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Hypertension Highlights

New US National Hypertension Guidelines -- JNC 8 -- To Be Announced?

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Abstract

The National Heart, Lung, and Blood Institute of the US National Institutes of Health has now reversed its previous position and announced that it will promulgate an updated version of the current national hypertension guidelines (JNC 7), for publication in 2009, along with updates of other key cardiology guidelines, to result in an overall cardiovascular knowledge network. The role of the American Society of Hypertension in this endeavor has also been clarified. In other news this month, several new analysis of key NHANES data or well-known clinical trial data provide insights into the prevalence of hypertension, its control or failure to persist in therapy to control, and its attendant comorbidities in important population subsets.

New US National Hypertension Guidelines (JNC 8) Scheduled for 2009

The National Heart, Lung, and Blood Institute (NHLBI)[1] announced that it is in the process of appointing an expert panel to review and update the US national hypertension guidelines. Since the first Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure was published in 1976, the guidelines have been updated every 4-5 years. The latest, the Seventh Report (JNC 7), was published in 2003;[2] however, since 2003, other hypertension management guidelines have appeared in the United States, including those published by the American Heart Association for patients at high cardiovascular risk,[3] and other national guidelines published the same year, such as those in Europe, have already been updated.[4,5] Some other national guidelines, such as those in Canada, are updated annually. The NHLBI has said that it expects to release the Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) in 2009.

JNC 8 will be one of 3 new updated guidelines scheduled for release by the NHLBI in 2009.[6] Separate expert panels are being convened to update and develop new guidelines for the prevention, detection, evaluation, and treatment of high blood

cholesterol/dyslipidemia -- Adult Treatment Panel (ATP) IV, an update of ATP III published in 2002[7] and updated in 2004,[8] -- and guidelines on overweight/obesity in adults, originally published in 1998.[9] The NHLBI does not expect that the previous guidelines will require a complete overhaul; instead the panels will be able to focus on updating the most pertinent issues that could improve important health outcomes. As part of the update process, the panels will also propose strategies for improving the dissemination and implementation of the updated guidelines.

As part of the NHLBI's longer term plan, all 3 updated guidelines will eventually be integrated into an evidence-based, comprehensive set of clinical guidelines for overall reduction of cardiovascular disease in adult patients directed mainly at primary care practitioners. These guidelines are scheduled to be released in 2010. An additional expert panel is being set up to review and update scientific evidence related to the assessment and management of cardiovascular risk factors for the integrated guidelines.

The NHLBI says the review "will be based on an evidence model that will give rise to a set of critical questions to be answered by the scientific evidence." The panel will focus on developing a comprehensive integrated guideline across all cardiovascular risk factors to more closely mimic "real world" clinical scenarios faced by individuals and clinicians. In addition to reviewing and updating the scientific content and integrating multiple cardiovascular risk factors into one comprehensive guideline, the expert panel will also focus on implementation, developing more user-friendly guidelines that will be easier for clinicians and patients to put into practice. This includes the development and use of "innovative tools to facilitate guideline adoption and adherence to recommendations in order to improve the current state of suboptimal risk factor assessment and management." This new effort will be the first of its kind to address overall cardiovascular risk factor identification and treatment in adults within 1 guideline, the NHLBI says. The update panels will function as subpanels of the integrated guidelines panel.

The Cardiovascular Knowledge Network

As part of its "longer term vision," the guideline development effort will feed into development of a cardiovascular knowledge network (CKN). The CKN is intended:

"to facilitate interaction among the domains of knowledge generation, knowledge translation and dissemination, knowledge utilization, and knowledge technology to bridge the gap between discovery and delivery, identify knowledge gaps that should be addressed by future research, bring user communities together to better meet their needs, and speed translation of research into practice through use of more effective approaches for synthesizing and organizing evidence."

