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REVIEW, US ENGLISH

Blood pressure lowering therapy in older people: does it really cause postural hypotension or falls?

AQ3 Anam Zia[1], Shahrul Bahyah Kamaruzzaman[1,2] & Maw Pin Tan[1,2]

[1]Ageing and Age-Associated Disorders Research Group, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, and [2]Department of Medicine, Division of Geriatric Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Abstract

Hypertension is a highly prevalent condition among older people, but many physicians avoid aggressive treatment in this age group due to concerns about adverse effects such as orthostatic hypotension and falls. Orthostatic hypotension, which also increases in prevalence with increasing age, has been considered to be associated with antihypertensive therapy. Both orthostatic hypotension and antihypertensive medications are considered independent yet closely related predictors for falls among older people. The prescription of antihypertensive therapy among the elderly remains a long-standing controversy in geriatric medicine due to ongoing concerns about potential complications such as falls, despite conclusive evidence supporting the treatment of hypertension even among the very elderly. However, recent evidence suggests a dose-dependent relationship between blood pressure lowering therapy and falls among older individuals with preexisting risk factors for falls. In response to the spate of revisions in hypertension treatment targets for older patients in international guidelines and the recent evidence on antihypertensive therapy and falls, this review article examines the complex relationship ~~among~~ hypertension, antihypertensives, orthostatic hypotension, and falls among older patients.

Keywords:

aged, orthostatic hypotension, accidental falls, antihypertensives, hypertension

History

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Introduction

The prevalence of hypertension increases with age and was reported as 66.7% in United States residents aged > 60 years in the National Health and Nutritional Examination Survey of 2009–2010 [1]. The prevalence of hypertension in the population aged ≥ 50 years in middle and lower income countries in the World Health Organization's Study on Global Ageing and Adult Health is 52.9% [2]. Although hypertension is a significant risk factor for renal, cardiovascular, and cerebrovascular morbidity [3], the treatment for hypertension in the elderly is one of the most debated issues among geriatricians currently. Concerns about complications and serious adverse effects associated with the use of antihypertensive medications such as orthostatic hypotension or falls has led to a spate of revisions in guidelines for the treatment of hypertension in older people [4,5]. The 2013 European Society of Cardiology and European Society of Hypertension Joint Guidelines recommended the initiation of blood pressure lowering therapy in individuals with systolic blood pressure (SBP) of ≥ 160 mm Hg with the aim of lowering it to < 150 mm Hg, with recommendations to treat those aged < 80 years with SBP > 140 mm Hg, aiming for a target SBP of < 140 mm Hg in those who are fit and able to tolerate treatment [4]. The latest US Joint National Committee guidelines released in 2014, however, are more conservative, recommending that in individuals aged > 60 years pharmacologic treatment should be initiated at SBP > 150 mm Hg or diastolic blood pressure (DBP) > 90 mm Hg with the treatment goal to lower SBP to < 150 mm Hg and DBP to < 90 mm Hg [5].

Both of the above guidelines recommend the efficient treatment of hypertension among the older population based on cardiovascular and all-cause mortality outcomes. The major concern of a geriatrician regarding aggressive hypertension treatment is the perceived risk of falls, which generally increases linearly with age and leads to a chain of potentially devastating consequences; 39% of accident and emergency attendances in patients aged > 50 years are due to falls. One in 10 falls in older individuals results in a serious injury, and about one in five results in a fracture [6]. Death rates from falls among the elderly have also risen sharply over the past 2 decades [7]. After the first fall, the risk of recurrent falls as well as fall-associated complications multiply [8], often leading to prolonged hospitalization or early institutionalization. The psychological fear of falling, which is reported in up to 80% of fallers, results in avoidance of physical and social activity and leads to poor quality of life, depression, physical deconditioning, and increased frailty [9].

