Patient-centered Blood Pressure: Thresholds, Targets, and Tools in Diabetes

Diabetes care has evolved into a patient-centered process, in which targets, strategies, and tools are decided in an individualized manner, based on an understanding of the patient’s attitudes, needs, and priorities. While multiple guidelines and recommendations have a broad consensus for targets and strategies in diabetes and dyslipidemia, similar consensus seems to be lacking with respect to targets of blood pressure management.

Hypertension care is guided by recommendations from professional bodies, which collate evidence and propose rational means of assessing and managing high blood pressure. We analyze three documents which guide blood pressure management in persons with diabetes and make an effort to find concordance between them. This review utilizes the evidence-based recommendations of the American Diabetes Association’s (ADA) Standards of Medical Care in Diabetes-2017, the European Society of Hypertension/European Society of Cardiology (ESH/ESC) 2013, and the panel members of the Eighth Joint National Committee (JNC8). It reinforces the need to interpret and follow their guidance, utilizing “good clinical sense,” without losing sight of our aim: To provide optimal health to people with diabetes and hypertension.

REPORT OF PANEL MEMBERS OF EIGHTH JOINT NATIONAL COMMITTEE

The panel members of the JNC8 have defined the target threshold, for various subgroups of people with hypertension. JNC8, however, does not specify any cutoff above which lifestyle modification should be initiated.

In the general population, the blood pressure threshold for initiating pharmacologic treatment is ≥140/90 mmHg in those aged <60 years, and ≥150/90 in those aged 60 or above. JNC8 does not suggest lower targets for persons with diabetes. At the same time, it reiterates that a person who has lower blood pressure should not modify therapy, as long as it is well tolerated.

The panelists of JNC8 justify their recommendation by explaining that the various trials used to support lower blood pressure targets for persons with diabetes have certain shortcomings. According to them, Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) included participants irrespective of baseline blood pressure and did not have randomized blood pressure treatment thresholds or goals. ADVANCE studied both macrovascular and microvascular outcomes, rather than focusing only on blood pressure. Blood pressure control, using a perindopril + indapamide-based strategy was used as a method of achieving better outcomes, and not as an end in itself. Therefore, the JNC8 omitted a large study with good outcome data.

The panelists also disregarded the lower incidence of stroke observed with lower blood pressure (systolic goal <120 mmHg, as compared to <140 mmHg) in Action to Control Cardiovascular Risk in Diabetes (ACCORD)-Blood Pressure, because of the low absolute numbers involved. The Hypertension Optimal Trial (HOT), which showed reduction in a composite cardiovascular disease outcome with a diastolic blood pressure goal of ≤80 mmHg as compared to ≤90 mmHg, was disregarded, perhaps because of the smaller number of participants with diabetes. JNC8 panelists also disregarded the United Kingdom Prospective Diabetes Study because it was a “mixed systolic and diastolic goal study and because it did not use a diastolic cutoff of 90 mmHg in one of its groups”. No evidence from recent, large trials has been published in the past few years to support these earlier reports.

JNC8 panelists do recommend ethnicity based choice of therapy including thiazide-type diuretic or calcium channel blocker (CCB) for the general black population (including those with diabetes), and ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) for blacks with chronic kidney disease (CKD). No specific guidance is provided for South Asians.

JNC8 panelists suggest initiating monotherapy or combination. Some members recommend initiation of combination therapy (2 or more drugs) when blood pressure is >160/100 mmHg or when it is >20/10 mmHg above goal and then titrating drug treatment by either maximizing dosage, or adding a second medication, or starting a fixed dose combination. It reiterates that more than one class of drugs will frequently be necessary and advocates use of thiazide-like diuretics, ACE or ARB and CCB, in varying combination. Only if these three classes prove inadequate, along with lifestyle modification, do they recommend the addition of beta blockers, aldosterone agonists, or other classes.

AMERICAN DIABETES ASSOCIATION STANDARDS OF CARE-2017

ADA reviews the very same evidence, including ACCORD, ADVANCE-Blood Pressure, and HOT trials analyzing their design and results.

It suggests a target of <140/90 mmHg for all people with diabetes, but advocates lower (not specified) targets in
specific situations. These include “younger patients” those with albuminuria, and/or those with one or more additional atherosclerotic cardiovascular disease (ASCVD) risk factors (dyslipidemia, obesity, and smoking). Such targets are proposed only if they can be achieved “without undue treatment burden.” Lower targets are especially important in persons with a high risk of stroke (systolic blood pressure control) or worsening of albuminuria, and “long life expectancy.” At the same time, when palliative care is needed in older adults (>65 years of age), ADA suggests that strict blood pressure control may not be necessary, and therapy may be withdrawn.[13] The threshold for beginning nonpharmacological intervention is also lower, at >120/80 mmHg.

