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RESEARCH ARTICLE

Treatment of hypertension in older patients in 2024: What's new?

Michel Burnier, MD

Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland

michel.burnier@netplus.ch

ABSTRACT

Older individuals represent the greatest proportion of patients with arterial hypertension. For several decades, the management of old (>60-65 years) and very old (>80 years) patients with hypertension has been relatively conservative because of the paucity of scientific evidence of clinical benefits and the fear of doing more harm than good. Yet, in recent years, major changes in the therapeutic approach of older hypertensive patients have occurred leading to lower thresholds and treatment targets in most recent guidelines such as those of the European Society of Hypertension. These latter now emphasize the need to assess frailty properly in all older patients to propose the most accurate drug treatments, to start antihypertensive therapy prudently with a monotherapy in very old hypertensive patients (>80 years) and to reassess periodically the overall medications to avoid overtreatments. In this review, the recent changes in the management of older patients are discussed comparing several recent recommendations from national and international guidelines.

Keywords: prevalence, thresholds, target, blood pressure, deprescription, frailty

Introduction

In the last decade, several expert recommendations for the management of adult patients with an elevated blood pressure (BP), or hypertension, have been published by International Societies such as the European Society of Hypertension (ESH)¹⁻³, The American College of Cardiology/American Heart Association (ACC/AHA)⁴, the International Society of Hypertension (ISH)⁵, or the Korean⁶ and Japanese⁷ and Canadian⁸ Societies of Hypertension, to name some of them. In these guidelines, published between 2013 and 2023, an always delicate chapter has been the one concerning older patients because strict definitions of old age and scientific evidence-based conclusions were often lacking. Thus, one question remains the definition of the age at which patients should be considered as old. Other unresolved questions are the optimal threshold and target BPs for this population of patients considering their overall health status and comorbidities and risk factors. At last, for many years, the level of evidence from prospective randomized clinical trials has been relatively weak in this population or at least not strong enough to provide firm recommendations⁹. In this context, what has changed during the last 10 years?

Definition of older patient populations

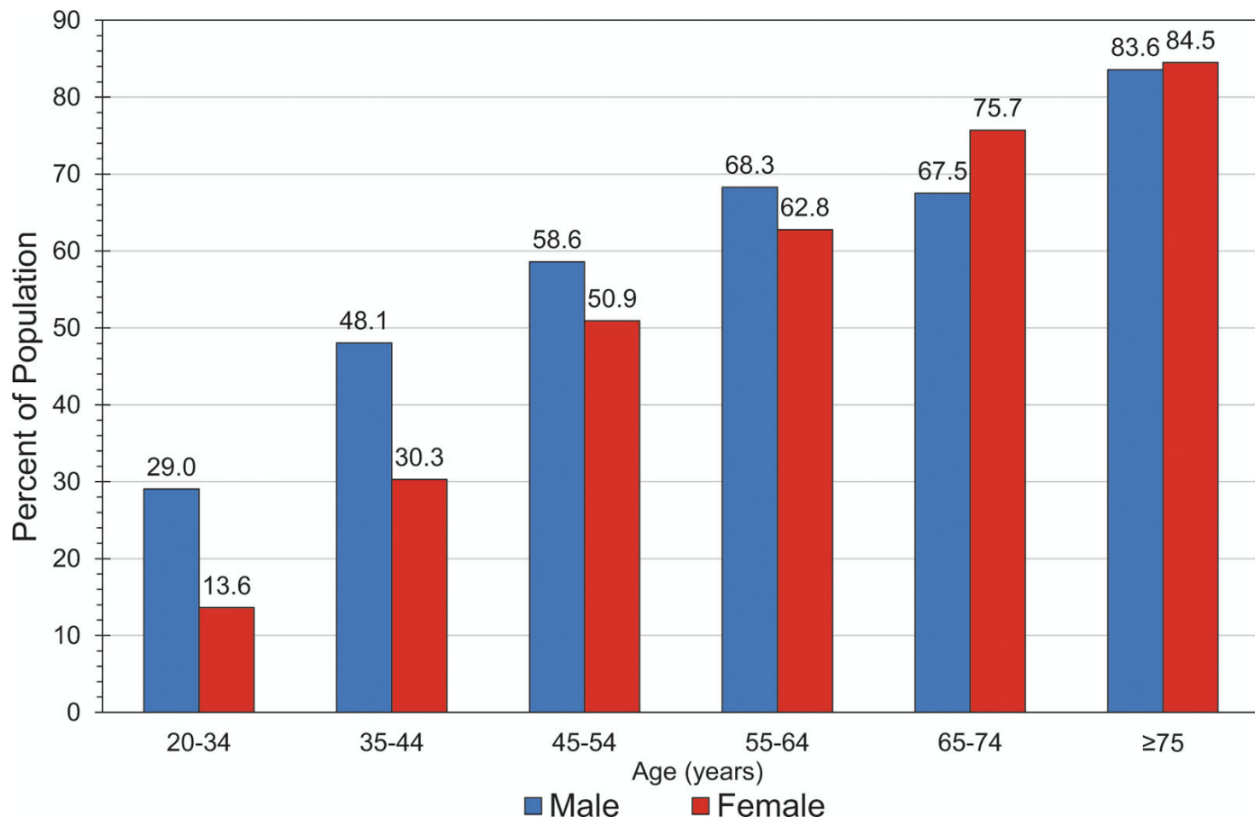
The definition of old age has varied considerably over the last 10 years starting at age 60 and evolving progressively to 65, 70, 75 and 80 years depending on the studies. Today, most guidelines define patients as old beyond the age of 65 years and very old when attaining more than 80 years^{2,4,5}. In few cases, authors include the category of centenarians for those