Orthostatic hypotension (OH) has been reported as an established risk factor for falls alongside other cardiovascular disorders such as carotid sinus hypersensitivity, vasovagal syncope, and cardiac arrhythmias [6]. In addition, certain classes of medications and polypharmacy are considered to

Correspondence: Maw Pin Tan, MD (UK), MRCP (UK), B MED SC (UK), MBBS (UK), Department of Medicine, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia. Tel: +60 3 79492429. Fax: +60 3 79494613. E-mail: mptan@ummc.edu.my

exacerbate OH and the other cardiovascular risk factors that subsequently lead to falls [10]. As a result, fall prevention guidelines currently recommend the withdrawal of culprit medications including antihypertensives as an intervention to reduce the risk of medication-induced OH and to prevent falls [11].

This review article summarizes the available literature on the association among antihypertensive therapy, orthostatic hypotension, and falls, so as to gain a better understanding of the complex relationship between antihypertensive therapy and the two common conditions affecting older individuals: falls and orthostatic hypotension.

Materials and methods

Targeted searches using the key terms *antihypertensives, orthostatic hypotension,* and *falls* were performed using electronic databases including PubMed, EMBASE, Web of Knowledge, and Science Direct. Relevant articles evaluating the use of antihypertensives and their association with orthostatic hypotension or falls and including older persons as participants and published in the English language were identified. We consulted recent international guidelines on hypertension (including European Joint Guidelines and US Joint National Committees guidelines), and reviewed our personal archives and relevant current textbooks.

Orthostatic hypotension and falls

Orthostatic hypotension, by consensus definition, is a sustained reduction in SBP of 20 mm Hg or in DBP of 10 mm Hg within 3 minutes of standing or head up tilt of ≥ 60° on a tilt table with reference to supine blood pressure [12]. It is not a disease in itself but rather a physical finding resulting from the complex interplay of multiple contributory factors. Orthostatic hypotension is likely to occur when there is impairment of the autonomic nervous system, decreased intravascular volume, reduced cardiac contractility, or reduced venous return. In addition, baroreflex-mediated cardio-acceleration and vasoconstriction are reduced in efficiency with age, and when superimposed with hypertension or potential culprit medications, these effects are exaggerated [13]. Due to these reasons, the prevalence of OH increases with age, ranging from 31% in individuals aged 75 to 79 years, to 35% in individuals aged 80 to 84 years, to 40% in those aged ≥ 85 years [14]. Among the community-dwelling elderly, the prevalence of OH is 18.2% [15], whereas among the hospitalized elderly it is 44% [16] due to increased frailty and greater aggregation of risk factors in the latter group.

It is postulated that the presence of OH may result in falls by causing loss of consciousness or postural instability as a result of cerebral hypoperfusion. However, the exact reproduction of symptoms of falls or loss of consciousness is rarely demonstrated in older fallers. Rubenstein *et al.* [17] suggested that OH is one of the primary causes of falls, whereas Craig [18] reported falls to be the most common presentation for OH patients, with medication-induced OH being responsible for 33% of these falls. These reports did not involve the use of case-control designs and did not acknowledge that falls are otherwise common among older patients, with > 30% of older community dwellers reporting ≥ 1 fall in the previous year regardless of the presence of OH [19]. Rutan *et al*. [15] found a weak association between OH and frequent falls, but did not report any results on the presence of falls and did not define "frequent falls." In contrast, a later study by Kario *et al*. [20] found no association between OH and falls despite demonstrating a significant relationship between lower standing SBP and falls.

Orthostatic hypotension may present as light-headedness, dizziness, blurred vision, nausea, pallor, shakiness, weakness, falls, and loss of consciousness immediately after standing [6]. The above-mentioned symptoms result from cerebral hypoperfusion, which may also be associated with other adverse events. Among the frail elderly, even a slight drop in postural blood pressure may increase the propensity to fall due to the increase in postural instability as a result of cerebral hypoperfusion [14]. In a study by Shibao *et al*. [21], 34% of patients with OH were symptomatic and 83% of these individuals with symptomatic OH experienced falls. The available evidence, therefore, indicates that the presence of the physical finding of OH alone may have no association with falls, whereas the evidence of the relationship between symptomatic OH and falls among frailer older individuals is more compelling.

