

Commentary

PASCAR commentary on the International Society of Hypertension global guidelines 2020: relevance to sub-Saharan Africa

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Abstract

Hypertension guidelines have been based on country-specific data until the publication of the International Society of Hypertension (ISH) global guidelines. The major differences between the ISH global guidelines and other international guidelines are the stratified recommendations to accommodate differences in available resources between countries and within countries. This is a key and novel proposal in the new ISH guidelines. There is the separation of optimal versus essential criteria for diagnosis and treatment according to availability of resources. This guideline includes recommendations for sub-Saharan Africa. The Pan-African Society of Cardiology (PASCAR) continues to promote awareness and recommendations on hypertension in Africa. This commentary provides a summary and discussion of the global guidelines in order to clarify the position of PASCAR.

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Most authoritative hypertension guidelines for the diagnosis and management of elevated blood pressure have been developed for specific regions or countries.¹⁻⁴ These guidelines have been based

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on studies that were predominantly performed in high-income countries (HICs), with the vast majority of participants being of non-sub-Saharan African (non-SSA) origin.^{2,5,6} No hypertension cardiovascular (CV) outcome study has been performed in SSA. Despite this, these international guidelines have been used to develop management protocols for SSA.

Until 2017, guidelines were unanimous that the cut-off point to diagnose hypertension was 140/90 mmHg, except in the elderly where the systolic blood pressure (SBP) was increased to 150 mmHg.⁷⁻⁹ Based on this definition, the World Health Organisation (WHO) estimated that Africa had the highest prevalence of hypertension.¹⁰ The Pan-African Society of Cardiology (PASCAR) hypertension roadmap¹¹ similarly used this diagnostic threshold. However, in 2017, the American College of Cardiology (ACC)/American Heart Association (AHA) revised their hypertension guidelines with radical changes, including lower cut-off points for the diagnosis of hypertension (BP \geq 130/80 mmHg).

Implications of these changes include an additional 31 million US individuals considered to have hypertension, just because of this change in threshold.¹ The lowering of the threshold of hypertension diagnosis was not replicated in the 2018 guidelines from the European Society of Hypertension (ESH)/European Society of Cardiology (ESC), which maintained the previously set 140/90 mmHg.²

In 2018, the International Society of Hypertension (ISH) questioned whether the ACC/AHA high blood pressure guidelines were fit for global purpose, especially in low- and middle-income countries (LMICs).¹² In 2020, the ISH published global hypertension practice guidelines, which have great relevance to SSA. Specific detail for the manner to achieve hypertension control is based on the needs, available resources and practice behaviours of a given population. This commentary aims to clarify the position of PASCAR on these global practice guidelines and their relevance to SSA.

Why do we have guidelines?

Before commenting on the ISH hypertension guidelines, it is important to consider why we need guidelines. The principles were particularly well summarised by Go *et al.*¹³ Briefly, they are required to identify people eligible for management; for monitoring at practice and population level; for increasing patient and provider awareness; providing an effective diagnosis and treatment plan; systematic follow up for initiation and

treatment intensification; clarifying the roles of healthcare providers; and reducing barriers for patients to receive and adhere to treatment and implement lifestyle modifications.

The impact of well-structured hypertension guidelines is typically illustrated by data derived from Lackland *et al.*,¹⁴ which showed that the decline in US population stroke mortality rates coincided with the reduction of population BP, which was consistent with the lowered BP thresholds and targets described in the sequential recommendations from the guidelines. PASCAR identified the creation or adoption of simple and practical clinical evidence-based hypertension management guidelines as one of its 10-point action plan to achieve 25% control of hypertension in Africa by 2025.¹¹

Summary of key proposals of the ISH global hypertension guideline and relevance to SSA

Essential versus optimal treatment

The major difference between the ISH global guidelines and other international guidelines is the stratified recommendations to accommodate differences in available resources between countries and within countries. This is a key and novel proposal in the new ISH guidelines. There is the separation of optimal versus essential criteria for diagnosis and treatment according to resource availability in LMICs versus HICs. Even within HICs there are areas with low-resource settings and vice versa.

