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Review Article

Management of blood pressure in stroke

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ABSTRACT

Objective: In this review and opinion piece, we discuss recent United States (US)-based guidance statements on the management of BP in stroke according to stroke type and stage of stroke.
Methods: We reviewed the most recent guidance statements on BP control from United States (US)-based organizations such as the American Heart Association/American Stroke Association (AHA/ASA) and American College of Cardiology (ACC), and articles available to the authors in their personal files.
Results: The key BP target before starting alteplase (t-PA) is < 185/110 mm Hg, and the maintenance BP after tPA administration is < 180/105 mm Hg. For IPH patients with systolic BP between 150 and 220 mm Hg and no contraindication to acute BP reduction therapy, acute lowering to 140 mm Hg systolic BP is safe. For persons with small vessel or lacunar cerebral ischemia, a reasonable BP lowering target is < 130 mm Hg systolic. For primary stroke prevention, the target BP for those with hypertension is < 140/90 mm Hg and self-measured BP is recommended to assist in BP control. Recent study and guidance suggest a BP target of <130/80 mm Hg for both primary and recurrent stroke prevention. BP control is reasonable for the prevention of cognitive decline or dementia.
Conclusions: BP targets for the proper management of stroke vary by chronological stage of stroke and by stroke subtype. Furthermore, consideration should be given to control of BP variability, especially in the acute phases of stroke, as it may play a role in conferring longer term outcomes.

1. Introduction

Proper management of blood pressure (BP) is an important theme for the acute treatment and prevention of first and recurrent stroke [1,2]. During the past 5–10 years, a number of new trials and guidance statements on the prevention and treatment of stroke have been published. In this review article and opinion piece we address the management of BP in relation to acute treatment, recurrent and first stroke prevention, and maintenance of cognition. The focus of the review is ischemic and hemorrhagic stroke subtypes, and each topical section includes discussion of background information, relevant guidance statements, and practical management advice. We conclude with a discussion of BP control for the maintenance of cognition, a topic that has recently received renewed attention. The publication does not have a formal literature review. Instead, we rely on the most recent guidance statements on BP control from United States (US)-based organizations such as the American Heart Association/American Stroke Association (AHA/ASA) and American College of Cardiology (ACC), and articles available to the authors in their personal files of predominantly clinical trials and major observational studies in the field.

2. Management of blood pressure in acute ischemic stroke

2.1. Background information

Controversy has shrouded the proper management of BP in acute ischemic stroke (AIS) [1]. AIS may be characterized by islands of infarcted cerebral tissue surrounded by potentially salvageable brain referred to as ischemic penumbra. Furthermore, the areas of cerebral infarction may have lost the ability to autoregulate and have increased

Abbreviations: AIS, acute ischemic stroke; BP, blood pressure; BPV, blood pressure variability; CBF, cerebral blood flow; IPH, intraparenchymal hemorrhage of the brain; tPA, tissue plasminogen activator (alteplase).

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blood vessel permeability [1]. Theoretically, in AIS a too aggressive approach to lowering of BP could lead to extension of cerebral infarction and worsening of neurological deficits. On the other hand, if BP is too high the local ischemic leaky blood vessels may serve as a conduit for occurrence of brain edema and hemorrhagic transformation of the brain infarct, and lead to neurologic deterioration. In normal persons, cerebral blood flow (CBF) is maintained as brain blood vessels are able to vasodilate and vasoconstrict. In persons with hypertension, however, the autoregulatory curve is shifted to the right, and these persons may be at higher risk that CBF will not be maintained when BP is more aggressively lowered [1].

2.1.1. Blood pressure variability and related metrics

Newer data suggest that the circumstances in relation to BP in AIS may be more complex as demonstrated by a series of studies from Korea [3–6]. Specifically, these studies characterize the influence of BP variability (BPV) and related metrics in relation stroke outcomes. BPV is a fluctuation of BP and is measured in a number of ways such as maximum-minimum, standard deviation or coefficient of variation of systolic or diastolic BP [3–6].