Previous studies have suggested that there is overlap between OH and the neurally mediated syncope disorders, vasovagal syncope, and carotid sinus hypersensitivity. However, Tan *et al*. [22] disputed these findings and demonstrated that there is no true overlap between there conditions, but OH, vasovagal syncope, and carotid sinus hypersensitivity may coexist in a patient, adding to the challenges of accurate diagnosis of syncopal disorders in the elderly. Therefore, it is possible that the occurrence of falls in individuals results from the coexistence of the other neurally mediated disorders. Studies evaluating the relationship between falls and carotid sinus hypersensitivity have found that cardioinhibitory carotid sinus hypersensitivity is present in 23% of individuals aged > 50 years presenting to the accident and emergency departments with unexplained or recurrent falls [23]. Furthermore, in two separate studies, amnesia for loss of consciousness was found in fallers with both carotid sinus hypersensitivity and vasovagal syncope [24,25]. ~~Furthermore,~~ although amnesia for loss of consciousness has not been reported in individuals with OH, it is likely that it may also be present in fallers with OH.

Hypertension and orthostatic hypotension

The increasing trends toward obesity and sedentary lifestyles have increased the prevalence of hypertension in both the elderly and nonelderly age groups. An English study involving 3515 older individuals aged ≥ 64 years found that 81% of the authors' nationally representative population fulfilled their criteria for hypertension during ≥ 1 time point, with 76% of those with untreated hypertension presenting with isolated systolic hypertension [26]. Isolated systolic hypertension, in turn, has been found to be strongly associated with

OH [15]. The increased pulse pressure and isolated systolic hypertension that are unique to hypertension in the elderly is presumed to add to the challenges of achieving blood pressure targets in that population, as lowering of SBP could then lead to unacceptably low DBP with the potential of increased adverse events.

Although randomized controlled studies such as the Hypertension in the Very Elderly Trial (HYVET) study have clearly demonstrated significant survival benefits in blood pressure treatment even among the very elderly [26], opinions among clinicians differ with respect to the how aggressively hypertension should be treated in older patients. Many geriatricians remain skeptical, as participants of the HYVET study consisted of physically healthy older individuals who did not necessarily represent the average older person attending a geriatric service.

Twenty-five percent of clinicians tend to prescribe fewer antihypertensives to older people as they believe it would do more harm than good [27]. The commonest reason for physicians' reluctance in prescribing antihypertensives effectively is the belief that antihypertensives lead to OH [28]. However, Vischer [29] reviewed the benefits and limitations of hypertension treatment among very old persons and concluded that hypertension should be treated efficiently, and drug-induced OH should not be a reason to refrain from treating hypertension [29]. The British Women Heart and Health Study (BWHHS) involving 3775 women aged 60 to 80 years found the prevalence of OH to be 24% higher among hypertensive women with a SBP > 140 mm Hg than among normotensive women [30]. The observational cohort in the Predictive Values of Blood Pressure and Arterial Stiffness in Institutionalized Very Aged Population (PARTAGE) study involving 994 participants aged ≥ 80 years demonstrated that elderly individuals with OH had significantly higher SBP and DBP than those without OH. On the other hand, both normotensive older individuals and those with well-controlled blood pressure (SBP ≤ 140 mm Hg) had a lower prevalence of OH than those with SBP > 140 mm Hg [31]. The MOBILIZE Boston (Maintenance of Balance, Independent living, Intellect and Zest in the elderly of Boston) study involving 722 community-dwelling adults aged ≥ 70 years found that both OH and the risk of falls is 2.5 times higher in individuals with uncontrolled hypertension compared with those with controlled hypertension using a cutoff value of ≥ 140/90 mm Hg [32].

Although the above studies have demonstrated a significant association between uncontrolled hypertension and OH, the Austrian Vorarlberg Health Monitoring and Prevention Programme involving 3544 community-dwelling seniors aged ≥ 60 years found that individuals with blood pressure > 120/80 mm Hg had a significantly lower risk of falls compared to those with lower blood pressures. They reported that an increase in SBP of 10 mm Hg and DBP of 5 mm Hg is associated with a 9% reduction in falls risk [33]. However, the values cited were not within the hypertensive range, and sitting blood pressure was measured without considering postural blood pressure changes.