patients older than 100 years. However, one important modification of the approach of older patients with hypertension is to consider the biological rather than the chronological age of the patient, considering several aspects of the aging patient such as frailty, independence, comorbidities and life expectancy^{2,4,5}.

Prevalence and characteristics of hypertension in older subjects

The prevalence of hypertension is very high in subjects older than 65 years. Thus, recent American data have reported that 67.5% of men and 75.7% of women aged 65 to 74 years were hypertensive and above the age of 75 years, ~84% of the population is hypertensive¹⁰ (Figure 1). Similar figures have been reported in Europe¹¹. As blood pressure increases with age, at the age of 55 to 65 years, the lifetime risk of developing hypertension is greater than 90%¹². In addition, with the ageing population in developed countries, the number of older people needing home and institutionalized care because of loss of autonomy or cognitive decline is rapidly increasing.

Figure 1: Prevalence of hypertension in US adults ≥ 20 years of age, by sex and age (NHANES, 2015–2018) (From ref. 9).



The main characteristic of hypertension in advanced age is the development of arterial stiffness leading to the phenotype of isolated systolic hypertension with an increase in pulse pressure, this latter being now recognized as an independent cardiovascular risk factor¹³. This is the consequence of several structural and functional changes developing with age in large arteries (calcifications, atheromatous lesions, loss of elasticity, endothelial dysfunction...) ¹³. In addition, comorbidities are common in older people including a decrease in renal function, coronary heart disease, stroke, vascular dementia and cognitive dysfunction, orthostatic hypotension and impaired baroreflex sensitivity¹⁴. Today, the progressive decline in physical, psychological, cognitive, and social functions contributes to the frailty and lack of autonomy observed in a

large fraction of very old hypertensive patients. This profile of very old patients, which is now increasing sharply in several areas of the World¹⁵, has important consequences on health care systems as it augments considerably the need of home and institutionalized care. Medically, it poses also important questions regarding the therapeutic attitude that should be followed regarding for example, the management of risk factors such as hypertension.

Blood pressure thresholds to treat older patients

For several decades, whether older hypertensive adults, particularly those >80 years, should be treated or not remained controversial mainly because of the fear that BP reductions may be

harmful in some older frail individuals and may, for example, increase all-cause mortality and accelerate cognitive decline¹⁶. Today, however, the benefits of lowering BP in older hypertensive patients are no longer dismayed. Indeed, in addition to the early studies conducted in patients with isolated systolic hypertension or in patients older than 80 years¹⁷⁻¹⁹, several more recent trials²⁰⁻²² and meta-analyses²³⁻²⁶ have now confirmed that treating hypertension in patients aged 60-79 years or older than 80 years is associated with a clear reduction in cardiovascular death, major cardiovascular events and all-cause death. Thus, in 2018 ESC/ESH guidelines, the thresholds to initiate antihypertensive therapy were >140/90 mmHg for patients aged 65-79 years and >160/90 mmHg for those older than 80 years whatever the comorbidities³. The target BPs were set at 130–139 mmHg for systolic BP and to <80 mmHg for diastolic BP taking into consideration the tolerability³. A key emphasis in treating older patients, and especially the very old, was to carefully monitor for any adverse effects associated with BP-lowering treatment, because adverse effects could be more frequent than reported in trials.