In a first study among 2271 AIS patients enrolled within 72 h of stroke onset and followed for a median of 8.7 days, BPV as measured by coefficient of variation, standard deviation, and standard deviation of the maximum-minimum for systolic BP, but not mean systolic BP, was independently associated with poor functional outcome at 3 months post stroke [3]. In a second observational study of 1161 AIS patients, BPV was independently and linearly associated with occurrence of early neurologic deterioration defined as an increase of at least 2 points on the National Institutes of Health Stroke Scale [4]. In a third study, a large registry-based one of 9840 AIS patients enrolled during the first 3 days of stroke onset, pulse pressure was shown to have nonlinear j-shaped associations with the occurrence of major vascular events and stroke recurrence during a 1-year follow up period [5]. In addition, pulse pressure had stronger predictive power than other commonly measured BP metrics such as systolic or diastolic BP [5]. Finally, 8376 AIS patients enrolled in a multi-center registry were categorized according to 5 systolic BP trajectory groups (low, moderate, rapidly stabilized, acutely elevated, and persistently high) within 24 h of stroke onset [6]. The risk of subsequent vascular events was significantly higher among those with acutely elevated and persistently high systolic BP trajectories [6].

2.2. Key guidance statements

The most relevant recent US guidance statement for BP management in AIS patients originates from AHA/ASA (2018) [7]. At the time of development of this manuscript, this guidance statement was undergoing revision [7]. Table 1 provides a summary of BP targets according to whether or not intravenous tissue plasminogen activator (tPA) (alteplase) or other endovascular therapy is administered, and Table 2 summarizes select acute BP control management strategies in AIS [7]. The key BP target before starting tPA (alteplase) is < 185/110 mm Hg, and the maintenance BP after tPA (alteplase) administration is < 180/105 mm Hg.

Table 1
Blood pressure targets in acute ischemic stroke [7].

Intravenous tPA (alteplase) Administration
1. If intravenous tPA (alteplase) is to be administered, carefully lower systolic BP to < 185 mm Hg and diastolic BP < 110 mm Hg before initiating fibrinolytic therapy.
2. In the first 24 h after intravenous tPA (alteplase) administration, maintain BP < 180/105 mm Hg.

Intra-arterial Fibrinolysis or Mechanical Thrombectomy Administration

The same BP targets and time windows are used for intra-arterial fibrinolysis or mechanical thrombectomy administration as are recommended before and after intravenous tPA (alteplase) (see above).

If the AIS Patient is Not an Intravenous tPA (alteplase), Intra-arterial Fibrinolysis or Mechanical Thrombectomy Candidate
1. If BP >/ = 220/120 mm Hg, it is reasonable to lower BP by 15% during the first 24 h.
2. If early treatment of hypertension is indicated for comorbid conditions (e.g., acute heart failure, acute coronary event, etc.), lowering BP by 15% is likely to be safe.

Restarting or Starting Antihypertensives During Hospitalization, if BP > 140/90 mm Hg
1. BP lowering is likely to be safe if the AIS patient is medically and neurologically stable, and there are no contraindications to BP lowering. The time window for administration of such therapy is often times 2 or 3 days after AIS onset.

2.3. Practical management advice

The AHA/ASA guidance statement (2018) serves as the main practice advice for the management of BP in AIS [7]. If intravenous tPA (alteplase) or endovascular therapy is implemented, the AHA/ASA BP targets and BP-lowering strategies should be followed (see Tables 1 and 2) [7]. Recent clinical trials such as Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial −2 (RIGHT-2), Efficacy of Nitric Oxide in Stroke (ENOS), and China Antihypertensive Trial in Acute Ischemic Stroke (CATIS) did not show improvement in functional outcome including death with BP lowering in acute stroke patients [8–10]. In another trial, Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED), the intensive BP control arm (systolic BP 130–140 mm Hg vs. standard BP lowering) did not show improvement of functional outcome at 90 days, however, fewer patients in the intensive BP control group had intracranial hemorrhage [11]. The latter finding may merit further exploration as a means to reduce hemorrhagic risk in persons receiving intravenous tPA (alteplase).