Optimal care refers to evidence-based standard of care articulated in recent major guidelines (ESH/ESC, ACC/AHA) but it is recognised that implementation of these standards is not always possible in LMICs. Essential standards refer to minimum standards of care for low-resourced settings. However, there was a paucity of evidence supporting this approach and the guideline committee applied expert opinion. The provision of these recommendations is based on the need to develop guidelines that are applicable to all areas of the globe rather than developing country-specific guidelines. This approach makes it possible to develop truly international hypertension guidelines.

However, the committee recognises that it may not be feasible for even the minimum standards to be implemented in many poorer countries in SSA due to lack of health professionals, infrastructure, equipment (ECG and BP machines for example) and finances. No guidance is provided for treating patients under these circumstances. However, it is suggested that the guidelines provide a framework for countries to strive for. Perhaps what is significantly lacking in the essential or minimum standards is their application to non-physician healthcare workers that are critical in providing care to the burgeoning numbers of hypertensive patients in poorer countries in SSA.

This review is not exhaustive and will focus on the essential recommendations of the ISH hypertension guideline and their relevance to SSA.

Definition of hypertension, BP measurement and target BP

The ISH guidelines maintained the traditional definition of hypertension at a level $\geq 140/90$ mmHg and have not aligned themselves with ACC/AHA guidelines at $\geq 130/80$ mmHg. In SSA more than 90% of hypertensives are not controlled because of lack of awareness (largely attributable to lack of screening),

failure to access treatment or persistence with treatment use, and failure of monitoring to ensure control.¹⁵

By redefining hypertension to a level of 130/80 mmHg, this will significantly increase the prevalence of hypertension. In the US it was estimated that the number of hypertensives will increase by 43% or 31.1 million people, and a similar increase would be expected in SSA, placing an unsustainable additional burden on health facilities.¹⁶ This, in the light of the lack of beneficial evidence for initiating treatment in patients at this lower threshold, does not support these diagnostic criteria for hypertension in SSA.

One weakness of the ISH guidelines is limiting the definition of hypertension into two grades (Table 1), excluding grade 3 hypertension: $\geq 180/110$ mmHg. In SSA, grade 3 hypertension is common¹⁷ and usually asymptomatic, but few present with features of hypertensive emergency. This grade of hypertension alerts the healthcare worker to a category of hypertension with a very high risk of adverse outcomes in a short time.

The guidelines make important recommendations regarding the essential requirements for measurement of BP. This has to be done on three separate occasions within a four-week period. Perhaps not completely recognised by the ISH guideline is the limited availability of functioning BP devices and the long distances patients may need to travel to have repeated measurements to establish the diagnosis. While it is ideal to have the BP repeated at different visits, high-risk patients with limited access should be treated based on a single set of readings, possibly if it is $> 160/100$ mmHg, but especially if $> 180/110$ mmHg. Similarly, repeated measurements at one clinic visit may enable a diagnosis to be made based on a single visit.

There are slight differences in BP re-evaluation: in those with high-normal BP, the BP should be checked in three years, unless the individual has a higher risk, in which case the BP should be checked in one year. If normal, the ESH/ESC recommends a BP review in five years. However, in SSA it may be more appropriate to make this recommendation three years, due to the high risk of complications.

However, home and 24-hour ambulatory BP monitoring are seen as essential for the diagnosis of hypertension. In the opinion of PASCAR, the latter represents optimal requirement. Even in a LMIC in SSA, such as South Africa, availability of 24-hour and home BP monitoring in the public sector that serves over 80% of the population is extremely limited. There is increasing availability of home-based monitoring devices, however validation of these devices is sub-optimal and needs to be improved. Furthermore, there needs to be training in the use of these devices, both for the patient and home-based carers.