Today, the BP thresholds at which antihypertensive pharmacotherapy should be started remain non-consensual among guidelines as illustrated in Table 1. According to the most recent ESH 2023 guidelines, antihypertensive treatment should be started (together with lifestyle recommendations) when BP is >140/90 mmHg in old patients (<80 y) and systolic BP is >160 mmHg in very old patients (>80 y)². However, these guidelines now consider the possibility to start at a lower BP threshold in very old patients e.g. when BP ranges between 140 and 159 mmHg, if

patients are still fit and physically active with preserved social and cognitive functions and diastolic BP is >70 mmHg². In contrast to these recommendations, ISH and ACC/AHA recommendations are more offensive. Indeed, ISH 2020 guidelines propose to start drug therapy when BP is >130/80 mmHg in individuals younger than 65 years and >140/90 mmHg when subjects are older than 65 years⁵. American recommendations do not consider age but rather the 10-year risk of developing a cardiovascular event in old patients. If the risk is below 10% the BP threshold is >140/90 mmHg but if the risk is greater than 10%, then the threshold is lowered to >130/80 mmHg⁴. However, the American College of Physicians and the American Academy of Family Physicians did not endorse the ACC/AHA recommendations considering that the level of evidence was not high enough²⁷. Hence, they rather recommend that clinicians initiate treatment in adults aged 60 years or older with systolic BP persistently at or above 150 mmHg²⁷. In patients with a high cardiovascular risk or a history of stroke or transient ischemic attack (TIA), they recommend starting or intensifying treatment based on a discussion with the patients of the benefits and potential harms of the treatment. Their main concern is the risk of overtreating the older adult population²⁷.

Table 1: Comparison of recent guidelines on the management of hypertension in adults from the European Society of Hypertension (ESH), International Society of Hypertension (ISH) and American College of Cardiology/American Heart Association (ACC/AHA).

| | ESH 2013 | ESC/ESH 2018 | ESH 2023 | ISH 2020 | ACC/AHA 2017 |
|--|---|---|---|---|---|
| Definition of older patients years (y) | >65 y | Old: 65-79 y Very Old: ≥80 y | Old: >60 or >65 y Very Old: > 80 y | Old: ≥ 65 y Very old: >80 y | ≥65 |
| BP threshold for initiation of pharmacotherapy (mmHg) | <80 y : >140/90 >80 y : >160/90 | Old ≥140/90 Very Old ≥160/90 | Old: >140 /90 Very Old: >160 Very Old: 140-159 may be considered | < 65 y: >130/80 ≥ 65 y: >140/90 | ≥130/80 if 10 y CVD risk >10% >140/90 If 10 y CVD risk <10% |
| BP targets (mmHg) | < 80 y: < 140/90 > 80 y: 140-150/90 Frail: individualize treatment | >65 y and >80 y SBP: 130-139 DBP: 70-79 Frail: individualize treatment CAVE: SBP not <120 DBP not <70 | 60-64 y: <130/80 65-79 y: <140/80 >80 y: 140-150 Consider 130-139 if DBP>70 Frail: individualize treatment CAVE : SBP not <120 DBP not <70 | < 65 y: <130/80 but >120/70 ≥ 65 y: <140/90 | <130/80 For all >130 if Multiple comorbidities Limited life expectancy Individualize treatment |
| Drug recommendations | All drugs CCB and D preferred | All drugs BB in second line Start monotherapy in very old and frail patients | All drugs including BB Cave: BB side effects Start monotherapy in very old and frail patients | All drugs Consider A +D in very old (>80 y) Start monotherapy in very old and frail patients | All drugs But BB in second line |

A: blockers of the renin-angiotensin system; BB: beta-blockers; CCB: calcium channel blockers; D: diuretics; SBP: systolic blood pressure; DBP: diastolic blood pressure; CVD: cardiovascular disease.

Blood pressure targets in old and very old individuals with hypertension

As far as BP targets are concerned, there is no real consensus between published guidelines although the general trend has been to lower BP targets in all age groups. ESH 2023 guidelines recommend specific BP targets for several age groups above 60 years². Thus, the proposed targets are <130/80 mmHg for patients aged 60-64 y, <140/80 mmHg for those aged 65 to 79 years and 140-150 mmHg systolic for those older than 80 years with or

without isolated systolic hypertension². In this latter subgroup, one may consider reaching a systolic BP between 130-139 mmHg if diastolic BP is >70 mmHg and the patient is fit. One important word of caution is that BP targets should not be below 120/70 mmHg to avoid harm. Recommendations from the International Society of Hypertension and Japanese Society of Hypertension are in the same range with a target at <130/80 mmHg in patients younger than 65 years (or between 65 and 74 years in Japan) and <140/90 in individuals older than 65 years (>75 years in

Japan)^{5,7}. Once again, ISH guidelines do not recommend targeting BP below 120/70 mmHg. ACC/AHA guidelines are simpler with a target <130/80 mmHg for all, except for high-risk patients with several comorbidities or a limited life expectancy⁴. In that case, systolic BP should remain above 130 mmHg. But once again, US family physicians and practicing physicians are more prudent proposing a systolic BP target of < 150 mmHg in adults older than 60 years. In patients with a history of stroke or TIA, the suggested target is <140 mmHg.²⁷