The Irish Longitudinal Study on Ageing (TILDA) research group classified orthostatic hypotension into three groups: a small drop in blood pressure with fast recovery, a medium drop with slow recovery, and large drop with no recovery. They found that severe OH with slow or no recovery was associated with uncontrolled systolic hypertension [34]. As previous studies had not evaluated the patterns of blood pressure drop in their OH subjects, the significance of the three classifications remains unclear. However, the study clearly showed the association between higher blood pressure readings and OH. The mechanism of this association can be partly explained by the assumption that normotensive individuals and those with treated hypertension have less arterial stiffness, improved baroreflex sensitivity, and consequently less OH as compared with hypertensives [35,36]. Although the above body of evidence suggests that OH is more prevalent among individuals with uncontrolled or untreated hypertension, there has been no published intevention study to date determining whether effective treatment of hypertension can reduce the severity of OH.

Is blood pressure lowering therapy associated with orthostatic hypotension?

Older patients are more sensitive to adverse drug events due to age-related changes in pharmacokinetics and pharmacodynamics. Furthermore, due to changes in drug handling abilities and an increase in comorbidities, drug–drug interactions, drug–disease interactions, and polypharmacy also increase the risk of adverse events with ~~the~~ increasing age. ~~However,~~ as medications are prescribed in response to illness, OH may occur either as a direct result of the medication or the consequence of an underlying illness, or a combination of both factors. Orthostatic hypotension is attributed to diseases like hypertension, diabetes, and parkinsonism [37], and is also widely considered to be a side effect of commonly prescribed medications for these conditions.

The effects of antihypertensive medication withdrawal on OH have been evaluated in a handful of limited studies (Table I). Fotherby and Potter [38] withdrew antihypertensive therapy from 47 subjects with blood pressure ≤ 175/100 mm Hg and reported a decrease in the prevalence of OH in the antihypertensive withdrawal group, whereas the prevalence of OH remained unchanged in the group that continued their antihypertensive therapy but only after exclusion of those with blood pressure > 175/100 mm Hg [38]. The antihypertensive therapy evaluated in this study consisted mainly of diuretics, calcium channel blockers, and β-blockers, as newer antihypertensive agents such as angiotensin receptor blockers (ARBs) were not yet available at the time of the study. In another study in which all cardiovascular medications (antihypertensive, antiarrhythmic, and antianginal medications) were withdrawn, 78% of subjects reported improvement in symptoms of syncope and falls and the physical finding of OH. Furthermore, the renewal of medications was not necessary in 70% of the group [39]. However, the criterion for antihypertensive withdrawal was a patient on antihypertensive therapy with blood pressure of ≤ 120/80 mm Hg, suggesting that withdrawal only occurred in individuals with overtreated hypertension.

Van der Velde *et al*. [40] also found the withdrawal of these culprit drugs to be effective in the resolution of OH. In

Table I. Summary of studies evaluating the relationship between antihypertensive medications with falls and OH.