The essential target BP recommended for all hypertensives is $< 140/90$ mmHg or a 20/10-mmHg reduction in BP by three months. For optimal treatment, it is $< 130/80$ mmHg if tolerated and not $< 120/70$ mmHg. In those 65 years old and above or

Table 1. Proposed SSA classification of hypertension, using office blood pressure measurements

	Normal BP	High-normal	Grade 1 hypertension	Grade 2 hypertension	Grade 3 hypertension
SBP*	< 130	130–139	140–159	160–179	> 180
DBP*	< 85	85–89	90–99	100–109	> 110

BP, blood pressure; SBP systolic BP; DBP, diastolic BP.
*Classification based on the presence of either or both SBP and DBP.

those with the presence of frailty, the cut-off value is < 140/90 mmHg. This recommendation is particularly applicable to SSA. However, in our view, the 20/10-mmHg reduction needs further comment. Although it is well recognised that this reduction in BP will substantially reduce cardiovascular events, it needs a degree of context. For example, if the initial BP is as high as 190/110 mmHg, a 20/10-mmHg reduction only to 170/100 mmHg would not be appropriate.

Clinical evaluation and diagnostic tests

The ISH guidelines recommend a full medical history addressing previous BP levels, risk factors, co-morbidities, and symptoms of secondary causes, together with a physical examination with a focus on the circulation, heart and signs of secondary causes. Laboratory investigations include Na⁺, K⁺, creatinine, estimated glomerular filtration rate (eGFR), dipstick urine, lipids and fasting glucose. A 12-lead ECG should be performed to detect left ventricular hypertrophy, atrial fibrillation and ischaemic heart disease. In PASCAR’s opinion these basic tests represent an optimal situation to assess hypertension-mediated organ damage (HMOD) and secondary causes at the primary-care level. While these tests are ideal, ECG machine availability and the skills to interpret are lacking in many SSA countries, especially in rural areas.

CV risk stratification

More than 50% of hypertensive patients have additional CV risk factors such as diabetes, the metabolic syndrome, dyslipidaemia and smoking. CV risk assessment is important and should be assessed in all hypertensive patients, and it relies on levels of BP, risk factors, and presence and/or absence of HMOD. The rationale is that patients at highest risk will achieve the greatest absolute reduction in adverse events and allow scarce resources to be optimally used. A simple risk chart is provided and is applicable to SSA. Alongside the chart is QRISK2, an online risk calculator that may be pertinent to SSA due to adjustment for black African race.

Non-pharmacological treatment of hypertension

Non-pharmacological treatment is a fundamental part of the management of hypertension. Healthy lifestyle choices can prevent or delay the onset of high BP and can reduce CV risk, are often the first line of antihypertensive treatment, and enhance the effects of antihypertensive treatment. The recommended changes are provided in Table 2. Briefly, the lifestyle changes

include a combination of optimising diet, exercise, weight, alcohol consumption and avoiding precipitants and smoking.

There is no differentiation in the recommendations between optimal and essential. Most of these recommendations are only implementable in HICs due to a variety of reasons. In the poorer communities of SSA, choice of food is determined by affordability and ability to store. Lack of electricity means that cooking and heating is done on open fires in crowded townships and rural villages, causing pollution, and exercise opportunities are limited due to safety concerns and lack of leisure time.

More pragmatic essential recommendations need to be considered for SSA. However, salt and sugar intake can be reduced and should be encouraged as salt is considered a major contributor to poor BP control in SSA. Legislative control of sodium content in processed foods is a feasible means to reduce salt intake at a population level.¹⁸ Further engagement with policy makers needs to address access to freshly grown produce.

Initiation and drug treatment of hypertension

ISH guidelines recommend drug treatment for all patients with established hypertension with BP ≥ 160/100 mmHg, which is certainly in line with PASCAR’s viewpoint. However, for patients with stage 1 hypertension, there is differentiation between optimal and essential. Patients at high risk, with HMOD or established CV or renal disease, should receive drug treatment, but those with low to moderate risk without these complications should receive drug treatment under optimal management.

Under essential treatment, if there is limited drug availability, then treatment should be considered for older people, 50–80 years old. In SSA this recommendation is not realistic as the majority of the population is below 50 years of age and hypertension presents at a younger age and is often more progressive (see below). PASCAR recommends treating all patients diagnosed with hypertension, including those with stage 1 hypertension who have not responded to lifestyle modifications.