The Role of the American Society of Hypertension

In the January issue of *The Journal of Clinical Hypertension*[10] Daniel Levy, MD, director of the NHLBI's Center for Population Studies and Framingham Heart Study and a director-at-large of the American Society of Hypertension (ASH), emphasizes the future role of ASH in the development of the new hypertension guidelines. "ASH will participate in a leadership capacity as a key stakeholder throughout this guideline development process," he says. He reports that Suzanne Oparil, MD (University of Alabama at Birmingham), current President of ASH, will represent ASH as a member of the newly formed NHLBI Clinical Guidelines Leadership Group for Cardiovascular Disease Risk Reduction. The Clinical Guidelines Leadership Group, which will meet annually, consists of representatives of major professional and patient stakeholder communities. Dr. Levy reassures ASH members that "As ASH's President, Dr. Oparil's membership in the guidelines leadership group means that the perspectives of ASH -- its membership and leadership -- will be heard throughout the guidelines development process." In 2005 ASH leaders proposed a new definition of hypertension and proposed expanding the definition and classification by incorporating the presence of absence of risk factors, early disease markers, and target organ damage in addition to blood pressure levels.[11] At that time, with no update of JNC 7 scheduled, the Society was discussing other ways in which new hypertension guidelines for the United States could be produced.

Hypertension Prevalence in the United States Remains Unchanged Since 1999

New data from the National Health and Nutrition Examination Survey (NHANES) show that between 1999 and 2006 there was no significant change in the prevalence of hypertension (systolic blood pressure [SBP] ≥ 140 mm Hg, diastolic blood pressure [DBP] ≥ 90 mm Hg, or current use of antihypertensive medication) in US adults. The overall age-adjusted prevalence of hypertension varied only slightly between 28% and 30%, and there were no changes in hypertension prevalence by gender, age, or race/ethnicity.

Data from NHANES 2005-2006,[12] summarized in the January 2008 issue of the *NCHS Data Brief*,[13] show that overall, 29% of all US adults aged 18 years or older had hypertension during this period. The prevalence of hypertension increased with age, from 7% among individuals aged 18-39 years to 67% in those 60 years of age or older. Non-Hispanic blacks had a significantly higher prevalence (41%) compared with non-Hispanic whites (28%) and Mexican Americans (22%). Overall, 37% of adults had prehypertension (ie, SBP 120-139 mm Hg or DBP 80-89 mm Hg) and were not taking antihypertensive medication. The prevalence of prehypertension also increased with age and was higher in men (43%) than women (39%) but did not differ significantly among racial/ethnic groups.

Of the total population of adults with blood pressure ≥ 140/90 mm Hg, 6.6% had never been told so by a healthcare provider. Among

adults with hypertension, 78% were aware of their hypertension and 68% were taking antihypertensive medication. Among those taking medication, 64% had their blood pressure controlled (< 140/90 mm Hg). Awareness of hypertension among those with the condition was higher in women aged 18-59 years compared with men in the same age group (87% vs 63%, respectively), whereas awareness and treatment were comparable between men and women 60 years of age and older. The same relation was seen for antihypertensive treatment, with 74% of women aged 18-59 years taking antihypertensive medication compared with 47% in the same age group. Overall, 64% of patients taking antihypertensive medication had their blood pressure successfully controlled. Blood pressure control was similar for men and women aged 18-59 years, but the proportion with control was higher for men than for women 60 years of age and older (64% vs 53%, respectively).

Mexican Americans with hypertension were less likely to be aware of their condition compared with non-Hispanic blacks and less likely to be treated compared with non-Hispanic blacks and non-Hispanic whites (50% vs 72% and 69%, respectively). There were no race/ethnic differences in the proportion of patients who had controlled blood pressure among those on medication.

Yechiam Ostchega, PhD, RN, and co-authors note that despite recent advances in medical treatment of hypertension and public health campaigns to reduce the prevalence of hypertension, the condition remains a significant public health problem in the United States. They believe that the information about awareness of hypertension, treatment, and control of blood pressure among those with the disease provides a basis for targeting public health efforts to reduce blood pressure levels and the prevalence of hypertension.

The National Health and Nutrition Examination Survey

NHANES is a nationally representative survey conducted by the US Centers for Disease Control and Prevention to monitor the health and nutritional status of the US population. The survey consists of interviews conducted in participants' homes, standardized physical examinations, and laboratory tests using blood and urine specimens provided by participants during the physical examination. The NHANES sample is selected through a complex, multistage design that includes selection of primary sampling units (counties), household segments within the counties, and sample persons from selected households. The sample design includes oversampling to obtain reliable estimates of health and nutritional measures for population subgroups. In 2005-2006, African Americans, Mexican Americans, persons with low income, persons 12-19 years of age, and persons 60 years of age and older were oversampled. In 1999, NHANES became a continuous survey, fielded on an ongoing basis. Each year of data collection is based on a representative sample covering all ages of the civilian, noninstitutionalized population. Public-use data files are released in 2-year cycles.