Ref.	Participants	Study design	Findings[a]
Fotherby and Iqbal. 1997 [51]	Hospital inpatients aged ≥ 60 years	Cross-sectional study	OH was not associated with antihypertensive treatment in the elderly
Ooi *et al*. 2000 [52]	844 people ≥ 65 years from nursing homes	Prospective cohort study	OH was not associated with the first fall, but among subjects with history of falls, those with OH had an increased risk of recurrent falls (RR, 2.1; 95% CI, 1.4–3.1)
Kario *et al*. 2001 [20]	266 community-dwelling elderly ≥ 65 years	Prospective study	Lower SBP on standing is associated with falls independently, but OH is not associated with falls. Antihypertensive therapy does not increase the falls risk (RR, 0.58; 95% CI, 0.29–1.2)
Heitterachi *et al*. 2002 [53]	70 participants aged 60–90 years	Prospective study	OH was significantly associated with falls (RR, 1.71; 95% CI, 1.14–2.59). Antihypertensives were strongly associated with OH but not with falls (RR, 0.91; 95% CI, 0.60–1.51). Other causes of OH need to be evaluated as antihypertensives are not related with falls
Fisher *et al*. 2003 [27]	119 patients aged > 80 years from residential care facilities	Case-control study	There was no significant association between antihypertensives and OH (OR, 0.8; 95% CI, 0.3–1.7) and antihypertensives and falls (OR, 0.8; 95% CI, 0.4–1.6).
Poon and Braun. 2005 [54]	342 elderly from geriatric clinic	Retrospective study	Prevalence of OH increased with the increase in number of culprit medicines including antihypertensives prescribed ($X^2 = 15.18$; $p = 0.002$) and was predictor of falls. Study is about the whole culprit medication group, but among antihypertensives thiazides were the most frequently used by patients having OH
Kamaruzzaman *et al.* 2010 [30]	4286 women aged 60–80 years recruited from general practice lists	Cross-sectional substudy of a large prospective study	OH was associated with ≥ 3 hypertensives (OR, 2.24; 95% CI, 1.47–3.40; $p < 0.001$). No other antihypertensives were associated with OH except β-blockers (OR, 1.58; 95% CI, 1.19–2.09; $p < 0.01$). This medication induced OH was not associated with falls
Gribbin *et al*. 2010 [49]	9682 participants aged > 65 years from primary care	Prospective case-control study	Thiazide diuretics were found to increase the risk of first fall significantly (OR, 1.25; 95% CI, 1.15–1.36), no other antihypertensive showed any significant association with falls
Shuto *et al*. 2010 [55]	349 patients who fell during hospital stay	Case-control study	Antihypertensives were strongly associated with falls risk (OR, 8.42; 95% CI, 3.12–22.72). As the patients are hospitalized, use of antihypertensive with another risk factor such as frailty may lead to falls
Coutaz *et al*. 2012 [16]	388 hospitalized elderly patients	Cross- sectional study	Antihypertensive therapy does not increase the risk of falls even in the presence of OH
Wong *et al*. 2013 [50]	520 community-dwelling older adults	Prospective cohort study	Antihypertensive medications were not associated with falls (OR, 1.05; 95% CI, 0.37–2.93). Angiotensin system blocking medicines showed protective effects against falls (OR, 0.68; 95% CI, 0.48–0.97)
Butt *et al*. 2013 [56]	543 572 new elderly users of antihypertensives	Prospective study	New antihypertensive users have 69% increased risk of having a fall (RR, 1.94; 95% CI, 1.75–2.16). This finding was consistent for thiazide diuretics, angiotensin-converting enzyme inhibitors, calcium channel blockers, and β-blockers, but not for angiotensin receptor blockers
Callisaya *et al*. 2014 [46]	409 participants aged 60 to 86 years randomly selected from community	Prospective population-based cohort study	Antihypertensives as a group were not associated with falls; however, higher dose of antihypertensives was independently associated with greater fall risk (RR, 1.07; 95% CI, 1.02–1.11; $p = 0.004$). The risk was 48% higher in those with > 3 times the daily defined dose (RR, 1.48; 95% CI, 1.06–2.08; $p = 0.02$)
Tinetti *et al*. 2014 [45]	4961 community-dwelling hypertensive older adults aged > 70 years	Prospective population-based cohort study	Antihypertensive medications by number or class were not associated with serious fall injuries, but in participants with previous falls or injurious falls use of high-intensity daily defined doses of antihypertensives was associated with serious fall injuries (HR, 2.31; 95% CI, 1.01–5.29)
Kuschel *et al*. 2014 [44]	64 399 community-dwelling persons aged ≥ 65 years	Case-control study	Twenty commonly prescribed medications were tested, and antihypertensives showed a protective effect against falls. The protective effect was highest for ACEIs and calcium channel blockers

[a]Risks are presented as OR, RR, and HR with 95% CI.
Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; HP, hazard ratio; OH, orthostatic hypotension; OR, odds ratio; RR, risk ratio.

addition, the withdrawal of cardiovascular drugs produced significantly larger reductions in OH than the withdrawal of psychotropic medications and other drugs. The authors reported that the drugs were withdrawn only if they were duplicative or if withdrawal was considered safe, but no clear cutoff values for BP or duplicative classes on antihypertensives were reported. The above studies citing the reduction in OH with the withdrawal of antihypertensive agents did not include longitudinal follow-up data on cardiovascular end points or all-cause mortality. We are therefore unable to

define the benefits of withdrawing antihypertensive agents and the extent to which they could be safely withdrawn.