The ISH guidelines recommend initiation of two drugs, preferably in a single-pill combination (SPC) in the majority of patients. The initial combination is an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) in combination with a calcium channel blocker (CCB). According to the ISH guidelines, in African patients an ARB is preferred over an ACE inhibitor due to risk of angioedema, despite the CREOLE study showing a low risk of non-severe angioedema.¹⁹

ACE inhibitors are generally less costly than ARBs and can be used unless there is a contra-indication. Furthermore, in African patients an initial combination of CCB plus thiazide/thiazide-like diuretic is recommended. In the CREOLE study

Table 2. Recommended lifestyle changes

	<i>Recommended to increase</i>	<i>Recommended to avoid</i>
Salt	Reduce salt in food preparation and at the table	High-salt foods (fast foods, processed foods, cereals)
Diet	Eat whole grains, nuts, seeds, legumes, tofu, fruit, vegetables (leafy vegetables, beetroot, avocados), polyunsaturated fats	High-sugar food, saturated and trans fats
Drinks	Coffee, green and black tea, hibiscus tea, pomegranate juice, beetroot juice, cocoa	Excessive (> 2/day) alcohol or binge drinking
Smoking		Smoking
Physical activity	Aerobic and resistance exercise 30 minutes/ day 5–7 days a week, strength training	
Stress	Transcendental meditation/ mindfulness	Chronic stress
Alternative therapies		Complementary, alternative or traditional medicines
Environment		Air pollution and cold temperature

this was more effective than ACE inhibitor-plus-thiazide combination, although potassium needs to be monitored due to risk of hypokalaemia. However, thiazide-like diuretics may not be widely available, in which case a thiazide diuretic would be used.

Importantly, the ISH guidelines stress the importance of controlling the BP, regardless of what drugs are available for use. They have provided alternatives to the standard first-line agents. They have also made it clear that, while it is optimal to use SPC, free combinations can be used in settings where SPC are limited. It is optimal to use agents with longer half-lives that require once-daily dosing. They recommend the use of single agents for BP control in the setting of frail elderly patients only or in the setting of stage I hypertension, where lifestyle measures have not improved the BP to target. The long half-life of amlodipine may make it the drug of choice in this setting, making it the preferred choice over a diuretic.

If BP is not controlled, the initial combination must have the dose optimised before adding a diuretic. This is an important difference to other major guidelines. Beta-blockers are only used for treatment of hypertension associated with specific cardiac conditions such as heart failure, ischaemic heart disease and atrial fibrillation.

The ISH guidelines have stressed the importance of ensuring good adherence, as have other international guidelines. They have highlighted means to improve adherence to antihypertensive therapy, both essential and optimal. It is essential that adherence to antihypertensive therapy is improved in whatever ways are available. While it is ideal to be able to monitor adherence, the methods available may not be feasible and have many limitations. However, where possible, it is recommended to monitor adherence using the best tools available/feasible in the particular setting.

Resistant hypertension

Resistant hypertension should be suspected if office BP is > 140/90 mmHg on treatment with at least three antihypertensives (in maximal or maximally tolerated doses), including a diuretic. It is essential to exclude pseudo-resistance (white-coat effect, non-adherence to treatment, incorrect BP measurements, errors in antihypertensive therapy) and substance-induced hypertension, such as non-steroidal anti-inflammatories (NSAIDs) as contributors. Health behaviours and lifestyle also need to be optimised.

If truly resistant, low-dose spironolactone is recommended, especially if K^+ is < 4.5 mmol/l and eGFR is > 45 ml/min. If this fails, then referral to a specialist or the investigation of secondary causes is recommended under the optimal approach. Under the essential approach, addition of other antihypertensive medication is recommended and a screen for secondary causes with a history, examination and basic tests, for example, thyroid-stimulating hormone, electrolytes, creatinine and eGFR, and dipstick urine.

