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REVIEW ARTICLE

Risk Assessment in Young Hypertensives

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ABSTRACT

Hypertension (HT) in young (< 40 years) is a significant problem in India. Preventing cardiovascular disease in these young hypertensives is a major challenge as management strategies for young hypertensives are not very clear. Risk assessment in young hypertensives is also limited as most of the risk assessment algorithms apply to population above 40 years. Unfortunately, we do not have a specific algorithm for Indian patients. The algorithm given by Joint British Societies (JBS-3) appears to be most suited for risk assessment in young Indian Hypertensive individuals. Additionally, multiple newer markers may be needed to understand the cardiovascular risk completely in the young hypertensive population.

Keywords: Cardiovascular risk assessment, Risk markers, Young hypertensives.

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INTRODUCTION

Hypertension (HT) is the leading cause of cardiovascular (CV) morbidity and mortality all over the globe. The incidence of HT is rising rapidly in the Asian countries including India. Approximately 30% adults (> 20 years of age), urban as well as rural, are suffering from HT in India.[1,2] A focused approach is required to manage this alarming increase in the incidence of hypertension and allied risk factors. Since the morbidity and mortality in HT results from CV events, every hypertensive must undergo assessment of risk for CV events. Aggressive management of high risk patients lowers the elevated risk. Aggressive management strategy today includes antihypertensive drugs, therapeutic lifestyle changes (TLC), statins and aspirin. Since TLC may be good for every adult, the issue of risk assessment boils down to use of statins and aspirin in young hypertensives. Thus, the purpose of risk assessment is to identify individuals who will derive significant benefits from drug therapy.

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Young Hypertensive

Although hypertension affects adult population (>18 years), most of the studies have included people over 50 years of age and limited data exists about younger people especially below 40 years of age. India is a young country with 65% of its population under 35 years of age. According to 2014 data, India has about 380 million individuals in the age group of 20 to 39 years.[3] Assuming a modest estimate of hypertension prevalence of 20% in this population, number of hypertensive individuals in this age group exceeds 75 million. This large number of hypertensive individuals if not detected and treated in time will exert tremendous burden on the healthcare systems in the years to come. Unfortunately, data about risk assessment and management of hypertension in this age group is sparse. Detection of hypertension in this group of young individuals is a challenge as most of them are asymptomatic. Even when hypertension is detected, physicians may be reluctant to label them with a medical diagnosis that may have implications for the future insurance, jobs and perceptions of health.[4] Besides, significance of isolated systolic hypertension (ISH) or isolated diastolic hypertension (IDH) at young age remains a matter of debate. However, recent data indicate that ISH even in young confers added CV risk.[5] Long-term follow-up data from Chicago Heart Association Detection Project in Industry study[6] showed that ISH in the young was associated with higher CV risk as compared to high normal blood pressure (BP) over follow-up of 31 years. Harvard Alumni Health study[7] also showed elevated BP in the early life (university entry) was associated with higher risk of all-cause mortality over follow-up of more than 40 years. Similar observations have been reported from follow-up of more than 4 decades in Glasgow University students.[8]

CARDIOVASCULAR RISK ASSESSMENT

Management of hypertension today focuses more on management of global CV risk in addition to of control hypertension.[9] Every hypertensive must be carefully evaluated for risk factor congregation and target organ damage at the baseline and during follow-up. Patient with target organ damage are high risk and need aggressive

therapy. Young hypertensives without target organ damage (no e/o LVH, CKD or vascular disease) must also be evaluated at baseline and during follow-up for global CV risk. In the clinical practice, it is difficult to estimate contribution of individual risk factor to the global risk in a given patient. Risk assessment algorithms help to quantify risk of 10 years CV events by offering the risk in numerical form. Quantifying risk in absolute number makes it easy for the clinician to use appropriate risk management strategies. Of the numerous risk scores available, commonly used scores include Framingham Risk Score (FRS),[10] European Systematic Coronary Risk Evaluation (SCORE),[11] the 2013 ACC/AHA ASCVD risk score[12] and JBS-3 by Joint British Societies (Table 1).[13,14] However, use of these risk score in young Indian population has certain limitations. Framingham score, ASCVD score and the SCORE tools are developed for population over 40 years of age and their applicability to people below 40 years is untested. The risk scores have been developed from large database like Framingham and have certain limitations in their applicability in the populations other than the original population. In this respect, the JBS-3 risk score developed by Joint British Societies can estimate risk for age group above 30 years up to 75 years. Further Indian ethnicity is specifically represented in JBS-3. A recent publication by Bansal et al[15] have found that the JBS-3 score provides more accurate estimation of CV risk in Indian subjects than ASCVD score. Thus for calculation of global CV risk in young Indian hypertensive population JBS-3 appears to be the best suited model in absence of one developed in India. The risk calculator is readily available online and using this can be very handy in assessing risk in clinical practice. Calculated risk above 20% is indicative of significant risk to qualify the patient for drug therapy for primary prevention.

