CURRENT TOPIC

Measurement and interpretation of blood pressure

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Mercury sphygmomanometry, the most widely used indirect method of blood pressure measurement, derived from the work of Scipione Riva-Rocci and Nicolai Korotkov forms the basis of our knowledge of the epidemiology of high blood pressure. Thus, recognised hypertension was first described as a specific clinical entity associated with an increased risk of strokes in the middle aged and elderly. However, it is now known that hypertension is a quantitative and not a qualitative deviation from the norm, and that there is no natural dividing line between normal and abnormal pressures.[1]

The problem

The main problem with interpreting measured blood pressure is its variability within the same individual and also between individuals, as determined by genetic and environmental factors. In addition, genetic and environmental influences can also vary from time to time within the same individual. Therefore, attempts at standardising blood pressure at a plateau before measurement (for example, British Hypertension Society criteria) have not been very successful because of diurnal variation and environmental influences (such as the "white coat effect"), particularly in children. This led to the tendency to use the mean value of several blood pressure measurements in clinical practice.

Even with this approach there are two basic concerns regarding the interpretation of measured blood pressure in children. The first is the identification of "hypertension" as a disease entity using an epidemiological definition (for example, blood pressure above the 95th centile,[2] or two standard deviations above the mean), which is purely a descriptive demarcation without an underlying biological meaning. This is because the association between increasing blood pressure and the increasing risk of future complications or shortening of life is continuous from lowest to highest values of systolic and diastolic blood pressure.[3] The second concern relates to the identification of hypertension in children using the above definition, which was introduced with adults and essential hypertension in mind. In other words, hypertension in younger children, which is often secondary, has been recognised and treated using a threshold based on the assumption that its risks are the same as that of primary or essential hypertension in adults. This is inappropriate because the former is a sign of a disease process whereas the latter, for all practical purposes, is a disease entity in its own right.

The same threshold for recognition of primary and secondary hypertension: does it matter?

Most children with hypertension (when defined as blood pressure above 95th percentile) have only a mild increase in blood pressure and are postpubertal. They usually lack another cause considered to be "essential" in character with possible increases of cardiovascular risk in later life.[4] There are a small number of children, clearly distinct from the majority and often younger with much higher blood pressure who, in most cases, suffer from secondary hypertension. In this situation, in contrast to essential hypertension, there is an associated high morbidity and mortality in the short term, and these children require urgent treatment. The prevalence of secondary hypertension in children is about 0.1%, similar to that of childhood diabetes mellitus. Most of the underlying conditions causing this type of hypertension are rare, with a relatively small number of disorders being responsible in over 90% of patients. Most of these children (60–70%) have renal abnormalities, with reflux nephropathy and obstructive uropathy being the most common. Approximately 10% of patients, many less than 5 years of age, have renovascular disease, commonly as a result of fibromuscular dysplasia. All other causes contribute to less than 25% of cases.

Secondary hypertension results from defects in identifiable systems that amplify physiological processes to raise blood pressure. Examples of these include mechanical obstruction (as in coarctation), volume overload (salt and water retention, as in renal diseases or mineralocorticoid excess states), hyper-reninaemia (as in renovascular disease), and catecholamine excess leading to increased peripheral vascular resistance (phaeochromocytoma).[5] Several genetic abnormalities associated with hypertensive syndromes have been identified—for example, Liddle's syndrome,[6] glucocorticoid remediable hypertension,[7] and apparent mineralocorticoid excess.[8] In contrast, primary hypertension is a heterogeneous disorder (that is, different individuals with hypertension might have different genetic defects) with polygenic manifestations (more than one gene or genetic defect is required to cause forms of the disease).[9]

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In children, although the sequelae of untreated hypertension depend on its severity, duration, and cause, serious complications (for example, encephalopathy) can arise at a relatively low blood pressure value, suggesting the involvement of mechanisms other than blood pressure alone for the onset of these complications.[10] Conversely, some children with extremely high blood pressure can remain completely asymptomatic at diagnosis. The most frequent complications of severe childhood hypertension involve the central nervous system and include hypertensive encephalopathy, facial palsy, visual impairment, cerebral infarction, and haemorrhage. Cardiac decompensation and renal failure are also well recognised sequelae of uncontrolled severe hypertension. Early intervention is known to be associated with a greater chance of reversibility of the damage that has occurred.

In children with secondary hypertension, the treatment is aimed at "normalising" blood pressure (< 95th centile), preferably with treatment that is specific for the aetiology. Confusion arises particularly when a subject at risk, such as a patient with reflux nephropathy, is followed up regularly to detect hypertension. A rise in blood pressure in these patients can be detrimental to the primary disease, cause target organ damage, and worsen renal impairment. Therefore, in these patients the necessity for intervention to achieve optimal blood pressure might arise even before blood pressure values have reached the current definitions of hypertension. This suggests that there might be a group of children with secondary hypertension who have normal blood pressure (using the current definitions) but who require treatment. This might partly explain the benefits of antihypertensive treatment in reducing the progression of renal disease at normal blood pressure values.[11–13] What is not clear is at what value blood pressure should be considered abnormal in such cases.