If intravenous tPA (alteplase) or endovascular treatment is not contemplated and there is no compelling medical condition to dictate acute BP lowering, AIS patients with BPs up to 220/120 mm Hg may be observed without BP lowering therapy in the first several days after stroke onset and before starting or restarting BP lowering therapy [12]. This strategy is referred to as 'permissive' hypertension. Some AIS patients with symptomatic high-grade large artery occlusive disease (e.g., basilar or carotid arteries) may deteriorate with lowering of BP and clinically manifest with worsening of neurologic signs [12]. Although unproven, strategies to augment BP (e.g., fluid challenge or vasopressor administration) may be tried in an attempt to improve CBF in such patients.

BPV should be minded and consideration given to treating and stabilizing elevated BP (e.g., systolic BP > 220 mm Hg) relatively soon after AIS and reducing fluctuations in BP in AIS patients [3–6]. It is reasonable to lower BP by 15% during the first 24 h after stroke onset.

There is evidence to suggest that although BP reduction in AIS if carefully done is safe, there may be worsening of secondary outcomes weeks to months later [13]. Thus, it may be prudent to delay BP lowering for several days after AIS for recurrent stroke prevention until the patient is medically (i.e., has suitable oral or enteral access) and neurologically (i.e., non-fluctuating neurological status) stable [12]. Once BP lowering medication is initiated for recurrent stroke prevention, getting to the BP goal (e.g., systolic BP < 130 mm Hg) is a trial and error process based on the patient's ability to tolerate BP lowering. Initiation of BP lowering therapy is recommended when BP is >/ = 140/90 mm Hg. An angiotensin converting enzyme inhibitor or angiotensin receptor blocker with a thiazide diuretic may be administered, however, getting BP to the

Table 2
Select blood pressure management strategies in acute ischemic stroke [7].

Labetolol 10–20 mg intravenous over 1–2 min and may repeat 1 time, or
Nicardipine 5 mg/h intravenous, titrate up by 2–5 mg/h every 5–15 min, maximum 15 mg/h; or
Clevidipine 1–2 mg/h intravenous, titrate by doubling the dose every 2–5 min (maximum 21 mg/h).
Other agents: hydralazine, enalaprilat.
If BP is not controlled or diastolic BP > 140 mm Hg, one may administer intravenous nitroprusside (may increase intracranial pressure).

target level is the main goal, and thus other oral BP lowering medication classes may be used.

3. Management of blood pressure in acute intraparencyhmal hemorrhage

3.1. Background information

Patients with intraparenchymal hemorrhage of the brain (IPH) frequently have elevated BP at onset of stroke [14]. Approximately 1/3 of such patients who present within several hours of an IPH have significant expansion of the hemorrhage within 24 h after onset. Hematoma expansion is a challenge for the clinician as it is associated with higher mortality and risk of neurologic deterioration. Acute lowering of BP after IPH has been considered a strategy to stunt hematoma growth [14], and pivotal clinical trials have been carried out to definitively determine if BP lowering is beneficial in IPH (discussed below in section 3.2).

Similar to AIS it has been shown that BPV may predict poor outcome in IPH [15]. Among 782 IPH patients enrolled in 2 healthcare systems over a 10-year time period, systolic BPV in the first 24 h of hospital admission including a novel index of BPV called functional successive variation, was associated with unfavorable in-hospital outcome (i.e., modified Rankin Scale disability score of 4–6) [15].

Perihematomal edema, a biomarker of secondary brain injury, appears as a ring of hypodensity around the IPH density depicted on cranial computed tomography [16]. In the Antihypertensive Treatment of Acute Cerebral Hemorrhage-2 (ATACH-2) trial, intensive BP lowering was associated with a reduction in the perihematomal edema expansion rate in deep IPH and with poor clinical outcome when there was basal ganglia brain hemorrhage [16]. The existence of a perihematomal ischemic zone, however, is the subject of controversy, as a study has shown that low blood flow around the hematoma may be secondary to reduced cerebral metabolism or possibly represents extravasation of plasma [14].