Table 1: Comparison of risk factors considered in different risk scores

	FRS	*ASCVD*	*JBS-3*	*SCORE*
Age	✓	✓	✓	✓
Gender	✓	✓	✓	✓
Total cholesterol	✓	✓	✓	✓
HDL	✓	✓	✓	✓
Systolic BP	✓	✓	✓	✓
BP treatment	✓	✓	✓	×
Diabetes	✓	✓	×	×
Smoking	✓	✓	✓	✓
Family h/o CVD	×	×	✓	×
BMI	×	×	✓	×
Region	×	×	✓	✓
Ethnicity	×	×	✓	×

FRS: Framingham risk score[10]; SCORE: European systematic coronary risk evaluation[11]; ASCVD: The 2013 ACC/AHA ASCVD risk score[12]; JBS–3: Joint British Societies[13]

As the morbidity and mortality attached to hypertension results from CV events secondary to atherosclerosis, assessment of subclinical damage may give important clues in individuals with hypertension. Risk calculators, however, do not consider markers of subclinical atherosclerosis/arteriosclerosis like hs-CRP (exception-Reynolds Score), Aortic Stiffness measured by pulse wave velocity (PWV), ankle-brachial index, carotid intima-media thickness (cIMT) and microalbuminuria. Due to limited data on integration of these markers of vascular health in global risk prediction, it is unclear how a clinician should use this knowledge. European society of cardiology recommends that subjects with evidence of subclinical atherosclerosis should be allocated to higher risk category than that calculated with SCORE.[16] An integrated approach to evaluation of CV risk is developed at Rasmussen Center for Cardiovascular disease prevention at the University of Minnesota, MN,[17] which involves 10 tests (Table 2) to generate a disease score (DS). Each test is scored as point 0 for normal, 1 for borderline abnormal and 2 for abnormal result. A disease score above 6 is considered high risk score and is related to higher occurrence of morbid CV events over 6 years follow-up.

Considerable data are accumulated about role of these added risk markers over past 2 decades. Estimation of these additional markers in young hypertensives can help in evaluating CV risk further especially for patients in intermediate risk category. In absence of large randomized data on addition of these markers to the classic risk scores, a clinician must use his clinical judgment in interpreting results of these tests on case to case basis. Current status of these markers is discussed briefly in the following section.

Abdominal Obesity

Abdominal obesity is now recognized as an important contributor in development of diabetes and atherosclerosis especially in Asian Indians. Traditionally, obesity is

Table 2: An integrated approach for CV risk assessment developed by Rasmussen Center, University of Minnesota

1. Resting sitting blood pressure
2. Small artery elasticity (pulse wave analysis)
3. Large artery elasticity (pulse wave analysis)
4. Exercise BP response (three minutes, 5 METS)
5. Carotid intima-media thickness + plaques
6. Retinal digital photograph
7. Urine sample for albumin/creatinine ratio
8. Electrocardiogram
9. Left ventricular ultrasound for thickness, mass
10. Blood sample for N-terminal pro b-type natriuretic peptide

defined on the basis of body mass index (BMI). However, recent findings indicate that waist circumference and/or waist to hip ratio may provide a better estimate of abdominal obesity and risk of cardiovascular disease.[18] Estimation of BMI alone may underestimate risk in South Asians as they tend to have increased visceral fat and greater insulin resistance at similar levels of BMI as compared to Europeans.[19] In fact, insulin resistance is commonly noted in south Asians at BMI levels below 25 kg/m^2.[20] Population specific definitions of abdominal obesity have been incorporated into diagnostic criteria for metabolic syndrome by the National Cholesterol Education Program Adult Treatment Panel III in the United States and the cut off for waist circumference for Asian men and women is 90 and 80 cm.[21] Simple inexpensive measurement of waist circumference in the young hypertensive patients can be used as a target thus helping in advising about weight reduction through regular exercise and diet modification.

