4%.

4 Management for hypertension in the very elderly

4.1 Clinical evidence for anti-hypertension

Early studies (European working party on high blood pressure in the very elderly trial, EWPHE)[15] showed that octogenarians do not be benefit from antihypertensive treatment. However, following studies and meta-analyses found that antihypertensive treatment in the very elderly decreased the risk of stroke and non-fatal stroke, but not total mortality (Table 1). A recent study (systolic hypertension in the very elderly program, SHEP) which followed patients for up to 22 years showed that compared to control group, patients in the treatment group were more likely to live up to 80 years old after 4.5 years of antihypertensive treatment (81.3% *vs*. 57.6%), 85 years old (58.1% *vs*. 37.4%), 90 years old (30.5% *vs*. 22.0%), 95 years old (11.9% *vs*. 8.8%) and 100 years old (3.7% *vs*. 2.8%). Subgroup analysis from Systolic Blood Pressure Intervention Trial (SPRINT) showed that aggressive control of systolic BP for those patients over 75 year old could decrease the risk of cardiovascular events and all-cause mortality.[16] The only randomized control clinical trial of antihypertensive treatment focus on octogenarians was HYVET, which showed a 30% decreased risk of stroke, 23% of cardiovascular death decreased, and 21% of total mortality, as well as reduced medical costs.[17] Subgroup analysis showed this benefit also persisted to those patients over 85 years old.[18]

4.2 BP level for initial treatment and target BP

General condition, co-existing disease, the risk of treatment and tolerance of medication should be considered in the decision making regarding the initial treatment. During treatment, the effect of lowering BP should be moni-

Table 1. Clinical trials in elderly hypertensive patients.

Name of trails	*n*	Age (yrs)	Average baseline BP (mmHg)	Average BP after treatment (mmHg)	Year of Publication	Following duration (yrs)	Results
INDANA meta analysis[21]: EWPHE, Coope and Warrender, SHEP-P, SHEP, STOP, CASTEL, Syst-Eur were enrolled	1679	81–99	173–204/ 73–101	–	1999	2.1–6.8	The risk of stroke decreased by 34%, MACE and HF decreased by 22% and 39%, respectively. Cardiac death was not affected. Total mortality increased by 6%.
HYVET-Pilot[28]	1283	79.5–96.1	181.5/99.6	151/84	2003	1.1	The risk of stroke decreased by 53%. The death from stroke decreased by 43%. Total mortality increased by 23%.
SCOPE subgroup analysis[23]	1051	80–89	168.7/82.0	146.2/71.6	2005	3.6	MACE decreased by 5%; non-fatal stroke decreased by 29%; fatal or non-fatal stroke decreased by 17%.
HYVET[28]	3845	80–105	173.0/90.8	144/78	2008	1.8	The risk of stroke decreased by 30%, the death from stroke decreased by 39%; cardiovascular death decreased 23%; heart failure decreased 64%; total mortality decreased 21%.

BP: blood pressure; EWPHE: European working party on high blood pressure in the elderly trial; HYVET: hypertension in the very elderly trial; HYVET-Pilot: Hypertension in the Very Elderly Trial-Pilot; MACE: Major Adverse Cardiovascular Events; SHEP: systolic hypertension in the elderly program; SHEP-P: systolic hypertension in the elderly program-Pilot; STOP: Swedish trial in old patients with hypertension; Syst-Eur: systolic hypertension in Europe; SCOPE: The study on cognition and prognosis in the elderly.

tored and the tolerance should be considered for the purpose of titrating the medication. Life style modification is recommended for those patients not appropriate for medications. BP monitoring, regular follow up, and re-evaluation is necessary.

BP level of initial treatment: ≥ 160/90 mmHg. The criteria for those clinical trials which enrolled very elderly hypertensive patients were systolic BP over 160 mmHg. In HYVET subgroup analysis, three groups were divided depending on initial BP level (160–169, 170–179 and ≥ 180 mmHg). There was no statistically significant difference among those groups in terms of reduction of mortality and cardiac events, but there was a difference in stroke prevention—the risk reduction of stroke was 0.82, 0.63 and 0.54 respectively, indicating that there was a declining trend of the benefit from the risk reduction of stroke accompanied by the decrease of initial BP level. For those octogenarians whose BP is over ≥ 160/90 mmHg, initiation of medication is recommended according to the present evidence.

Target BP for management: for those very elderly patients who do not have co-existing disease, such as stroke, CAD, heart failure (HF), diabetes and chronic renal failure, the target BP is < 145/90 mmHg.