Hypertension Control in the United States Remains Poor in Adults With Cardiovascular Comorbidities

Nearly three fourths of American adults with conditions such as coronary artery disease (CAD), congestive heart failure (CHF), stroke, diabetes mellitus, or other conditions that raise their risk for cardiovascular disease also have hypertension, according to a study published in the December 2007 issue of *Archives of Internal Medicine*.[14] Although 75% of these individuals with hypertension were being treated -- a high rate compared with patients with uncomplicated hypertension, say the authors -- only one third to one half had their blood pressure controlled. "Recent estimates indicate little change in the prevalence of hypertension, and, although there seem to be some recent improvements in treatment and control rates, hypertension in many persons remains inadequately controlled," the authors write.

In the study, which was supported by a contract from Bristol-Myers Squibb to the University of California at Irvine, Nathan D. Wong, PhD (University of California, Irvine) and colleagues analyzed data from adults participating in the NHANES (see above). In NHANES for 2003-2004,[15] 4646 adults provided demographic and socioeconomic information and underwent laboratory testing and physiologic measurements that included complete data on blood pressure values. A total of 1671 (31.4%) of these participants had hypertension, defined as SBP ≥ 140 mm Hg or 130 mm Hg in those with diabetes or chronic kidney disease (CKD), or DBP ≥ 90 or 80 mm Hg, respectively, or reported use of blood pressure-lowering medication. The prevalence of hypertension increased with age and was greatest in African-American participants (37.4%). Of these participants with hypertension, 68.5% were being treated and 52.9% of those under treatment had their hypertension in control. Women and men had similar treatment rates, but control tended to be higher in men than women (56.5% vs 49.4%, respectively). Although treatment rates increased with age, control rates decreased with age. Treatment and control rates were similar in black, Hispanic, and non-Hispanic white patients.

Overall, 23.1% of individuals without cardiovascular comorbidities had hypertension compared with 51.8% to 81.8% ($P < .01$). Specifically, hypertension was found in:

- 81.8% of those with CKD;
- 76.8% of those with diabetes;
- 73.7% of those with peripheral artery disease (PAD);

- 73.0% of those with CAD;
- 71.4% of those with CHF;
- 61.5% of those with the metabolic syndrome;
- 69.5% of those with stroke; and
- 51.8% of individuals with dyslipidemia.

Among individuals with ≥ 2 cardiovascular disease conditions (CAD, CKD, PAD, CHF, or stroke), 76.9% had hypertension. All these hypertension rates were significantly higher than the hypertension prevalence in the no-disease group ($P < .01$).

The most common hypertensive subtype identified in the study was isolated systolic hypertension (ISH), in 57.0% overall of participants with hypertension. Compared with the rate of ISH in participants with no comorbidities (41.9%), however, ISH prevalence was significantly higher in participants with dyslipidemia, diabetes mellitus, CKD, CHF, or PAD (68.8% to 95.2%; $P < .05$ to $P < .01$). These findings provide further evidence that the notion that systolic hypertension need not be treated if DBP is lower than 90 mm Hg "is mistaken," Dr. Wong and his colleagues emphasize.

Despite hypertension treatment rates for diabetes mellitus, stroke, CHF, and CAD that were higher (83.4% to 89.3%) than the rates of those without these conditions (66.5%) ($P < .01$), control rates for treatment were low (23.2%-49.3%) ($P < .001$ to $P = .048$). Dr. Wong and his colleagues note that if they had applied newer recommendations that blood pressure in patients with CAD and other high-risk conditions be reduced to < 130/80 mm Hg,[3,4] control rates would have been even lower. Rates of control to blood pressure < 130/80 mm Hg in the patients with diabetes mellitus or CKD were even poorer, at 35.3% and 23.2%, respectively ($P < .01$ vs no-disease group).

The finding of poor control in diabetes patients suggests that there has been no improvement in hypertension in this group since the 1999-2000, when a control rate of 36% was reported,[16] the investigators suggest. They describe the prevalence, treatment, and control rates in CKD patients as "a cause for great concern," pointing out that hypertension has been reported to be present in > 80% of CKD patients.[17] They attribute the poor treatment and control rates in part to an inability to recognize advanced renal disease from serum

creatinine level alone and the failure to determine creatinine clearance in these patients.