Interestingly, some national recommendations for the management of hypertension in adults are based essentially on the cardiovascular risk such as the 10-year global risk greater or inferior to 10 %. This is the case, for example, of Canadian and Korean Hypertension guidelines^{6,8}. According to this approach, BP thresholds are >160/100 mmHg in low risk, >140/90 mmHg in moderate to high-risk and >130 mmHg in high-risk patients. The target BP is then <120 mmHg in high-risk patients and <140/90 mmHg in low- and moderate-to-high-risk patients. In Korean hypertension guidelines, the target BP is <140/90 mmHg in older hypertensive patients without complications and a low to intermediate risk and <130/80 mmHg whenever hypertension is associated with complications or a high cardiovascular risk such as patients with coronary heart disease, heart failure, left ventricular hypertrophy or peripheral artery disease⁶.

Taken together, these recommendations tend to confirm the trend towards lower BP targets in general hypertensive population including older patients with sometimes a lower target in high-risk individuals. In the absence of

evidence for additional benefits, and perhaps increased harm, when lowering BP excessively, most guidelines do not recommend targeting BP below 120/70 mmHg.

Assessment of patients' frailty and individualization of drug treatments

The most prominent improvement in recent recommendations on the management of older patients with an elevated BP is the importance attributed to the recognition and diagnosis of frailty and cognitive impairment. Indeed, in the past, frailty was also mentioned in guidelines³, but no practical tool was proposed to help physicians or other health care providers assessing the frailty level in an easy, rapid and standardized way using a validated tool. This is now available in the recent 2023 ESH guidelines with the proposal to use a clinical frailty score before starting any antihypertensive treatment but also to monitor the evolution of this score and hence the patients' functionality and autonomy². This may help adapting the treatment strategies.

Frailty is a multidimensional syndrome, which is predictive of the risk of dependence, hospitalization, institutionalization, and death²⁸. In patients older than 80 years, the Canadian clinical frailty score is a 9 stage functional score based on the ability to perform activities of daily living either totally independently or with various levels of speed and/or external help^{29,30}. In addition, the score may be completed with an assessment of the level of cognitive dysfunction and dementia. Depending on the level of frailty, recent guidelines recommend individualizing treatment targets to avoid aggravations of cognitive function and global functionality and social life. In

accordance with this approach, family physicians from the US insist on scheduling periodic discussions of the benefits and harms of specific BP targets with the patient.²⁷

Antihypertensive drug classes recommended in older patients

A priori, all main classes of BP lowering drugs, e.g. diuretics, beta-blockers, calcium channel blockers and blockers of the renin-angiotensin system can be used to control BP in older patients. However, some guidelines propose preferences in very old patients such as the use of diuretics and blockers of the renin-angiotensin system as first line therapy in very old patients in ISH guidelines⁵ or the use of beta-blockers as second line because of a higher susceptibility to side-effects such as fatigue and sleep disturbances in older subjects in ESH guidelines². As observed in younger patients, adherence to drug therapy is an important issue³¹. Indeed, in an Italian survey, adherence with antihypertensive drug treatment was also associated with a lower risk of cardiovascular mortality in frail old patients, but the benefit is less marked than in those with a good clinical status³².

One major recommendation for very old patients (>80 years) with hypertension and comorbidities is to start with a monotherapy rather than with single-pill combinations as recommended in younger patients. Thus, the principle of *Start Low and Go Slow* is put forward for this group of patients².

Another important issue in older patients is to avoid withdrawing antihypertensive drugs based only on the criteria of age, even when patients attain an age > 80 years². If patients are well controlled, antihypertensive drug therapy

should not be stopped unless there is a strong clinical indication because treatment interruptions at this age have been associated with an increase in cardiovascular events. Nevertheless, in some circumstances it may be desirable to down-titrate or even deprescribe drugs in older patients^{33,34}, but most of the time, this does not concern BP lowering drugs but rather hypnotics or anti-inflammatory agents. Yet, a recent analysis of the benefit/risk ratio of antihypertensive in older hypertensive patients has suggested an absence of benefits in patients with hypertension older than 90 years.³⁴

Conclusion

Patients older than 65 years probably represent the largest proportion of the hypertensive population in developed countries. For many decades, the therapeutic approach of this group of hypertensive patients, particularly those older than 80 years, has been rather conservative for various reasons, among which the lack of strong evidence from prospective randomized controlled trials and the fear to cause more harm than clinical benefits. In recent years, the management strategies have changed markedly based on new studies resulting in lower thresholds to initiate drug therapy and lower therapeutic targets. Yet, recommendations remain prudent in very old patients and most guidelines emphasize the need to assess the degree of frailty, cognitive impairment, social involvement, and life expectancy in order to propose the most appropriate therapeutic plan to these patients.

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