For those patients who have cardiovascular or renal dysfunction, the target BP is < 150/90 mmHg. Further BP reduction to < 140/90 mmHg is acceptable if the patient tolerate the medication (Figure 1).

BP should not be lower than 130/60 mmHg for very elderly patients.

BP reduction should be smoothly controlled to avoid a rapid decline. BP level is suggested to reach the target within three months.

The HYVET study enrolled relatively healthy elderly patients with Chinese participants accounted for 40% of all patients. Mortality was significantly deceased when SBP lowered to 144 mmHg.[19,20] A meta-analysis, which included systolic hypertension in the very elderly program-Pilot (SHEP-Pilot), SHEP, EWPHE, Coope and Warrender, Swedish trial in old patients with hypertension (STOP), systolic hypertension in Europe (Syst-Eur), hypertension in the very elderly trial-Pilot (HYVET-Pilot), HYVET, indicated there was heterogeneity on the effects of antihypertensive treatment among the very elderly. [21]A mortality benefit was only seen in HYVET and STOP study which indicated over anti-hypertension and hypotension may be detrimental for those frailer very elderly patients. A Japanese trial to assess optimal SBP in very elderly hypertensive

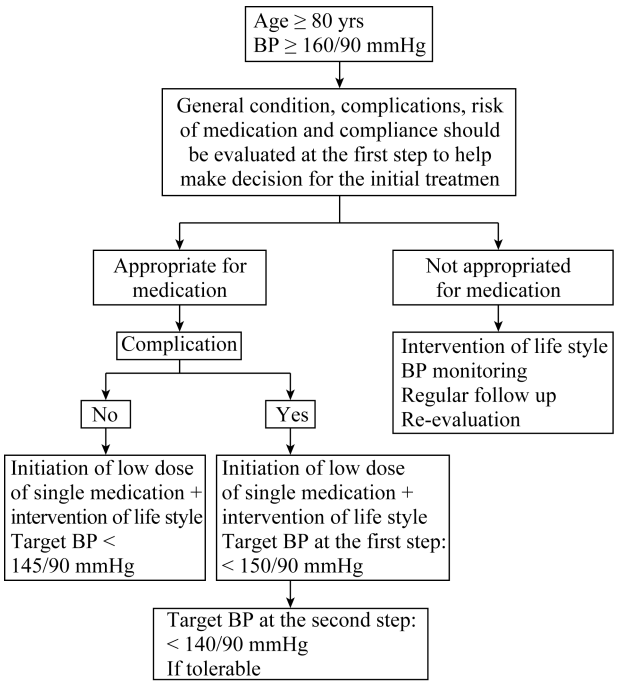

Figure 1. Flowchart for the initial treatment of hypertension in the very elderly. BP: blood pressure.

patients (JATOS) enrolled 1869 participants whose age ranging from 75–85 years old. The target BP for aggressive group and general group was 132.3/74.0 mmHg and 146.6/78.3 mmHg, respectively. Prognosis was not different between the two groups.[22] Subgroup analysis from international verapamil SR/trandolapril study (INVEST) showed the cutoff of benefit from anti-hypertension floated up accompanied with an increase in age. For those stable CHD patients age over 80 years old, the risk of death, myocardial infarction and stroke was lower in SBP around 140 mmHg group than SBP < 130 mmHg group. Furthermore, the risk of cardiac event would increase when DBP < 70 mmHg.[23] Another study enrolled 4071 very elderly hypertensive patients and followed them for 2 years, which showed the risk of death increased 18% (95% CI: 0.74–0.91) and 15% (95% CI: 0.78–0.92) respectively for every 10 mmHg interval of BP drop from baseline of SBP of 139 mmHg and DBP of 89 mmHg.[24] Taking all the above data together, it is suggested that BP below 130/60 mmHg should be avoided in very elderly patients.

5 Management of hypertension in the very elderly

5.1 Intervention of life style in the very elderly

Non-medication treatment is helpful for BP control, such as salt restriction, reasonable diet, total calories intake, tobacco and alcohol cessation, weight loss, moderate exercise, and release of psychological stress. There is one thing need to point out that there is a lack of strong evidence for outcomes of treating hypertension in the very elderly. Malnutrition often appears in very elderly patients. Risk of weakness could increase due to a rapid decrease of body weight. Strict dietary control and salt restriction may contribute to malnutrition and electrolyte disorders. Aerobic exercise is not appropriate for all elderly, especially those with comorbidities and debility. In terms of lifestyle modification in the very elderly, individualized management and close follow up is recommended.