Aortic Stiffness and Pulse Wave Velocity

Aortic stiffness is a marker of arterial stiffening (arteriosclerosis) and indicates arterial wall damage in the subclinical stage.[22] Measurement of carotid femoral pulse wave velocity (CFPWV) reflects stiffness of large arteries and is a strong predictor of future CV events.[23] Carotid femoral pulse wave velocity above 10 m/s is now considered abnormal according to the expert consensus statement of ESC (2012). Significant data indicate that use of CFPWV improves risk prediction in patients with hypertension without overt cardiovascular disease.[23-25] With measurement of CFPWV in the Framingham study,[26] 15.7% of patients at intermediate risk could be reclassified into higher (14.3%) or lower (1.4%) risk. In another meta-analysis,[27] 19 and 22% of the intermediate risk individuals were reclassified into higher or lower quartiles of risk. However, data on modulation of aortic stiffness and its impact on CV risk is limited[28] and will be evaluated in 4 years prospective Strategie de prevention Cardiovasculaire Basée sur la Rigidité Arterielle (SPARTE) Study. Smaller studies indicate that ACE inhibitors, angiotensin receptor blockers and spironolactone reduce the aortic stiffness beyond their BP reducing effects while beta-blockers limit de-stiffening of arterial wall and in fact can increase it in some patient population.[22]

C-reactive Protein

High sensitivity C-reactive protein (hs-CRP) is an inflammatory biomarker which independently predicts future vascular events in diverse population ranging from healthy individuals[29,30] to patients with acute coronary syndromes regardless of LDL cholesterol levels. Utility of elevated levels of hs-CRP over and above traditional risk factors in predicting 10 year CV events was clearly demonstrated in CV health study[31] which included men and women above 65 years of age without vascular disease. Data from JUPITER trial[32] shows that treatment of apparently healthy individuals above 50 years of age and elevated levels of hs-CRP (>2 mg/l) with rosuvastatin reduces major CV events significantly. Although utility of hs-CRP in younger individuals is not specifically demonstrated in a large randomized study, it should be equally powerful marker in this population too. The 2013 ACC/AHA guidelines[12] on the assessment of CV risk do not recommend use of this marker routinely in low risk individuals. However, it remains a very useful marker in people with intermediate risk (FRS 5 to 20%) to identify candidates for statin therapy (ACC/AHA IIb/B).

Carotid Intima-Media Thickness

Imaging the carotid arteries provide a window to detect subclinical atherosclerosis by direct visualization of wall thickening measured as cIMT.[33] Elevated cIMT and/or presence of plaques in carotid arteries has been shown to predict occurrence of stroke and myocardial infarction independent of traditional risk factors.[34-37] The relationship between cIMT and CV events is continuous and determining a threshold for CV events is rather arbitrary. Although, ESC guidelines 2007 considered cIMT >0.9 mm indicative of existing abnormality, threshold value for high CV risk was > 1.0 mm in the middle aged patients of European Lacidipine Atherosclerosis (ELSA) study.[38] In the atherosclerosis in the communities (ARIC) study[39] addition of cIMT and carotid plaques added little value for predicting CV events and reclassifying the patients into another risk category. Despite of these uncertainties a recent systematic review indicates added predictive value of cIMT in asymptomatic individuals at intermediate risk.[40]

Ankle-brachial Index (ABI)

Ratio of systolic BP measured at the ankle to brachia systolic BP provides useful assessment of peripheral vasculature. Ankle-brachial index (ABI) < 0.9 indicates advanced peripheral vascular disease[41] and is related to 2-fold increase in the 10 years CV risk in each Framingham category.[42] Despite this, addition of ABI to Framingham risk score improved risk prediction only marginally. Thus, measurement of ABI although indicates peripheral atherosclerosis, integration of this information in risk assessment has limited value in nonselected patients. A low ABI may help patients in the intermediate risk