3.2. Key guidance statements

The most recent focused US-based guidance statement for the management of BP in IPH is from the ASA/AHA (2015) [17]. The main BP lowering recommendations according to the guidance statement are as follows:

1. For IPH patients with systolic BP between 150 and 220 mm Hg and no contraindication to acute BP reduction therapy, acute lowering to 140 mm Hg systolic BP is safe and may be effective to improve functional outcome; and
2. For IPH patients with systolic BP > 220 mm Hg, it may be reasonable to implement aggressive BP lowering with a continuous intravenous infusion and to initiate frequent BP monitoring [17].

The above recommendations were influenced by the Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage-2 (INTERACT-2) trial, a pivotal study comparing intensive BP lowering (<140 mm Hg systolic BP) vs. standard lowering (<180 mm Hg systolic BP) within 6 h of IPH by administration of a variety of intravenous and oral BP lowering agents based on local protocols [18]. Although the primary outcome, death or major disability, did not quite reach statistical significance favoring the intensive treatment group, secondary endpoints such as functional recovery based on an ordinal analysis and quality of life did [18]. Furthermore, there was no significant effect of intensive BP lowering on hematoma expansion, although BP lowering was safe. The ATACH-2 trial, another pivotal study of intensive BP treatment (110–139 mm Hg systolic BP) vs. standard BP therapy (140–179 mm Hg systolic BP) within 2 h of IPH onset, showed no significant benefit of the intervention on poor clinical outcome at 3 months or hematoma expansion [19]. ATACH-2 utilized intravenous nicardipine [19] and was published after the AHA/ASA focused guidance on IPH was released [17].

In subsequent publications from the above 2 studies, an exploratory analysis of the ATACH-2 data showed that intensive BP lowering was associated with reduction of hematoma growth when there was deep IPH (i.e., basal ganglia hemorrhage) [20]. Furthermore, in a preplanned pooled analysis of individual patient data from the 2 trials, achievement of early and stable systolic BP was safe and associated with favorable clinical outcomes in acute IPH [21]. In the pooled analysis, the mean magnitude of early systolic BP reduction was 29 mm Hg with a mean systolic BP of 147 mm Hg. Symptomatic hypotension occurred in 1%, serious renal events in 1%, and serious cardiac events in 3% [21]. Thus, the pooled analysis supports the value of early and stable systolic BP reduction.

3.3. Practical management advice

In the acute phase of IPH if systolic BP is > 220 mm Hg it may be reasonable to administer continuous intravenous BP lowering medication [17,22]. For those with systolic BP between 150 and 220 mm Hg, it is reasonable to lower BP to the 140 to 150 or 160 mm Hg range. Lowering systolic BP to <140 mm Hg may be associated with harm, especially if done too quickly and in a pronounced manner [19,22,23]. The choice of BP lowering agents is at the discretion of the clinician though those used in the ATACH-2 or INTERACT-2 trials may be considered [18,19]. Additionally, BPV in IPH may have a detrimental effect on clinical outcome, and it may be worth attempting to control fluctuation of BP [23]. Finally, although the optimal time to start BP lowering therapy after IPH in relation to recurrent stroke prevention is not known, a target BP of <130/80 mm Hg is recommended [17]. Furthermore, BP lowering treatment may be started when the patient is considered to be medically and neurologically stable. Paradoxically, early reductions in mean arterial pressure may be associated with ischemic brain injury thought to be associated with an active vasculopathy as an underlying mechanism [24].

Table 3 summarizes practical management advice for hypertension in IPH.

4. Recurrent stroke prevention

4.1. Background information

Of an estimated 795,000 incident strokes in the US annually, almost 25% are recurrent strokes [25]. Stroke may be broadly divided into ischemic and hemorrhagic types and further subdivided into ischemic subtypes (e.g., large artery atherosclerotic occlusive disease, lacunar or small vessel infarction, cerebral embolism including cardiac source embolism, non-atherosclerotic stroke, and cryptogenic stroke) and hemorrhagic subtypes (e.g., IPH, subarachnoid hemorrhage and intraventricular hemorrhage) [26]. It is generally accepted that any

Table 3
Practical management of hypertension in intraparenchymal hemorrhage.