ADA states that high ASCVD risk associated with diabetes, and the high prevalence of undiagnosed ASCVD in these patients, favors the use of renin-angiotensin system (RAS) inhibitors. ADA suggests administration of one or more antihypertensive medications at bedtime and reminds us that more often than not, multiple drugs will be needed to achieve control. No attempt is made to prioritize either ACEi or ARBs over each other, but mention is made of outcomes benefits with perindopril + indapamide and benazepril + amlodipine combinations. ACEi and ARB may be substituted for each other if one class is not tolerated. Both should never be used together. Serum creatinine/estimated glomerular filtration rate (eGFR) and serum potassium levels should be monitored during long term of RAS blockers.

**European Society of Hypertension/European Society of Cardiology 2013 Guidelines**

The 2013 ESH/ESC guidelines[6] propose a therapeutic approach based on an assessment of overall cardiovascular risk, aiming to reduce it by appropriate diagnosis management and follow-up of hypertension. The authors describe their literature search methodology, including a description of the Appropriate Blood Pressure Control in Diabetes and Randomized Olmesartan and Diabetes Microalbuminuria Prevention trials.[14,15]

All persons with diabetes are classified alongside those with organ damage of hypertension or with CKD stage 3. Patients with diabetes and evidence of organ damage, or with other risk factors, as categorized are being equivalent to those with symptomatic cardiovascular disease or CKD stage 4. Thus, the ESH/ESC taxonomy classifies diabetes into two grades of risk. A color coded table, using shades of green, yellow, and red is used to emphasize this concept. To paraphrase the ESH/ESC guidance: Persons with uncomplicated diabetes have a risk equivalent to that of CKD stage 3 or end organ damage. Those with diabetes + other risk factors, or diabetes + end organ damage, are equivalent in risk to CKD stage 4.

The role of asymptomatic organ damage is through to be crucial in risk stratification. Four markers (microalbuminuria, increased pulse wave velocity, left ventricular hypertrophy, and carotid plaques) are considered important risk prognosticators. Among investigations, echocardiography with Doppler is considered to have the highest predictive value, while electrocardiography, estimation of glomerular filtration rate, microalbuminuria, carotid intima-media thickness, arterial stiffness, ankle-brachial index, and fundoscopy are considered useful, available, reproducible, and cost-effective alternatives.

The 2013 ESH/ESC guidelines suggest institution of pharmacotherapy above a threshold of 140/90 mmHg, in all patients with low-moderate cardiovascular risk, or previous stroke/transient ischemic attack, or coronary heart disease or diabetic/nondiabetic kidney disease. The only exception is made for the elderly (who are offered a higher systolic target) and for diabetes (who are given a lower diastolic target). The recommended diastolic target in diabetes is <85 mmHg, with the reminder that values between 80 and 85 mmHg are safe and well tolerated. If overt proteinuria is present, systolic blood pressure targets of <130 mmHg may be considered, provided that changed in eGFR are monitored. Lifestyle modification is encouraged in all diabetics at a level of 130/85 mmHg or more.

The 2013 ESH/ESC authors list metabolic syndrome and glucose intolerance as possible contraindications for thiazide diuretics and beta-blockers but refrain from describing this contraindication as compelling. The choice of class of drugs, or an individual drug, is expected to be based on comorbidities. All classes of antihypertensive drugs can be used in diabetes, but RAS blockers are preferred, especially in the presence of proteinuria or microalbuminuria. Again, no attempt is made to compare ACEi and ARB, though simultaneous administration is strongly discouraged. They also favor the use of fixed-dose combinations, and initiation of combination therapy in persons with marked blood pressure elevation, or those at high/very high cardiovascular risk.

**Patient-centered Approach**

There have been calls for a patient-centered approach to management of hypertension. These calls relate to the active involvement of patients in their own care, and to improving the quality of this care, using modern technology such as ambulatory blood pressure monitoring and home blood pressure monitoring. To the best of our knowledge, there has been no discussion using the phrase “patient-centered choice of targets” in blood pressure treatment. This is in stark contrast to the guidance followed in hyperglycemia management, where patient-centered goals are set for glycemia.

**Patient-centered Approach to Deciding Targets**

Hypertension management, too, needs patient-centered management. This is easier said than done, however. Current guidelines differ with each other in certain aspects and need to be reconciled before suggestions can be shared with other physicians and prescribers.

The subtle differences between the guidance from the three respected sources can be resolved by taking the best from each of them. We suggest following this advice from a...
48-word long sentence written by the JNC8 panelists: “(their) recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.”