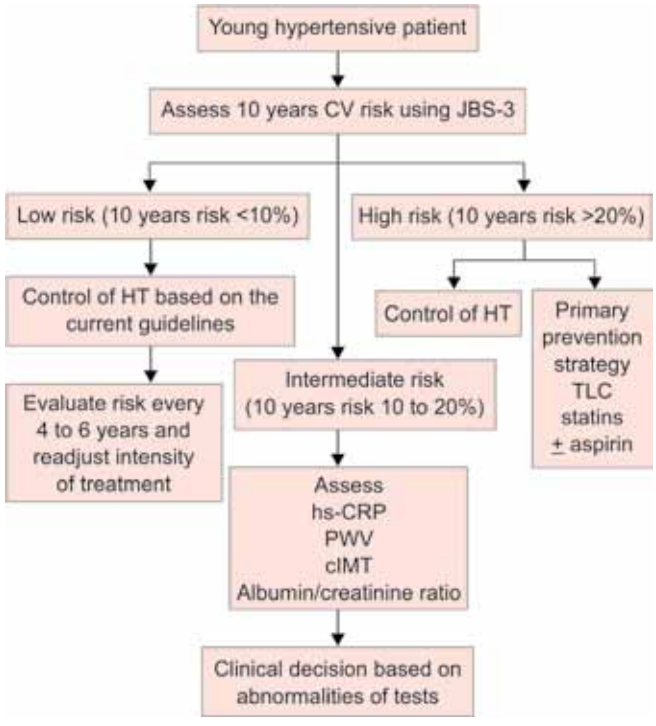
category to be reclassified into higher risk category and eligible for aggressive treatment.

MICROALBUMINURIA

Microalbuminuria is a marker for generalized vascular dysfunction. It is also an important, independent marker for endothelial dysfunction and CV diseases.[43] Traditionally, it is used in diabetic patients to monitor the development and progression of kidney disease. An international survey i-SEARCH[44] conducted to evaluate microalbuminuria in approximately 22000 hypertensive patients with or without CV disease showed the prevalence of microalbuminuria ranging from 53 to 71% patients. Highest rate of microalbuminuria was observed in patients with uncontrolled hypertension. Microalbuminuria had been shown to correlate with 4-fold increased risk of ischemic heart disease among hypertensive or borderline hypertensive subjects in 10 years follow-up analysis of all subjects with untreated arterial hypertension or borderline hypertension identified within the World Health Organization (WHO) multinational monitoring of trends and determinants in cardiovascular disease (MONICA) study.[43] Microalbuminuria is typically defined as a 24 hours urinary albumin excretion rate of 30 to 300 mg (20–200 μg/min) or urinary albumin creatinine ratio (UACR) of 2.5 to 30 mg/mmol in men 3.5 to 30 mg/mmol in women. The assessment of UACR along with the other markers of subclinical atherosclerosis can be helpful in global risk assessment of hypertensive patients. Urinary albumin excretion should be measured regularly in a hypertension clinic, and a rigorous control of BP and of other atherosclerotic risk factors is recommended in hypertensive patients with microalbuminuria. Reduction in microalbuminuria with ACE/ARB inhibitors have been shown to reduce the progression of atherosclerosis.[45,46]

Large population of young hypertensive patients in India demands early detection and optimal management to reduce subsequent morbidity and mortality. Unfortunately, strategies to optimally manage these young patients are lacking and we need to extrapolate the existing data about managing CV risk derived from older patient population. On one hand overestimation of CV risk in a young hypertensive can unnecessarily expose him to long-term drug therapy, on the other hand inadequate evaluation may lead to loss of opportunities of preventing CV events. Ideally, we need to develop specific strategies for this large pool of young hypertensive patients by systematic follow-up. Till such data are available, one can use the existing risk calculators (like JBS-3) as an initial tool to identify high risk group

Flow Chart 1: Suggested algorithm for risk assessment in young hypertensives



who clearly will benefit from intensive TLC and drug therapy (Flow Chart 1). Individuals in the intermediate risk category can undergo further evaluation for subclinical atherosclerosis. Intermediate risk patients exhibiting sub-clinical atherosclerosis are likely to benefit by aggressive preventive strategy including drugs like statins. Low risk patients may be followed up on TLC and antihypertensive therapy for adequate control of hypertensive with periodic assessment of risk development every 4 to 6 years.

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