Intensely prescribed antihypertensive therapy, however, could increase the risk of OH. Intensive hypertensive treatment could be determined by higher doses of antihypertensive medications, increased number of antihypertensive drugs, or lowering blood pressure to a target < 140/90 mm Hg. It has been suggested that the total number of blood pressure lowering medications [41] or the use of ≥ 3 antihypertensive drugs is a significant predictor of OH [30]. Conversely, a study by Hiitola *et al*. [14] reported that OH was associated only with the total number of medications consumed but not with any particular antihypertensive medications or the number of cardiac medications. However, in Hiitola *et al*.'s study the use of medications was very high, with participants taking up to 23 medications. To date, there have been no studies linking the dosage of antihypertensives with OH.

The degree of association of antihypertensives with OH differs according to the individual classes of blood pressure lowering medications. Angiotensin-converting enzyme inhibitors (ACEIs), ARBs, and calcium-channel blockers are less likely to be associated with OH compared with β-blockers and thiazide diuretics. The PARTAGE study reported that β-blockers had a significantly higher impact on OH due to increased sympathomimetic activity, whereas OH was less common among ARB users [31]. Supporting this evidence, the TILDA study reported an association between OH with β-blockers and α-blockers, whereas calcium channel blockers were shown to be protective against OH. Except for one study in which thiazides were found to be protective [27], most previous studies suggest that thiazides are associated with OH [30]. A randomized, double-blind trial comparing the use of an ARB and a thiazide diuretic with an ARB and a calcium channel blocker found that both combinations were equally effective in controlling high blood pressure, but the ARB and thiazide combination group was more likely to develop OH [42].

The evidence from older studies linking blood pressure lowering drugs to postural hypotension can be considered relatively outdated, as most of the studies were performed while patients were on older hypertensive medications such as methyldopa, prazosin, thiazide diuretics, or propranolol, which had more side effects and a higher propensity to cause orthostatic hypotension. The newer antihypertensive agents such as ACEIs and ARBs that have been developed in response to the unsatisfactory side effects of older antihypertensive medications have fewer side effects and better compliance profiles [42]. Therefore, there is an urgent need for well-designed studies to measure the risk of adverse cardiovascular and mortality outcomes of withdrawal of blood pressure lowering therapy.

Is blood pressure lowering therapy associated with falls?

Although antihypertensives have been considered culprit medications for falls among older individuals, published evidence supporting this assumption has been limited. A meta-analysis by Zang [43] involving 42 studies concluded that there is no clear evidence for the association between blood pressure lowering medications and serious and injurious falls. However, the use of higher doses of antihypertensives in the presence of other risk factors including frailty, history of previous falls, and very old age may be associated with falls. In a case-control study involving 64 399 older fallers admitted to a hospital in Sweden, cardiovascular medications were actually found to be protective against falls [44].

Two recently published studies have provided further insight into this relationship. Using the Medicare Current Beneficiary Survey Cohort of 4961 participants, Tinetti *et al*. [45]. demonstrated that among patients with a previous fall higher intensity antihypertensive treatment was significantly associated with future serious falls. The mean age of the cohort in the study was 80 years. In another study that evaluated the dosage of hypertensives and falls among participants aged 60 to 86 years, a higher dosage of antihypertensives was independently associated with falls [46]. However, patients with mild and moderate doses had a mean SBP of 145 mm Hg, whereas individuals with higher doses had a mean blood pressure of 135 mm Hg. In addition, the participants with higher daily doses had a higher prevalence of falls at baseline.