Patient-centered care for hypertension involves what we term the Five T’s [Table 1]. Both ADA[5] and ESH/ESC[6] convey the message of choosing patient-centered targets and goals while managing hypertension in diabetes. While the general target for blood pressure may be made more stringent for “younger” individuals with longer life expectancy; additional risk factors (smoking, obesity, dyslipidemia); high risk of stroke or progression of albuminuria. Such a step should be contemplated only if therapy is well tolerated, and does not pose an unacceptable cost or bill burden on the patient. The <140/85 mmHg goal in diabetes is supported by Ferrannini and Cushman who advocate the initial use of a thiazide-like diuretic (for cardiovascular protection) and RAS blocker (for renoprotection) in hypertensive diabetes.[16] At the same time, less stringent targets may be in order for the elderly, those with a high risk of postural hypotension, or falls (such as limited fluid intake/frequent fasting, leading to dehydration, especially in hot climates) and osteoporosis; and inability or unwillingness to cope with prescribed pills [Table 2].

Although rarely discussed in modern medicine, symptoms of hypertension may determine treatment goals as well. Patients who complain of symptoms suggestive of high blood pressure, such as headache, anger, and irritability, may benefit from lower blood pressure levels, provided they remain asymptomatic and enjoy a better quality of life. Asymptomatic patients may be managed using conventional targets (<140/90 mmHg). It is unlikely, however, for persons to report symptoms at blood pressure levels near currently suggested therapeutic targets.

### Summary

We admit that the patient-centered method of setting blood pressure goals is not a purely evidence-based approach. It does not attempt to draw water-tight lines or compartments, but endeavors to empower physicians (and their patients) choose appropriate targets for blood pressure control. In this regards, it is similar to globally accepted approaches to hyperglycemia and dyslipidemia management.[13] The outline presented in Table 3 attempts to collate expert opinion from some of the most respected organizations in the world. It then utilizes this guidance to create a framework [Table 1] which reminds prescribers of the need to achieve maximal efficacy, while ensuring safety and tolerability. It also reinforces the need to

### Table 1: The five T’s of patient-centered blood pressure management

| Technique, of measurement | Threshold, for intervention, both nonpharmacological and pharmacological | Targets, to be achieved | Tools, to be used (lifestyle, drugs) | Tactics, to be followed |
|---------------------------|------------------------------------------------------------------------|------------------------|--------------------------------------|------------------------|
|                            | Initiation - of monotherapy or combination therapy; of loose combination or fixed dose combination | Intensification - if initial drug choice proves ineffective | Up-titration of dose | Switch to new drug within same class |
|                            | Interchange - if initial drug choice is not well tolerated/proves unsafe |                        | Switch to new drug from different class | Addition of new drug |

### Table 2: Suggested patient-centered approach to determining blood pressure targets in diabetes

| Stringent targets | Relaxed targets |
|-------------------|-----------------|
| Age               | Young           | Elderly              |
| Expected life expectancy | Long         | Short                |
| Symptoms          | Symptomatic     | Asymptomatic         |
| Risk factors      | AVSCD risk factors, for example, obesity, dyslipidemia, smoking | Chances of dehydration, for example, fasting, hot climate; risk of falls, for example, osteoporosis |
| Complications     | Proteinuria     | Orthostatic hypotension |
| Pill burden       | Low             | High                 |
| Cost burden       | Low             | High                 |
| Patient motivation| High            | Low                  |

ASCVD: Atherosclerotic cardiovascular disease

### Table 3: Comparison of blood pressure targets and interventional thresholds in diabetes

| Authors/parameter | Panel members of JNC8 | ADA-SMC 2017 | ESH/ESC 2013 |
|------------------|-----------------------|--------------|--------------|
| Target SBP       | <140                  | <140         | <140         |
| Target DBP       | <90                   | <90          | <85          |
| Threshold for initiating lifestyle changes | Not discussed | >120/80 | >130/85 |
| Higher targets suggested for | >60 years (SBP>150) | Older adults (>65 years) requiring palliative care | Elderly (SBP >150) |
| Lower targets suggested for | | Younger patients | Overt proteinuria (SBP <130) |
|                   | | High risk of stroke albuminuria | Additional ASCVD risk factor |

ADA: American Diabetes Association, DBP: Diastolic blood pressure, ESC: European Society of Cardiology, ESH: European Society of Hypertension, JNC8: Eighth Joint National Committee, SBP: Systolic blood pressure, SMC: Standards of Medical Care, ASCVD: Atherosclerotic cardiovascular disease
treat the patient as an equal partner in shared decision-making, basing these decisions on not only biomedical but also psychosocial determinants as well.

Such a patient-centered outline needs to be debated and critiqued while serving as a framework for future research and evidence generation. In the end, however, clinical judgment or rather, “good clinical sense,”[8] should prevail.

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