5.2 Comprehensive evaluation and assessment in elderly

Comprehensive evaluation in very elderly is a new idea and core technique in the field of geriatrics.[25] The definition includes multi-level evaluation for disease, physical ability, cognition, psychology and social status. On the basis of overall maintenance of health in very elderly, we should pay particular attention on the different stages of medical problems. The main purpose for treatment is to maintain function, improving the quality of life, rather than to target a single disease. On the basis of a comprehensive assessment, Individual nutritional plans, aerobic exercise and resistance exercise program will help to improve the management level of BP in very elderly.[26,27]

Multiple risk factors of CHD, target organ damage and coexisting disease of heart, brain and kidney are commonly involved in very elderly hypertensive patients. During management of hypertension, clinical history, physical exam and auxiliary data should be taken and recorded carefully. At the meantime, in addition to more stringent BP goal, it's also important on active control of cardiovascular risk factors, treatment of target organ damage and comorbidity, such as blood lipids, blood glucose control, and rational use of antithrombotic drugs. The risk of polypharmacy should be alert to prevent potential adverse effect.

5.3 Promoting families, communities and community health services support

5.3.1 Diversity of BP may appear in very elderly patients accompanied with aging. Except the common type of hypertension which is characterized as high systolic BP and low diastolic BP, abnormality of BP rhythm is common such as morning hypertension, hypertension with postprandial hypotension and orthostatic hypotension, so home BP monitoring need to be strengthened.

Multidisciplinary approach including physicians, nurses, therapists and psychologists are need to be involved because multi-concomitant diseases, poly-pharmacy, decreased function, increased frailty and cognitive impairment and psychological problem are prominent in very elderly. Beneficial populations, reasonable BP target and comprehensive plan are supposed to be established after overall evaluation.

Debility and limited exercise ability in very elderly need considered for long term compliance of life style modification and follow up. Support from family, society and health care facilities at different levels are required to ensure safety and efficiency of treatment.

With the development of Internet technology, remote management of BP has become possible. At present, the platform for remote management of hypertension and related disease has officially launched the pilot project. To use smart medical facilities and telemedicine programs, together with family members and the community of medical and health services, the BP management to very elderly patients could be more easily, which may help to improve BP target achievement.

5.4 Choice of medication

The initial treatment should be started with a single medication at a low dose to avoid hypotension.

Appropriately effective, safe drugs with minimal side effect should be recommended first, such as diuretics, long effective calcium channel blocker (CCB), angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB).

In HYVET study, low dose of diuretics plus low dose of ACEIs were effective which resulted in a success rate of 71% and 78% for SBP and DBP respectively.[28] Data from INVEST and a study on cognition and prognosis in the elderly (SCOPE) indicated long acting CCBs and ARBs were both appropriate for elder hypertensive patients.

Drug combination is recommended if BP could not be controlled by single drug. In HYVET study, if BP could not be controlled satisfactory by low dose of diuretic, small dose of ACEI would be combined with which lead to a doubling of the success rate.[28] It is appropriate for an initial single drug or low dose combination therapy in Chinese elder patient because of the low rate of resistant hypertension in China.[29] Eighty percent of participants got standard BP control in Hypertension Optimal Treatment in Chinese Hypertensive Patients (HOT- CHINA)[30] which enrolled 3050 hypertensive elderly Chinese. It is helpful to increase medication compliance by using low dose of single compound preparations, such as ACEI/diuretic, ARB/diuretic, ACEI/long effective CCB, ARB/long effective CCB, compound reserpine triamterene.[30,31]β blockers are recommended for hypertensive patients with MI, chronic HF or arrhythmia if there are no contraindication.

α receptor blockers could be used in hypertensive male patients with symptomatic benign prostatic hyperplasia (BPH).

Risks of polypharmacy and drug adverse reaction.[30,31] Multiple drugs are often prescribed for very elderly. Results from Predictive Values of BP and Arterial Stiffness in Institutionalized Very Aged Population (PARTAGE) showed the highest mortality rate (HR: 2.05, 95% CI: 1.37–3.06) was found in patients who taken more than two kinds of antihypertensive drugs and SBP below 130 mmHg.[32] Disadvantage from over use of medication should be considered.[33,34] Side effects and incontradictions of common antihypertensive drugs for very elderly hypertensive patients are listed in Table 2.

For morning hypertension patients, smooth, long acting antihypertensive agents are recommended according to the characteristics of their BP. For postprandial hypotension patients, Incentives should be avoided (such as eating too full, high carbohydrate meals) and adjustment of medication should be considered.