The available evidence, therefore, suggests that in robust older individuals, aggressive blood pressure lowering therapy is beneficial, whereas in frail individuals with predilection to falls, blood pressure lowering therapy may increase the risk of falls in a dose-dependent fashion. In frail individuals with a high risk of falls, blood pressure lowering therapy should be initiated and monitored cautiously, and the withdrawal of antihypertensive therapy may reduce further the risk of falls in this group. Butt *et al*. [47] found the initiation of antihypertensive therapy to be associated with a 43% increased risk of hip fracture. Although van der Velde *et al*. [48] found a significant reduction in the incidence of falls following the withdrawal of all potential culprit drugs, including antiarrhythmics, nitrates, digoxin, analgesics, antihistamines, and antiparkinsonian and hypoglycemic agents, in patients attending their geriatric outpatient clinic, the benefit was greatest with the withdrawal of cardiovascular medications.

The evidence for individual classes of antihypertensive medications and falls is less robust than that for OH. The risk of falls has been found to be higher within the first 3 weeks of diuretic treatment, whereas there was no significant association between other antihypertensive medications and falls [49]. Angiotensin-converting enzyme inhibitors showed a negative association with falls in a recent report [34]. In another recent prospective study involving 520 community-dwelling participants, there was again no association between cardiovascular drugs and falls. In fact, angiotensin system blocking medications (ACEIs and ARBs) were found to be protective against falls after adjusting for confounders [50].

The possible mechanisms by which blood pressure lowering medications are associated with falls remain unclear. It has often been assumed that the relationship between antihypertensive medications and falls may be explained by the increased risk of OH in individuals treated with the blood pressure lowering drugs. To date, there has been no published