Comment

In an accompanying editorial,[18] Theodore A. Kotchen, MD (Medical College of Wisconsin, Milwaukee), suggests several explanations for the gap between recommended treatment guidelines and clinical practice. "These reasons may include the complexity or difficulty of achieving the recommended guidelines, patient or physician behavior and/or deficiencies in the system of healthcare," he says. "Achieving these target goals requires more intensive interventions, an increased potential for adverse effects, and frequent monitoring. Both physicians and asymptomatic patients may be unaware of the added benefits of optimum control. Alternatively, they may be satisfied with less-than-optimum control and may consider that the potential added benefits of more rigorous control do not warrant the added investment of time, energy, expense, and potential for adverse effects. Indeed, there may be skepticism about the scientific validity of guidelines recommended by expert panels." He adds that limited access to care and the cost of medications may also contribute to less-than-optimum control. "Developing effective strategies to address the slow pace of dissemination into healthcare will require a better understanding of the potential barriers," he concludes.

Nonpersistence With Antihypertensive Therapy

Although the prevalence of nonpersistence with antihypertensive medication (complete discontinuation of therapy prematurely) has decreased in recent years, nonpersistence remains significantly higher in certain sections of the US population, according to a study reported in the January 2008 issue of the *American Journal of Hypertension*.[19] By analyzing data collected by NHANES between 1988 and 2002, Leonelo E. Bautista, MD, MPH, DrPH (University of Wisconsin, Madison), calculated that nonpersistence with antihypertensive medication is significantly increased in younger people, in men, and among Hispanics. It is also increased in people with low income, no health insurance, and a history of failure to consult a doctor in the previous year.

Dr. Bautista believes that his study, which was funded by the American Heart Association, is the first of its kind to simultaneously measure the independent effect of patient's predisposing, enabling, and need characteristics on persistence with antihypertensive medication. Since the study used nationally representative samples, its findings were unlikely to be affected by selection bias and so can be extrapolated to the US population, he says. Previous studies mostly comprised elderly people enrolled in single health insurance plans and had poor representation of ethnic minorities, he notes.

Dr. Bautista used data from a total of 6100 subjects who participated in NHANES III (1988-1994),[20] NHANES 1999-2000,[21] and

NHANES 2001-2002[22] and who had been prescribed antihypertensive medication. Among this group, 903 individuals were not taking antihypertensive medication, corresponding to a sampling weighted national prevalence of 12.5%. Multivariate analysis showed that age, gender, and race were the only predisposing factors independently associated with nonpersistence. After adjustment for other risk factors, nonpersistence was found to be 2.5 times higher in people aged 30-49 years and 12 times higher in people aged < 30 years than in those 50 years of age or older (both $P < .001$). The effect of age was stronger than seen in previous studies, probably because this study included subjects from a wider age range, Dr. Bautista suggests. Nonpersistence was also 31% higher in men than in women ($P = .011$), and 43% higher in Hispanics compared with other racial groups ($P = .027$). Dr Bautista suggests that the increased nonpersistence in Hispanics could be partly explained by communication difficulties resulting from linguistic barriers and poor understanding between patients and physicians.

Low Income, No Insurance, No Doctor Visits

All enabling factors were independently and significantly associated with nonpersistence. Patients on a low income (< $55,000 per year) were almost twice (1.96 times) as likely to be nonpersistent as those with a higher income ($P < .001$). Having no health insurance increased nonpersistence by 88% ($P = .002$). The enabling factors with the strongest effect on nonpersistence was visiting the doctor during the last year; patients who made no visit were 10 times more likely to be nonpersistent than those who made ≥ 1 medical visit ($P < .001$). Together these 3 risk factors increased nonpersistence 2.56 times and accounted for an excess of 53.1% of all cases. None of the need factors studied (body mass index, self-reported health status, or coexisting disease) was significantly associated with nonpersistence. Between 1988 and 1994 and 2001 and 2002, the prevalence of nonpersistence decreased by 27%.

Noting that, in addition to young age, factors related to access to healthcare and medications (low income, health insurance, and visits to the doctor) were the main predictors of nonpersistence, Dr. Bautista suggest that policies to improve access to healthcare care and patient follow-up may have a major impact in maintaining persistence.

