

Age, Race, Sex and Other Indices of Risk in Hypertension

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Among the various criteria used in evaluating the prognosis of hypertensive patients the level of the diastolic blood pressure averaged over three or more visits is the most important index. Other indices also are useful and are essential in deciding on treating patients with average diastolic blood pressures below 105 mm Hg. Included among these are sex, age and race. Male sex, young age and black race are all associated with increased risk of morbidity and mortality.

The lability of the hypertension is another indicator of risk. Patients with labile hypertension—high casual in relation to basal blood pressure—have a better prognosis than those who do not. Family history also should be considered. A history of premature death from hypertensive complications in a parent or sibling suggests that the patient may be at increased risk. Finally, the presence and extent of detectable target organ damage provides a major criterion of prognosis and indication for treatment.

It has been demonstrated repeatedly that morbidity and mortality in hypertension are quantitatively related to the level of blood pressure; the higher the blood pressure, the worse the prognosis [1-3]. This conclusion is supported by a large body of epidemiological data of which the life insurance statistics provide the largest experience [2].

It should be recognized, however, that epidemiologic data relating morbidity and mortality to levels of blood pressure are based on a comparison of frequency of events occurring in *groups* of patients. Individual members of a group may exhibit a different course than the average. In some the course may progress more rapidly and in others less rapidly than the average. Blood pressure alone, therefore only indicates whether the individual patient is in a high or low risk group at the time of examination. Unless the hypertension is quite severe, the predictive value of blood pressure alone is limited when applied prognostically to the individual case.

Because of the marked variability of blood pressure in many patients an estimate of risk should never be based on readings taken at a single office or clinic visit. The patient may have come to the physician because of discomfort or pain, or he may be apprehensive, all factors known to elevate the blood pressure. An estimate of the average blood pressure will be much more reliable if the blood pressure is measured on three

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separate office visits, under as basal conditions as possible, and the three readings are averaged.

In using blood pressure as a guide to prognosis it also should be recognized that the pattern of blood pressure change can vary considerably with time. Although the course of the blood pressure is often one of gradual progression to higher levels there are many exceptions. Heyden and his associates [4] reported on the outcome after 7 years in 30 adolescents with initial blood pressures in the range of 140/90 to 159/94 mm Hg. None of these subjects received treatment. Follow-up after 7 years, however, revealed that blood pressure levels in 12 had reverted to normal, remained unchanged in 7 and showed progression in 11; 2 of the latter died from cerebral hemorrhage. This example illustrates clearly that although as a group these subjects with borderline hypertension were at increased risk, some of them reverted to a class or group at much lower risk whereas others, whose blood pressure levels had risen, entered a group at higher risk than the one they were in originally.

Despite these reservations the blood pressure average over three or more visits, or, better yet, the average of blood pressures recorded several times daily in the hospital or at home by the patient or a member of his family, does represent the most valuable single criterion of prognosis. Probably all patients whose diastolic blood pressures average 105 mm Hg or higher should receive treatment. Not only are they at high risk as indicated by epidemiologic data [2,3], but treatment with antihypertensive agents will also give them a significant degree of protection against major complications. The Veterans Administration trial [5] indicated that in male patients with diastolic blood pressures averaging 105 through 114 mm Hg morbidity was three times as high in the control group as in the treated group. In patients with initial diastolic blood pressures averaging 90 through 104 mm Hg, however, the difference in incidence of major complications between control and treated groups was less than 2 to 1. It is particularly in this latter group of patients that other prognostic indices in addition to average blood pressure are needed to estimate the desirability of treatment or, if not immediate treatment, of the need for close and frequent follow-up. Of the various factors other than level of blood pressure that influence prognosis the most readily determinable are race, sex and age.

RACE

Not only is hypertension more prevalent in blacks than in whites but it also is more severe. With re-

spect to prevalence the National Health Survey found a blood pressure of either 160 systolic or 95 mm Hg diastolic or higher in 27 per cent of black adults as compared to 14 per cent of white adults [6]. Since the National Health Survey conducted a representative sampling of the national population, we can conclude that the prevalence of hypertension in the United States is almost twice as high in blacks as in whites. The excess prevalence in blacks was approximately the same, that is, almost 2 to 1, in every age group from youth to old age.

In addition to increased prevalence the reported death rates for hypertension and hypertensive heart disease indicate that in blacks the severity of hypertension is also increased. Not only is the disorder more common; it is also more severe. For example, vital statistics for the year 1967 indicate a death rate of 66 per 100,000 for hypertension in black men as compared to 16 per 100,000 in white men [7]. This represents a difference of approximately 4 to 1 in mortality from hypertension. A similar ratio is found in women, the mortality rates being 58 per 100,000 in black women. After correcting for the higher prevalence of hypertension in blacks, the vital statistics indicate that the mortality risk in black patients with hypertension is approximately twice that in white patients with hypertension.

When the mortality rates for hypertension in blacks and whites are subdivided according to age it becomes evident that in blacks hypertension occurring at a relatively young age carries an extremely high risk. Before age 50, reported death rates from hypertension and hypertensive heart disease are about six to seven times higher in blacks than in whites. After age 50, the death rates are two and a half times higher in blacks. However, the prevalence of hypertension is about twice as high in blacks as in whites in all age groups. Therefore, the higher death rate among blacks after age 50 can be explained largely on the basis of the increased prevalence of hypertension. Under age 50, however, the excess of mortality greatly exceeds the excess of prevalence of hypertension between blacks and whites and indicates the very high risk associated with hypertension in blacks in this younger age group. As a prognostic index the racial difference applies most importantly to black patients who are less than 50 years old.