1. If systolic BP is > 220 mm Hg, it is reasonable to administer continuous intravenous BP lowering therapy (see Table 2 for select intravenous treatment options) [17]. Initial BP lowering by 15% is generally safe.
2. If systolic BP is in the 150–220 mm Hg range, aim for a systolic BP in the 140–150 or 160 mm Hg range.
3. Control of blood pressure variability may be useful.
4. Too fast and too pronounced acute BP lowering (e.g., to <140 mm Hg) may be harmful.
5. Choice of acute BP lowering agents is at the discretion of the clinician, however, use of BP lowering agents as in the ATACH-2 and INTERACT-2 protocols may be considered [18,19].
6. After IPH the optimal timing of initiation of BP lowering for recurrent stroke prevention has not been established, however, when the patient is medically and neurologically stable it may be a reasonable time point to administer such treatment. The BP goal for recurrent stroke prevention is < 130/80 mm Hg [17,22]. Blood pressure lowering agents such as those recommended in the recurrent stroke prevention section (see section 4) may be considered.

patient no matter the stroke subtype is a candidate for BP lowering therapy in the presence of persistent elevation of BP. With the occurrence of recurrent stroke, there is a consequent increase in morbidity and mortality emphasizing the importance of recurrent stroke prevention [26]. In relation to the estimate of the annual incidence of recurrent stroke, figures ranging as high as 3–4% are reasonable [27].

The approach to recurrent stroke prevention is multifactorial and takes into account not only BP lowering, but in addition a number of other therapies including but not limited to administration of antithrombotics, lipid lowering treatments, carotid endarterectomy and stenting, patent foramen ovale closure, and atrial ablation and occlusion therapies when indicated [26,27]. In this section we will focus only on BP lowering in recurrent ischemic stroke prevention. In section 3.3 of the article there is reference to BP lowering in IPH for recurrent stroke prevention.

4.2. Key guidance statements

The AHA/ASA guidance on prevention of stroke in patients with stroke or transient cerebral ischemia is the main US-based recommendation on the topic (2014) [27]. For BP lowering to achieve recurrent stroke prevention in ischemic stroke or transient cerebral ischemia the AHA/ASA guidance is as follows [27]:

1. For persons with established elevation of BP >/ = 140 mm Hg systolic or >/ = 90 mm Hg diastolic, BP lowering therapy is indicated.
2. A reasonable target for BP lowering is < 140/90 mm Hg.
3. For persons with small vessel or lacunar cerebral ischemia, a reasonable BP lowering target is < 130 mm Hg systolic.

The above recommendations are currently undergoing revision by a new writing group formed by AHA/ASA in 2019. However, features of the plan have been supported in a more recent collaborative US guidance publication (2018) whereby the elevated BP threshold target to lower BP, >/ = 140/90 mm Hg has been endorsed [22]. Furthermore, treatment may begin several days after the index stroke, a goal of <130/80 mm Hg is now considered a reasonable BP target, and treatment of BP when BP is below 140/90 mm Hg or there is no evidence of a prior history of hypertension is associated with no evidence of therapeutic benefit. In relation to administration of a specific BP lowering agent, the 2018 guidance indicates that treatment with an angiotensin converting enzyme inhibitor or angiotensin receptor blocker with a thiazide diuretic is useful, however, drugs from other BP lowering classes may be used [22].