High or Low Blood Pressure After Myocardial Infarction Increases Risk of Cardiovascular Events

The dangers associated with having hypertension at the time of an acute myocardial infarction (MI), and also with having elevated or low blood pressure during follow-up have been shown by a post hoc analysis of data from the Valsartan in Acute Myocardial Infarction Trial (VALIANT). In the January 2008 issue of *Circulation*,[23] Jens J. Thune, MD (Brigham and Women's Hospital, Boston, Massachusetts), reported that among the VALIANT patients, a well-treated post-acute MI population, those with antecedent hypertension had an increased risk of cardiovascular events. Both high and low SBP after MI were also associated with adverse cardiovascular outcomes.

In VALIANT, a study sponsored by Novartis Pharmaceuticals, patients with left ventricular (LV) function (LV ejection fraction < 35%), heart failure, or both, plus SBP > 100 mm Hg between 12 hours and 10 days after an acute MI were randomly assigned to treatment with valsartan (160 mg twice daily), captopril (50 mg thrice daily), or both (valsartan 80 twice daily plus captopril 50 mg thrice daily).[24,25] Of 14,703 patients enrolled in the trial, 8575 (58.3%) reported antecedent hypertension, 7609 (88.7%) of whom reported receiving medical treatment. Multivariate analysis adjusted for age, gender, body mass index (BMI), estimated glomerular filtration rate (eGFR), previous MI, heart failure, or stroke, baseline diabetes peripheral vascular disease, and New York Heart Association (NYHA) class, antecedent hypertension was associated with a statistically significant increased risk of cardiovascular outcomes: cardiovascular death (by 11%), MI (27%), heart failure hospitalization (19%), stroke (27%), sudden death or resuscitated cardiac arrest (9%), as well as a composite of all these endpoints (13%).

Different Risks for High or Low Blood Pressure

Of 10,532 patients who had not had a cardiovascular event by 6 months of follow-up, 1522 had elevated blood pressure (SBP > 140 mm Hg) and 602 low blood pressure (SBP < 100 mm Hg) at 2 of 3 follow-up visits during the first 6 months. Over a median post MI follow-up of 24.7 months, patients with elevated SBP were at significantly higher risk of a combined cardiovascular outcome (as above) and stroke compared with patients with normal SBP. This risk was highest in patients taking a statin or not taking long-lasting nitrates. Patients with low SBP had a higher risk of heart failure, cardiovascular death, all-cause death, and the combined cardiovascular outcome. They were also more likely to have renal impairment, although this was not true of patients with high SBP. The effects on the risk associated with high or low SBP over the first 6 months after MI was seen in patients with and without antecedent hypertension. Classification of patients based on DBP (> 90 mm Hg or < 60 mm Hg) showed similar trends to those seen for SBP, but the relationships were not significant because of the lower number of patients with consistent DBP.

Dr. Thune and his colleagues note that patients with a history of hypertension have been shown to be at the greatest risk for adverse LV remodeling post-MI, which is associated with an increased likelihood of adverse outcomes. Similarly, LV hypertrophy (LVH), a consequence of hypertension, is itself an independent predictor of both adverse remodeling and clinical outcomes after MI. However, since few data are available on patients with high-risk MI from large, randomized, placebo-controlled

hypertension trials, which either excluded patients with heart failure or included few post-MI patients, it remains unknown whether aggressive blood pressure treatment in the post-MI population would reduce the risk of stroke or other cardiovascular events.

The finding that high blood pressure at follow-up increased post-MI cardiovascular risk is in contrast with the conclusions of other

studies in patients with heart failure, which have reported that increasing blood pressure improves prognosis. The investigators note that only 11% of the VALIANT patients had NYHA class III or IV heart failure at 6 months follow-up and that in patients without overt heart failure, elevated blood pressure may be more common and reflect an increased risk of ischemic events.

Comment -- Time for the "J" Curve?