Ethnic differences

In populations of African descent, hypertension and HMOD occur at younger ages. There is greater resistance to treatment, more nocturnal hypertension, and increased risk of kidney

disease, stroke, heart failure and mortality.²⁰ This may be related to physiological differences in the renin-angiotensin-aldosterone system, altered renal sodium handling, CV reactivity and early vascular aging. These are important considerations when treating patients from SSA. Studies done in SSA suggest amiloride is a useful agent in controlling BP in patients with resistant hypertension,²¹ but amiloride is not mentioned in the ISH guideline.

Hypertensive emergencies/urgencies

Hypertensive emergency is a severely elevated BP associated with acute HMOD and requires immediate BP lowering, usually with intravenous therapy. Urgency refers to severely elevated BP without acute HMOD and can be managed with oral antihypertensive agents. In SSA these complications of hypertension are relatively common, but an evidence-based approach to management is lacking.

The essential requirements are a clinical examination, evaluation of HMOD, including fundoscopy, and the following investigations: haemoglobin, platelets, creatinine, sodium, potassium, lactate dehydrogenase, haptoglobin, urinalysis for protein, urine sediment and ECG. In SSA, access to ECG and urinary sediment is limited, and measurement of lactate dehydrogenase and haptoglobin is unnecessary. A simple dipstick and creatinine will alert the clinician to kidney damage, which is the most common complication of a hypertensive emergency.

Hypertensive emergencies require immediate BP lowering to prevent or limit further HMOD, but unfortunately there is sparse evidence to guide management, and recommendations are largely consensus based. The time to lower BP and the magnitude of BP reduction depends on the clinical context, but in general a 25% immediate reduction is recommended. Large drops in BP can precipitate stroke due to loss of cerebral autoregulation.

The ISH guidelines recommend intravenous labetalol and nicardipine, which are generally safe to use in all hypertensive emergencies. However, intravenous labetalol has limited availability in SSA and nicardipine is not listed on the WHO essential drugs list and in 2010 was only available in Cameroon and Senegal.²² Nitroglycerine is an option, however, access to high-care and intensive-care units is very limited. In the absence of the above, an oral long-acting CCB²³ or oral labetalol is probably the safest choice and a loop diuretic is an option in the setting of pulmonary oedema. All patients should be followed up and should achieve optimal BP control.

Hypertension and co-morbidities

A detailed analysis of this section is beyond the scope of the review. In addition to BP control under optimal and essential recommendations, effective treatment of the other risk factors to reduce the residual cardiovascular risk is essential. Low-density lipoprotein (LDL) cholesterol should be reduced according to risk profile: (1) > 50% and < 1.8 mmol/l in hypertension and cardiovascular disease (CVD), chronic kidney disease, diabetes mellitus or no CVD and high risk; (2) > 50% and < 2.6 mmol/l in high-risk patients; (3) < 3 mmol/l in moderate-risk patients. The fasting serum glucose levels should be reduced below 7 mmol/l or glycated haemoglobin (HbA_{1c}) below 7%. Serum urate should be maintained below 0.387 mmol/l, and < 0.357 mmol/l in patients

with gout. Antiplatelet therapy should be considered in patients with CVD (secondary prevention only).

From the PASCAR perspective, the lipid guidelines are too complex and rely on web-based risk charts for implementation, and the recommendation for treating asymptomatic hyperuricaemia is considered very controversial. In addition, aspirin should be used in all patients with established atherosclerotic CVD, unless there is a contra-indication.

Other

In SSA, where there is the highest prevalence of people living with HIV and, with around one of every four of them having hypertension, it is important to be aware of the drug interactions between CCB and antiretroviral therapies. Amlodipine dose should be reduced when used in combination with protease inhibitors due to the risk of prolonging the PR interval.²⁴ Other antihypertensives that are affected by various anti-retrovirals are detailed by van Zoest *et al.*²⁵ Otherwise the treatment of hypertension remains the same as in general hypertensives.