4.3. Practical management advice

Elevated BP is an important and modifiable predictor of recurrent stroke [28]. The relationship was substantially publicized after release of the findings of the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) [29,30]. In PROGRESS an average 9/4 mm Hg BP lowering in the perindopril-based treatment group (~12/5 mm Hg BP lowering in the perindopril plus indapamide treatment group) resulted in a 28% relative risk reduction of the primary endpoint stroke when compared to matching placebo [29]. In addition, other key outcomes were reduced in the perindopril-based treatment group including fatal or disabling stroke, non-fatal or disabling stroke, ischemic stroke, cerebral hemorrhage, non-fatal myocardial infarction, and non-fatal stroke. Benefits of therapy were most pronounced in the dual perindopril plus indapamide treatment group. The main findings of the Heart Outcomes Prevention Evaluation (HOPE) Study, which compared add-on therapy with ramipril among high-risk cardiovascular disease patients, were complimentary to those of PROGRESS [31]. On the one hand, HOPE was based on add-on BP lowering medication with no specific BP lowering target, whereas PROGRESS had a BP lowering target (8–9 systolic BP/4–5 mm Hg diastolic BP). Furthermore, the main results of PROGRESS primarily showed prevention of recurrent stroke, whereas HOPE showed primarily prevention of recurrent myocardial infarction and first stroke [30].

Based on the most recent guidance for stroke prevention, it is reasonable to aim for a BP lowering target of <130/80 mm Hg [22]. This recommendation has been supported by a recent systematic review and meta-regression analysis of randomized trials which concluded that strict and aggressive control of BP were important for effective secondary prevention of stroke [32]. In addition, a recent clinical trial and meta-analysis concluded that intensive BP lowering tended to reduce recurrence of stroke, and a BP target <130/80 mm Hg was reasonable [33]. In another study, intensive BP therapy (systolic BP < 130 mm Hg) was beneficial no matter if an angiotensin converting enzyme inhibitor, angiotensin receptor blocker, calcium channel blocker or beta-blocker was compared to a thiazide diuretic [34].

A backdrop to the PROGRESS trial was concern over lowering BP for recurrent stroke prevention for fear of BP lowering being associated with adverse events such as incident recurrent stroke [29]. This concern was not validated in PROGRESS as BP lowering was safe and effective. However, clinicians still may confront situations in which intensification of or overly aggressive BP lowering may be associated with adverse outcomes. For example, in a recently published observational study of 4056 patients (mean age 77 years) in the US Veterans Health Administration system hospitalized for non-cardiac conditions, intensification of antihypertensive therapy at the time of discharge was associated with an increased risk of readmission and serious adverse events within 30 days [35]. Finally, it was shown that BPV, instability and episodic hypertension may explain the risk of first and recurrent stroke [36].

Table 4 summarizes practical management advice for hypertension in recurrent stroke prevention.

5. Prevention of a first stroke

5.1. Background information

Raised BP is considered by some as the 'crown jewel' of modifiable risk factors for stroke prevention as it has a high prevalence in the population, a high relative and population attributable risk in relation to first stroke, and consistent findings from clinical trials that BP lowering results in reduction of stroke [30]. BP lowering may be associated with an approximate 35–40% reduction of stroke risk.

5.2. Key guidance studies and practical management advice

The main US-based guidance for prevention of a first stroke is an AHA/ASA statement (2014) which makes the following recommendations [37]:

1. Regular BP screening and treatment of raised BP with lifestyle modification and pharmacotherapy are recommended.
2. The target BP for those with hypertension is < 140/90 mm Hg.
3. Individualize BP treatment based on specific patient characteristics and tolerance to medication. Successful reduction of BP is emphasized over administration of a specific BP lowering agent.
4. Self-measured BP is recommended to assist in BP control.

Since the publication of the aforementioned AHA/ASA guidance

Table 4
Practical management of hypertension in recurrent stroke prevention [22,27].

1. For persons with established elevation of BP >/ = 140 mm Hg systolic BP or >/ = 90 mm Hg diastolic BP, BP lowering therapy is indicated.
2. A reasonable target for BP lowering is < 130/80 mm Hg.
3. An angiotensin converting enzyme inhibitor or angiotensin receptor blocker plus a thiazide diuretic may be useful, however, other classes of BP lowering therapy may be used to achieve the target BP goal (e.g., calcium channel blocker, later generation beta blocker).

statement [37], the target BP goal based on newer data has been lowered to <130/80 mm Hg for prevention of major cardiovascular outcomes including stroke [22].