Persistence of a blood pressure rank ("tracking") from childhood into adulthood has been documented.[14] Despite this, there is no common practice in the follow up of such cases in the context of viewing blood pressure increases as abnormal if they cross the centile lines, even though they might not have reached a value considered as hypertensive by current definitions. Should such patients be treated early? Similarly, do healthy asymptomatic children who are picked up as hypertensive on routine examination, but who have no underlying recognisable disease, have an increased cardiovascular risk? Should they receive treatment based on blood pressure value alone?

Therefore, "hypertension" in children is best defined as a "syndrome" that is associated with increased cardiovascular risk, and high blood pressure is a sign that is often (but not always) seen. Unfortunately, a better test than blood pressure measurement that will recognise this population at cardiovascular risk is yet to be described.

Nomograms for interpretation of blood pressure

The rapid increases in blood pressure found with development and maturation led to the use of age and or height, race, and sex specific centiles to identify children for further follow up and treatment.[2 15–17] Using such criteria the prevalence of sustained high blood pressure in childhood is described as 1–2%.

In contrast, hypertension, as defined by a casual blood pressure measurement of 140/90 mm Hg or higher, in adults, occurs with increasing prevalence with age, ranging from 9% in individuals 18 to 24 years old to 64% in 65 to 74 year old individuals. This suggests a false increase in the prevalence with age, which probably results from the absence of standardisation of normal age related changes of blood pressure. On the other hand, antihypertensive treatment using the above empirical threshold has been shown to be of benefit, suggesting that the treatment of blood pressure, even if "normal" for age, might be of benefit and that manipulation of blood pressure might be a tool for the prolongation of normal life span. In other words, the redefinition of hypertension in adults standardised for age might even lead to a reduction in the benefits of treatment that we have already seen. This is because many adults who are diagnosed as hypertensive under the current definition might be reclassified as normal under an age related definition and hence go untreated.

The differences between published nomograms

Published blood pressure nomograms are not interchangeable because of racial and geographical variations and methodological differences. An example of this is blood pressure interpretation, which can be relative to weight, height, or age,[2 16 17] although there are other shortcomings.[18] There are also concerns over errors between devices used for establishing blood pressure nomograms. Unfortunately, with the current rapid turnover of electronic blood pressure monitoring devices, the generation of normal data by means of a single type of a device from a reasonable sample of normal children can often become purely an academic exercise because the instrument in question is obsolete by the time the nomograms are published. This creates a need for device specific nomograms and the use of a correction factor that will allow the comparison of data between nomograms.

Instrument validation for clinical use: errors by default

The definition of normal blood pressure values in adults and children[2] is based on mercury sphygmomanometry (the inflatable cuff, limb occlusion, and auscultation technique) and, therefore, is "method specific" and not absolute. Accurate blood pressure measurement by mercury sphygmomanometry is particularly difficult in children because of the wide misinterpretation of Korotkov sounds.[2 19] Conventionally, therefore, systolic blood pressure has been used in young children, and difficulties in

auscultation, particularly in very young children, have been overcome by the use of a Doppler device.[20] In this context, some investigators have suggested that oscillometric devices might be superior to the auscultatory method, particularly in children, as a result of increased accuracy, reduced variability, and ease of use.[21 22]

Unfortunately, the differences between methods of blood pressure measurement—for example, between oscillometry and mercury sphygmomanometry—have been interpreted as "inaccuracies" as opposed to "differences" in the methods[23] because of the preconceived aim of standardising all blood pressure monitoring devices to agree with mercury sphygmomanometry. Earlier oscillometric devices often overestimated blood pressure compared with mercury sphygmomanometry, but newer models produce estimations of blood pressure that are very close to those of mercury sphygmomanometry.[24–26] It is not clear, however, whether the improvements seen in these automatic devices, particularly after the introduction of the validation protocols by the American Association for the Advancement of Medical Instrumentation (AAMI) and British Hypertension Society (BHS),[27] were truly the result of the refinement of technique or because of covert electronic manipulations within these devices. It is noteworthy that a new blood pressure device, which undertakes measurement of blood pressure by oscillometric and Korotkov methods simultaneously, has failed BHS criteria for oscillometry, but has satisfied clinical grading for Korotkov measurement.[28]

In the process of instrument validation, protocols place most emphasis upon bias (differences in measurements between the devices), with repeatability (the ability of the instrument to reproduce the same results at the same blood pressure value) receiving much less attention.[29] Therefore, certified blood pressure measuring devices on the market today might still have an inherent variability. Because of this, individual measurements of blood pressure obtained using such devices in clinical practice could be misleading, although the mean of several readings might be acceptable for routine clinical use.