Rationale for creating this commentary

The ISH guidelines were developed in order to create a uniform platform that is accessible and usable to all environments, both high and low income. In order to improve accessibility, they were published in two major hypertension journals. The aim was to create recommendations that can be adopted in different settings but that are accepted international standards of care.

The guidelines provide a tool to promote the improvement of BP control to 25% in Africa as developed by the PASCAR task force.¹¹ Adopting the ISH guidelines will provide a standard of care for African hypertension groups to lobby healthcare providers and governments to develop basic standards of care for the diagnosis and treatment of hypertension. However, this commentary serves to underline that some of the recommendations are not realisable in SSA at the current time. There is also a need to develop a guideline to enable nurse practitioners to treat hypertension and provide greater access to basic care for patients.

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Elderly may benefit from more invasive treatment: large seven-year study

Elderly patients suffering the most common type of heart attack may benefit from more invasive treatment, research has shown. The study draws on data captured over seven years from 1 500 patients aged 80 years or over. It was conducted by researchers from the National Institute of Health Research Health Informatics Collaborative (NIHR-HIC), led by Imperial College Healthcare NHS Trust and Imperial College London.

The research looks at elderly patients admitted to hospital with a non-ST-segment elevated myocardial infarction (NSTEMI). It found patients who underwent invasive treatment with a coronary angiogram, followed up with bypass surgery or coronary stenting as appropriate, had higher survival rates than those who were treated with medication alone. Patients who had coronary angiograms were also less likely to be re-admitted to hospital with a second heart attack or heart failure.

Coronary angiograms are specialist X-rays to identify blockages in the blood supply to the heart. They can help a clinician determine the cause of an NSTEMI and decide on effective treatment, such as increasing blood flow through a coronary stent or bypass grafting.

Previous trials have shown increased survival rates in younger patients with NSTEMI following invasive treatment, but there has been conflicting evidence as to whether these benefits extend into patients over 80 years. Only 38% of NSTEMI patients in this older age group currently receive invasive treatment, compared to 78% of the under 60 years.

Dr Amit Kaura, lead author of the research, British Heart Foundation clinical research fellow and NIHR clinical research fellow with the National Heart and Lung Institute at Imperial College London explained: 'Because there has been no clear consensus on how best to manage elderly patients with this type of heart attack, many doctors have erred on the side of caution, not wanting to risk complications in their more vulnerable patients. These results show they can now be more confident of the benefits that invasive treatment can bring for this group.'

The study, funded by the NIHR Imperial Biomedical Research Centre, identified just under 2 000 patients aged over 80 years who were diagnosed with an NSTEMI at five hospitals between 2010 and 2017. To ensure the robustness of the study, the researchers used sophisticated statistical techniques to apply the kind of criteria used in a clinical trial, to determine which of these patients would be included in the analysis. In total, 1 500 patients were included, with just over half having invasive treatment. After five years, 31% of those in the invasive treatment group had died, compared to 61% in the non-invasive group.

The team estimates that if all patients had received invasive treatment, just 36% would have died, compared to 55% if all had received non-invasive treatment. These figures take into account over 70 variables that might have affected prognosis, such as other medical conditions.

The analysis also showed that patients were at no greater risk of stroke or bleeding if they received invasive treatment, as there were similar rates across both groups. Patients who had invasive treatment were also a third less likely to be re-admitted to hospital for heart failure or heart attack.

Kaura said: 'The gold standard is to base treatment decisions on evidence from randomised control trials, but that doesn't yet exist for this group of patients. In the interim, we've done the next best thing, by looking at retrospective data gathered from these five large hospitals and using it like a clinical trial. The results are clear: clinicians should positively consider invasive management for any patients over 80 diagnosed with an NSTEMI.'

The data used in the study was gathered through the National Institute for Health Research Health Informatics Collaborative (NIHR-HIC), which involves: Imperial College Healthcare NHS Trust, Oxford University Hospitals NHS Foundation Trust, University College London Hospitals NHS Foundation Trust, King's College Hospital NHS Foundation Trust and Guy's and St Thomas' NHS Foundation Trust.

Source: Medical Brief 2020