In summary, prevention of a first stroke is highly dependent on successful BP reduction. BP reduction may be achieved by lifestyle modification and medication administration. Reaching the target BP goal of <130/80 mm Hg is emphasized over administration of a specific BP lowering agent, unless there is a compelling indication to administer a certain class of BP lowering drugs [22]. Since many patients with hypertension will require more than 1 BP lowering drug to achieve the target BP goal, the clinician may have a number of drug classes to choose from to affect stroke and other cardiovascular disease prevention.

6. Maintenance of cognition

6.1. Background information

There is substantial scientific and clinical interest in successfully achieving maintenance of cognition and brain health [38,39]. Whereas observational epidemiological studies have provided supportive data for the role of elevated BP in conferring cognitive decline over time, uncertainty has existed in relation to the role of direct BP lowering in the maintenance of cognitive health [40–43]. Observational epidemiological studies consistently show that midlife hypertension is associated with later life cognitive decline and brain injury [40–43]. Most recently, the investigators of the Systolic Blood Pressure Intervention Trial (SPRINT) have raised hope that BP lowering may help to preserve cognition and maintain brain integrity [44,45].

6.2. Key guidance studies

US-based guidance statements include those from AHA/ASA, the American Society of Hypertension and the National Academies of Sciences, Engineering and Medicine (NASEM) [38–40,46]. The scientific backing for the statements is largely based on observational epidemiologic studies. Key recent recommendations from AHA/ASA [22] and NASEM [46] for BP control and prevention of cognitive decline or dementia are broadly summarized and reflect clinical equipoise:

1. It is reasonable to treat BP [22].
2. There is encouraging but inconclusive evidence for BP control [46].

However, the SPRINT trial showed that among 9361 non-diabetic, hypertensive randomized participants (target systolic BP goal of <120 mm Hg vs. <140 mm Hg) with an average age of 67.9 years and median intervention/follow-up periods of 3.34 years/5.11 years, respectively, intensive BP control did not significantly reduce the risk of the primary trial outcome, probable dementia. However, it did reduce the risk of secondary outcomes including mild cognitive impairment and the combined rate of mild cognitive impairment and probable dementia [44]. Limited follow-up time may explain why the main outcome, probable dementia, was not statistically significantly impacted. In addition, although the differences were small, intensive BP control was significantly associated with a smaller increase in cerebral white matter lesions but a greater decrease in total brain volume as determined by magnetic resonance imaging [45].

6.3. Practical advice for management

Based on results from observational epidemiologic studies, other guidance statements and SPRINT, in Table 5 we make recommendations in relation to BP control for maintenance of cognition and brain health [43,47].

Table 5
Blood pressure management recommendations for the maintenance of cognition and brain health [39,43,47].

1. BP lowering is a reasonable overall strategy as at the very least it will reduce risk of stroke and other cardiovascular diseases.
2. There is no definitive evidence that one class of antihypertensive drugs is superior to another for achievement of cognitive maintenance. It is reasonable to consider the SPRINT BP lowering therapeutic regimen and BP lowering target (<120 mm Hg systolic).
3. It is reasonable to control BP in middle-aged and young elderly to lower risk of cognitive impairment and dementia.
4. In those with stroke, lowering of blood pressure may reduce the risk of post-stroke dementia.
5. In those at risk for vascular cognitive impairment (e.g., multiple cardiovascular risks), lowering of BP may reduce the risk of cognitive impairment.
6. For persons 80 years of age and older, the usefulness of BP lowering for prevention of dementia in not established. In fact, there is concern that with BP lowering in for example certain older patients, there may be an increase of small subcortical infarcts based on brain blood pressure gradients [48].

7. Conclusion

We have reviewed guidance and provided our opinion on the management of BP in acute ischemic and hemorrhagic strokes, first and recurrent stroke prevention, and the maintenance of cognition. Additional study of BPV in major subtypes of stroke and intensive BP control for maintenance of cognition are areas in need of further study as they may enhance our knowledge to successfully manage BP in stroke and prevent its devastating complications.

Declaration

Dr. Gorelick serves on a Data Safety and Monitoring Board for Novartis in relation to LCZ 696 in heart failure and received honorarium for serving on this board. Drs. Qureshi and Farooq have nothing to declare.

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