Furthermore, for new blood pressure monitor validation in children, the BHS protocol[19] recommends the use of two different "gold standards", namely: the Doppler mercury technique, as described by de Swiet *et al* for under 5 year olds,[15 20] and conventional mercury sphygmomanometry for 5–15 year olds. This might have introduced a considerable bias into blood pressure monitor validation because there is a substantial disagreement between the two reference techniques.[30]

In addition, the first readings of oscillometric devices, once discarded because of overestimation, are the only valid readings used in ambulatory blood pressure monitors. This might have contributed to the recording of slightly higher mean ambulatory blood pressures using these monitors initially,[31] yet new models seem to perform equally with mercury sphygmomanometry.[32]

Mercury sphygmomanometry, although conventionally regarded as the reference method, has inherent variability as a result of technique and human error, which has not been assessed comprehensively. This might also influence clinical validation results. These factors suggest that even "approved" blood pressure measuring devices on the market today are probably less than perfect.

White coat effect: poor standardisation or pathological variation?

It has been known for many years that clinic blood pressure values tend to be higher than home values in hypertensive patients, sometimes by as much as 40 mm Hg. This difference between clinic and home blood pressure was seen mostly in individuals with hypertension; however, with time, predisposed individuals who were hypertensive under office conditions but normotensive otherwise were recognised and labelled as "white coat hypertensives". Clinic pressure in these subjects on repeated visits also fell over time with no corresponding change in their home or ambulatory blood pressure.[33] The prognosis in such subjects remains uncertain.[34] Some argue that white coat hypertension is a precursor of essential hypertension,[35 36] whereas others do not identify any increased risk of cardiovascular disease or target organ damage in this population.[34] Is it the end result of non-standardised blood pressure recording in relation to the time and place of measurement and the mental status of the subject? In other words, a selection bias seems to exist.[37] Although the solution would be to measure blood pressure under normal circumstances, the definition of a normal circumstance is equally difficult. Is it the weekend when at home or during the week when at school or work? This confusion further illustrates the lack of specificity of measured blood pressure alone in the correct identification of subjects with increased future cardiovascular risk. The existence of such a risk, even in the absence of "hypertension" as defined today, illustrates poor sensitivity of the existing method of blood pressure interpretation in identifying all subjects needing antihypertensive treatment to reduce the risk.

Ambulatory blood pressure

Although the knowledge of a diurnal rhythm in blood pressure in not new, hitherto, this had not been taken into account in the interpretation of blood pressure. With advances in technology, ambulatory blood pressure monitoring has become common practice, but has introduced further confusion. Ambulatory blood pressure defined as a day time, night time or 24 hour mean does not adequately quantify fluctuation in blood pressure, which is a known risk factor.[38 39] Mean day time blood pressure measured by ambulatory blood pressure monitoring is higher than both age and height related casual blood pressure recordings.[40] Twenty four hour mean systolic and diastolic

blood pressure correlates poorly with resting casual blood pressure in the same individual.[41] Furthermore, a lower mean blood pressure might not necessarily mean better control of blood pressure because this does not recognise the trough to peak ratio, a further index predicting the risks–benefits of antihypertensive treatment.[42 43] The importance of assessing the variability (fluctuation) in blood pressure[44 45] and pulse rate[46 47] in the identification of subjects with increased cardiovascular risk has been recognised, but such indices are not yet being used quantitatively in clinical practice.

Conclusions

The historic definition of hypertension, by cross sectional epidemiological means (rather than by estimating positive predictive values), has made blood pressure alone a less sensitive and a less specific marker of future cardiovascular risk. However, antihypertensive treatment reduces the incidence of strokes in hypertension defined in this way, but not coronary morbidity and mortality,[48] and it is still not known whether this is a direct result of the reduction of blood pressure. Therefore, the measurement of blood pressure must be considered merely as a screening test that alerts the physician to initiate investigation, but not necessarily a diagnostic test leading to treatment. Pharmacological treatment of blood pressure in the absence of any evidence of target organ damage and without adequate investigation should be avoided, although close supervision of such cases is required. Patients at high risk of developing hypertension (for example, those with reflux nephropathy) should be considered for antihypertensive treatment if an abnormal rise in blood pressure (such as crossing centile lines) occurs, even if the blood pressure itself has not reached the currently defined thresholds.

Blood pressure and pulse behaviour during day to day activity are likely to be more informative, in a similar fashion to that of beat to beat variability of the heart rate offering prognostic information after myocardial infarction.[39 49] The "nocturnal dip"[50] and the white coat effect[51] can be considered as preliminary observations of blood pressure behaviour, but still needing clarification to understand their real biological meanings. Thus, "hypertension syndrome" requiring antihypertensive treatment is probably best recognised by a score rather than just a threshold of blood pressure. This would not only allow the benefits of intervention to be extended to the currently undiagnosed cases, but could also help reduce the number of normal individuals receiving unnecessary intervention.

Finally, there is a clear need and potential to improve our methods of blood pressure measurement and interpretation. Elimination of new monitors with poor repeatability at an early stage of instrument development, clinical validation of blood pressure monitors against a reference method with maximal reliability (that is, a very low or zero repeatability coefficient, such as a direct arterial pressure transducer), and the introduction of device specific or device corrected (against mercury sphygmomanometry) nomograms, particularly for children, are manoeuvres that might result in improvement. Correction factors in this context will reduce bias originating from methodological differences and introduce the concept of method specificity among physicians and paediatricians, leading to improved interpretation of high blood pressure.

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