BP including orthostatic BP should be monitored closely during the treatment. Evaluation of drug tolerance is necessary as well. If the patients develop symptoms of low perfusion, postural hypotension or other intolerance, the intensity of antihypertensive therapy should be reduced, especially when combined. Other factors which may influence BP should be re-examined, including some drugs associated with BP fluctuation.

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Table 2. Side effects and contraindications of of antihypertensive medications.

Category	Side effects	Contraindications	Notes
Diuretics			
Thiazide	Hyponatremia, hypokalemia, glucose increase, hyperuricemia, gout, hypotension, dehydration	Gout	Helpful for HF The use of Indapamide has been improved by HYVET study Low dose of diuretic (dihydrochlorothizide 25 mg) is safe and well tolerated.
Loop diuretics	Hyponatremia, hypokalemia, hypocalcemia, hypomegnicemia, hypotension, dehydration, hyperuricemia, gout, glucose incease		There are no clear indications in elder hypertensive patients except severe renal dysfunction (Ccr < 30 mL·min^{-1}·1.73 m^{-2}) Single use in hypertensive patients with HF Dose should be low initially and increase gradually depending volume status. Sometimes, volume status is hard to evaluate, especially in weak patients because edema could also appear in malnutrition patients. Electrolyte and creatinine should be monitored closely. Risk of hyponatremia increases when combined with antidepressants of elective 5 – hydroxytryptamine reuptake inhibitors. Urinary incontinence could be aggravated in weak patients which lead to difficulty of care. Loop diuretics should be avoided in elderly patients who have regular outdoor activities.
Aldosterone antagonist	Hyperkalemia, hyponatremia, spasm, diarrhea, GI symptom, gynecomastia in male	Renal failure, hyperkalemia	Helpful in HF patients Electrolyte and creatinine should be monitored during dosage increase.
CCB			
Long-acting dihydropyridines	Dizzy, blush, headache, hypotension, peripheral edema, tachycardia.		Helpful to PAD and stable CAD patients. Edema is common side effect which could be suspected of presence of HF. Social and physical activities would decrease because of edema (Walking difficulty wearing shoes).
Non dihydropyridines	Tachycardia, AVB, HF exacerbation, constipation, hypotension, fatigue, dyspnea.	More than 2nd AVB, HF	Helpful for prinzmetal angina and PSVT. Edema could be caused by diltiazem. Verapamil normally would not cause edema, but may lead to nausea, anorexia, delirium and dysfunction induced by constipation. Verapamil is not recommended in combination with a β-blocker
ACEI	Dry cough, hyperkalemia, rash, angioneurotic edema, hypotension, dizzy, fatigue, acute renal dysfunction.	Gestation, hyperkelamia, bilateral renal artery stenosis.	Helpful to HF, CAD, LVH, renal disease/proteinuria, metabolic syndrome. Its effect was approved by HYVET study. Contraindicate to suspected dehydration patient. Avoid to combine with diuretics to prevent from renal dysfunction.
ARB	Hyperkelamia, rash, angioneurotic edema, hypotension, dizzy, fatigue, acute renal dysfunction.	Gestation, hyperkalemia, bilateral renal artery stenosis	Same to ACEI. Avoid combining with ACEI or aldosterone antagonist.
Beta blocker	Bradycardia, HF, peripheral vessel contraction, bronchial spasm, fatigue, depression, dizzy, confusion, glucose dysequilibirium.	More than 2nd AVB, asthma	Appropriate for those combined with CAD, arrhythmias with rapid rhythm and CHF. Fatigue induced by B-blocker is easily overstated. Fatigue in elderly maybe due to many factors. B blockers can pass through the BBB, lead to nightmares, sleep disorders, depression and loss of consciousness. Conduction dysfunction could be worse after usage of β blocker. The risk of bradycardia can increase when combined with acetylcholinesterase inhibitor (for Alzheimer's)
Alfa receptor blocker	Dizzy, fatigue, nausea, urinary incontinence, orthostatic hypotension, syncope.	Orthostatic hypotension	Helpful for patients with prostatic hyperplasia No effect on lipids. May cause hypotension (orthostatic or postprandial), increases risk of syncope.

ACEI: angiotensin converting enzyme inhibitors; ARB: angiotensin receptor blockers; AVB: atrium ventricular block; BBB: blood brain barriers; CAD: coronary artery disease; CCB: calcium channel blocker; CHF: congestive heart failure; Ccr: creatinine clearance rate; HF: heart failure; HYVET: hypertension in the very elderly trial; LVH: left ventricular hypertrophy; PAD: peripheral artery disease.

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