In an accompanying editorial commentary,[26] Scott J. Denardo, MD, and co-authors comment that with the exception of clinically stable patients with CAD who have undergone bypass grafting, the optimal blood pressure after MI appears to be within the range 120-139/75-89 mm Hg. They note that current guidelines for the management of patients with ST-segment elevation MI (STEMI) or non-STEMI[27,28] recommend a target blood pressure of < 140/90 mm Hg (< 130/80 mm Hg in patients with diabetes mellitus or renal failure), with "lower is better" as the overall message in secondary prevention. However, the results of the study by Thune and colleagues,[23] the International Verapamil SR-Trandolapril Study,[29] and others who include excessively low pressures for analysis do show a "V-," "J-," or "U-" shaped curve, and therefore suggest that there should be a lower limit set for the target SBP and DBP except for, perhaps, DBP in patients with previous bypass grafting. Dr. Denardo and co-authors believe that it is not yet time to update the acute MI guidelines to include a lower limit to the target blood pressure, but that some caution might be prudent until more data are available. "If an appropriately powered randomized trial confirms that excessively low blood pressure (< 120/75 mm Hg) indeed increases adverse outcomes, compared with patients assigned a low blood pressure target (120 to 130/75 to 80 mm Hg), then the time will be on us to update the guidelines," they suggest.

Left Ventricular Hypertrophy Highly Prevalent in African Americans Despite Blood Pressure Control

An "extremely high prevalence" of LVH has been identified in a large cohort of African Americans with hypertensive renal disease, despite evidence of good blood pressure control. This finding comes from the African-American Study of Kidney Disease (AASK) Cohort Study, an extension of the original AASK trial, and indicates that LVH is likely multifactorial in these patients, but also suggests that African Americans may have a genetic predisposition to LVH, say Gail E. Peterson, MD (University of Texas Southwestern Medical Center Dallas) and co-investigators in the December 2007 issue of *Hypertension*.[30]

African Americans are at increased risk for cardiovascular disease morbidity and mortality, and more frequently progress to end-stage renal disease compared with other ethnic groups. AASK, carried out between 1994 and 2001, investigated the effects of 3 medications used as initial antihypertensive therapy (ramipril, metoprolol, and amlodipine) and usual (mean arterial pressure 102-107 mm Hg) or lower (mean arterial pressure < 93 mm Hg) blood pressure control.[31] The trial enrolled 1094 African-American hypertensive adults

with DBP ≥ 95 mm Hg, GFR 20-65 mL/min/1.73 m^2, and no apparent cause of renal insufficiency other than hypertension, who were followed for 3-6.4 years.

Patients in AASK achieved blood pressures averaging 128/78 mm Hg in the lower blood pressure group and 141/85 mm Hg in the usual blood pressure group. There was no difference in the clinical composite outcome, reduction in GFR by 50% from baseline, the development of end-stage renal disease, or death, or in the progression of renal disease. The ramipril group showed a significant reduction in the composite outcome compared with the metoprolol and amlodipine groups. Based on these results, and in the absence of contraindications, patients in the AASK Cohort Study were treated with an angiotensin-converting enzyme inhibitor.

All participants in AASK who had not died or reached end-stage renal disease were invited to enroll in the Cohort Study, which was funded by the National Institute of Diabetes and Digestive and Kidney Diseases, and the National Institutes of Health, as well as industry support from Pfizer , AstraZeneca Pharmaceuticals, and King Pharmaceuticals.[32] Of the 691 patients who agreed to participate in the Cohort Study, 599 had interpretable baseline echocardiograms and 24-hour ambulatory blood pressure monitoring (ABPM) performed at baseline. Despite good pressure control over 5 years before evaluation, LVH, defined as left ventricular mass index 49.2 $g/m^{2.7}$ in men and > 46.7 $g/m^{2.7}$ in women, was present in the majority of patients (69.4%) including 66.7% of men and 73.9% of women. This finding contrasts with a prevalence of about 30% reported in hypertensive patients in other studies.

Multiple regression analysis showed that higher average day and nighttime SBP, younger age, and lower eGFR were associated with LVH, but albuminuria was not. ABPM values were highly correlated with LVH, the most predictive being average daytime SBP based on ABPM, consistent with previous reports. Although average SBP was well controlled in this population, average nighttime SBP, which was also strongly predictive of LVH, was elevated. The researchers note that African Americans have been shown to have higher nighttime blood pressure than whites, despite similar daytime values, and that the absence of a fall in nocturnal blood pressure has been linked to target organ damage. Observational studies in hypertensive patients have shown that patients with elevated nighttime blood pressure are at increased risk of cardiovascular events. In the AASK Cohort Study population, there was an additive relationship between daytime and nighttime ambulatory blood pressure, with the greatest left ventricular mass (LVM) occurring in patients with upper quartile measures of both.