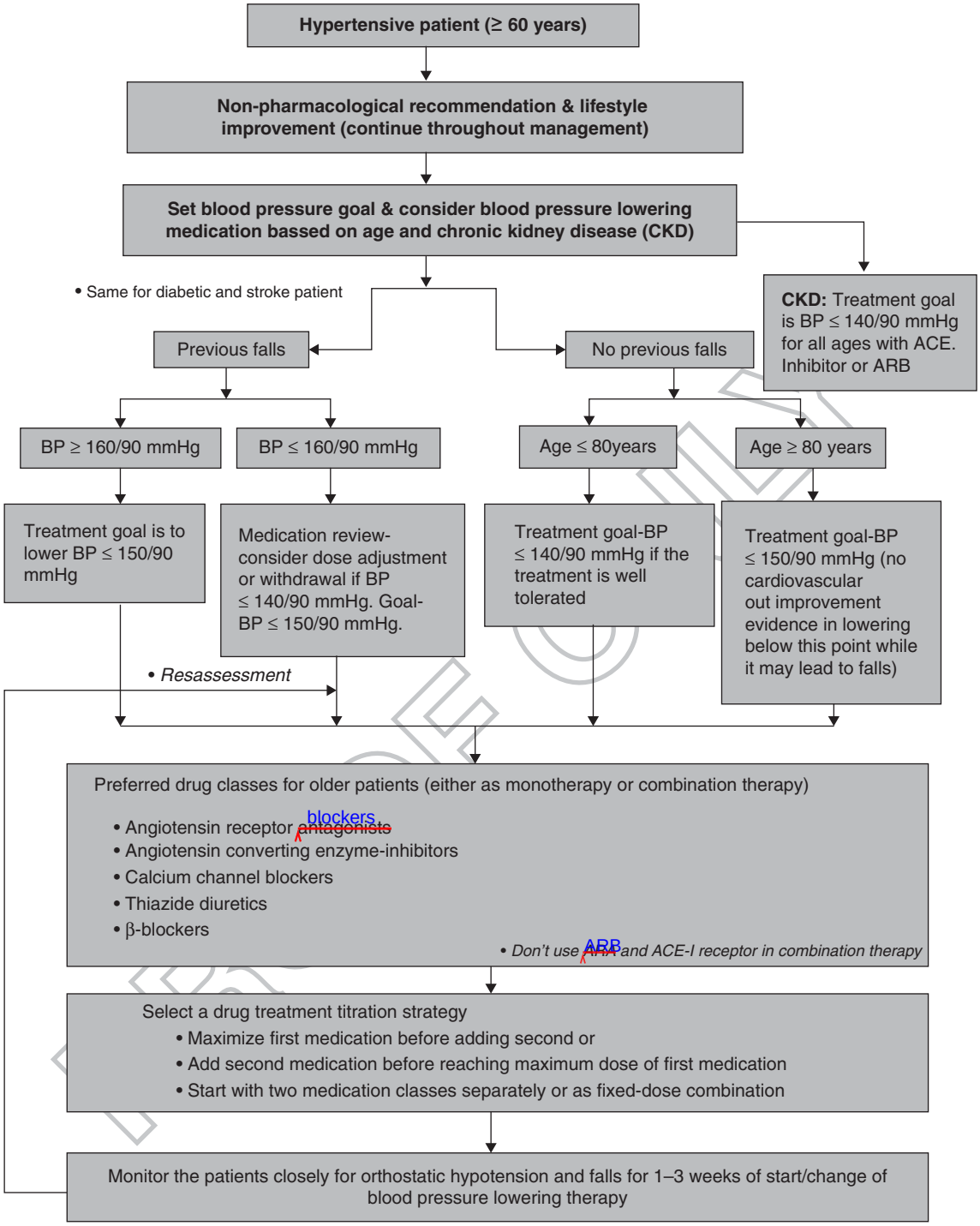

Figure 1. Flowchart for the management of hypertension among older individuals.

study directly linking medication induced OH with falls among older patients [13] or evaluating the effects of continuation or withdrawal of therapy in a longitudinal manner. Therefore, the risk of falls in individuals on blood pressure lowering medications may actually be attributable to underlying cerebrovascular disorders associated with hypertension and aging, rather than the direct side effects of the antihypertensive medications. Similarly, it remains to be established whether withdrawal or dose adjustment of antihypertensive medications alone is associated with prospective reductions in falls. Such a study should take into account the potential increased risk of cardiovascular end points that may be associated with the reduction in blood pressure control.

Management of hypertension in older patients

Figure 1 is a flowchart of the recommended treatment strategy of hypertension in older fallers and non-fallers based on the current guidelines and available evidence [4,5]. Prior to prescribing any blood pressure lowering treatment, the physician should take into account the factors of age and a previous history of falls and frailty. Intensive blood pressure

treatment should be prescribed among robust older individuals aged < 80 years. In individuals aged ≥ 80 years, it is currently not advisable to treat high blood pressure aggressively. In individuals with established risk factors for falls, aggressive blood pressure lowering treatment should be avoided, and in individuals previously on antihypertensive treatment with a treatment target of < 140/90 mm Hg, their treatment targets should be revised to < 150/90 mm Hg, and medication withdrawal should be considered. Close monitoring is required for the potential onset or exacerbation of OH in these individuals, particularly in the first month of initiation of therapy. The blood pressure lowering agents ARB, ACEI, and calcium channel blockers should be used preferentially, especially among patients at high risk of falls, as diuretics and β-blockers have been found to be associated with OH and falls and should be avoided in at-risk individuals. Should any older individual on antihypertensive treatment sustain a fall, the blood pressure management should be revised and treatment targets adjusted accordingly.

Conclusion

This review article has mapped the landscape surrounding the relationship between OH and falls. The role of blood pressure lowering medications in both these conditions ~~was~~ is reviewed, and areas for future research ~~were~~ are highlighted. We have found that the evidence for OH and falls induced by antihypertensives is weak. The use of blood pressure lowering treatment alone is not associated with falls, but in the presence of risk factors higher intensity treatment may be associated with falls. The presence of untreated or uncontrolled hypertension is associated with OH, with adequate treatment of hypertension potentially reducing the risk of developing OH as well as falls. Therefore, robust older individuals may benefit from intensive blood pressure lowering therapy with a treatment goal of 140/90 mm Hg. Among individuals with preexisting symptomatic OH or individuals with a history of falls, a more cautious approach with a treatment goal of 150/90 mm Hg is recommended. However, current recommendations are not a substitute for clinical judgment, and antihypertensive therapy in older people needs to be highly individualized according to the patient's age and physical condition. For future research, longer term randomized controlled studies are urgently required to determine the net risk-to-benefit ratio of aggressive blood pressure lowering and withdrawal of culprit medications against the potential risk of OH and falls.

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