Possible Explanations

The investigators say that the association between younger age and LVH may have been due to a survival bias in the study. The finding of a lack of a relationship between albuminuria and LVH may have been a result of using ABPM values, as other studies using

ABPM also reported a lack of this association. Another reason may have been the use of angiotensin-converting enzyme inhibitors. The relationship between eGFR and LVH may represent an indirect of blood pressure elevation over time and factors associated with renal impairment may contribute to the target organ damage and cardiovascular risk in these patients.

"The association between renal dysfunction and LVH may explain in part the high cardiovascular morbidity and mortality observed in African-Americans with hypertensive kidney disease," the researchers suggest. They raise the question of whether LVH itself should be a therapeutic target. "Our own findings that LVH and LVM were significantly associated with daytime and nighttime SBP provide a strong rationale for additional research, particularly clinical trials, that test whether reduction in ABP and targeted treatment of nighttime blood pressure reduce LVM and prevent cardiovascular events."

Blood Pressure Values No Predictor of Left Ventricular Hypertrophy in Children With Primary Hypertension

In contradistinction to the previous finding concerning LVH, another study has found that it appears to be common in children with hypertension, suggesting that many children are already showing the adverse cardiovascular consequences of their hypertension when they are diagnosed. A new study in an ethnically and geographically diverse sample of children with newly diagnosed primary hypertension has reported that 41% had LVH, a result consistent with findings in several other studies. However, unlike other studies that found higher casual blood pressure to be associated with LVH or ABPM to be correlated with LVH, this study did not find any blood pressure variable to be predictive of the presence or absence of LVH in these children. Reporting their study in *The Journal of Pediatrics*,[33] lead author Tammy M. Brady, MD, MHS (Johns Hopkins University, Baltimore, Maryland) and other investigators write that since neither the severity of blood pressure elevation nor the presence of abnormal ambulatory blood pressure at initial diagnosis are predictors of LVH, all children with hypertension should undergo echocardiography for evaluation of LV structure at initial examination.

Brady and colleagues[34] carried out a cross-sectional study in 184 children (mean age 12.9 years, 65% male, 49% nonwhite) who were referred for initial evaluation of raised blood pressure at 1 of 3 tertiary care centers. All children had a diagnosis of primary hypertension after a standardized evaluation[34] and as recommended by US guidelines.[35] Casual blood pressure and various ambulatory blood pressure variables were analyzed to determine their association with LVH, defined after echocardiography by cardiologist diagnosis or a left ventricular mass index , calculated as LVM/height ≥ 95th percentile (36.88 $g/m^{2.7}$ for girls and 39.36 $g/m^{2.7}$ for boys).

A total of 41% of children who had echocardiograms (57/140) had LVH. Children with LVH were significantly more likely to be

nonwhite and have a higher BMI z-score. The prevalence of LVH was higher in children who were nonwhite and obese (BMI ≥ 95th percentile) at 61% compared with 39% in nonwhite nonobese, 35% in white obese, and 26% in white nonobese.

Among the 94 children who had echocardiograms and ABPM, children with LVH did not differ significantly from children without LVH with respect to mean daytime, nighttime, or 24-hour blood pressure, blood pressure index, or blood pressure load, although all mean blood pressure, 24-hour, and daytime blood pressure index values tended to be higher in children with LVH. There was also no difference in casual SBP or DBP index in children with LVH and children without LVH. Additional analyses showed no difference in the prevalence of LVH between children with both 24-hour SBP load > 50% and ambulatory 24-hour SBP index > 1.0 and children without these criteria (40% vs 41.5%, respectively).

Predictors of Left Ventricular Hypertrophy in Children

Dr. Brady and her colleagues conclude that in children with newly diagnosed hypertension, the degree of blood pressure elevation cannot predict the absence of LVH and that race and BMI may be more important in identifying LVH. "The high prevalence of LVH in all children leads us to recommend echocardiography in all children with primary hypertension as part of their initial workup," they write. "Moreover, future studies are warranted to determine which children are at risk for the development of left ventricular disease and whether current antihypertensive treatment regimens are adequate to promote LVH regression."

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