SEX

All epidemiologic studies indicate that the prognosis in women is better than in men. According to the follow-up data of untreated hyper-

tensive patients, several investigators have observed that mortality was approximately twice as high in men as in women [8,9]. The actuarial data indicate a somewhat smaller difference in mortality between men and women [2]. For example, with a blood pressure of 150/100 mm Hg at age 45 life expectancy was reduced from normal by an average of 8.5 years in women and 11.5 years in men. On the basis of the available data it is justifiable to conclude that the prognosis is better in women than in men at any given level of blood pressure, the extent of the difference probably being somewhat less than 2 to 1.

AGE

For any given level of blood pressure the younger the patient at the onset of hypertension the greater is the reduction in life expectancy as compared to the normal subject of similar age. The life insurance data [2] indicate that at a blood pressure level of 150/100 mm Hg men aged 50 to 59 years have twice the 20 year mortality rate as do normotensive persons in the same age group. In the 40 to 49 year age group for the same blood pressure level (150/100 mm Hg) the 20 year mortality increases to 3.6 times the standard risk for that age; and at ages 30 to 39 the 20 year mortality rises to 5 times the normal. Thus, even a modest elevation of blood pressure is associated with greatly increased risk when the hypertension appears at a relatively early age.

As already mentioned, risk is lower in women than in men at all ages and according to some studies approaches the standard risk (average life expectancy for the normal population) in women age 50 and above with mild hypertension. Thus, Bechgaard et al. [10] found during a follow-up of approximately 20 years that the mortality rate in women age 50 and above with systolic blood pressures below 200 mm Hg was not significantly different from that of the general population of similar age and sex. Other data, however, do not support this conclusion. The Framingham Study indicated that with respect to stroke, for example, the risk was higher in older women as compared to older men and that the probability of developing a stroke was directly related to systolic blood pressure regardless of sex or age [3]. Nevertheless, most of the available data indicate that elderly women with hypertension have a better chance of living out their normal life span than do other age-sex groups of patients.

LABILITY OF BLOOD PRESSURE

Blood pressure varies considerably over a 24 hour period not only in hypertensive patients but also in

normal subjects [11,12]. Physical, mental and especially emotional stress elevate the blood pressure for the period that the stress is present. Physical and mental rest lower blood pressure, the lowest levels usually being recorded during sleep. Because of such lability a single recording of blood pressure may be quite misleading. The experience of screening programs indicates that many subjects who are found to be "hypertensive" at the time of the initial examination will have normal blood pressures when referred for further examination. This emphasizes the importance of obtaining a series of blood pressure readings before deciding on a therapeutic program for the patient.

Various investigators have found that the risk of major complications is much less in patients with labile hypertension whose blood pressures fluctuate widely between hypertensive and normotensive levels. Smirk et al. [13] observed that the supplemental blood pressure bore no relationship to prognosis. In contrast, basal blood pressure and, to a lesser extent, the casual blood pressure were related to prognosis. Supplemental blood pressure is the difference between casual and basal pressure and is a measure of lability. In a 16 year follow-up of 290 patients Mathison and his associates [14] found that the mortality of patients with labile hypertension was only one-third that of patients with more fixed hypertension. Lability in this case was defined as a diastolic blood pressure which dropped below 95 mm Hg with rest and sedation.

Sokolow and his associates [15] used a portable semiautomatic blood pressure recorder to measure the blood pressure throughout a day of relatively normal activity in 124 patients. They found that the average blood pressure as determined by recorder readings correlated closely with the extent of end-organ damage exhibited by the patient, the higher the average blood pressure the greater the degree of damage. Although the casual blood pressure (office recording) also was related to vascular disease, the degree of correlation was not as close as was the average of the portable recordings. Another interesting observation was that approximately one third of the patients who had a moderate elevation of both systolic and diastolic casual pressures had average blood pressures within the "normal" range.

In both the experimental animal and in man the evidence presently available indicates that the cardiovascular complications of hypertension are either secondary to or are aggravated by the elevated blood pressure. In rats with spontaneous hypertension the cardiovascular lesions are com-

pletely prevented by keeping the blood pressure from rising using antihypertensive drugs [16]. In man it has been shown that long-term control of blood pressure will reduce complications in hypertensive patients [5]. If, as the available evidence indicates, the end-organ damage found in hypertension is indeed the result of the elevated blood pressure, then it is reasonable to expect that the complications will be related to the average blood pressure rather than to occasional transient elevations. Thus, the findings by Sokolow of a close relationship between height of the average of blood pressures recorded throughout the day and the extent of end-organ damage is consistent with the general concept of a causal relationship between elevation of blood pressure and vascular complications. On the other hand, patients with labile hypertension may exhibit normal average blood pressures with only occasional elevations of relatively brief duration. It is in such patients that Sokolow found minimal or no end-organ damage resulting from hypertension.

To determine the degree of lability of the hypertension it is necessary to obtain an estimate of the so-called basal blood pressure for comparison with casual reading. The more reliable methods for obtaining basal blood pressure include (1) hospitalization with blood pressure recorded from three to five times daily for at least 3 or 4 days, and the readings obtained during the last day or two averaged; (2) recordings of blood pressure in the home twice a day by the patient or a member of his family for a period of 2 weeks; or (3) hourly recordings of blood pressure throughout an 8 hour period by a technician during a day-long clinic visit.

All these methods admittedly are time-consuming, and modifications have been used to make the procedure more adaptable to office practice. One such method is to have the patient lie quietly in a semi-darkened room while a nurse or technician records the blood pressure every 5 minutes for 30 minutes. It is important that the technician does not engage the patient in conversation during this time. The lowest reading is then taken as the basal blood pressure. Patients often react to the blood pressure measuring procedure with a pressor response. This apprehension begins to wear off as the measurements are repeated. Because 30 minutes may not be long enough for the deconditioning process to take place, this method is not as reliable as some others but may be a more practical way of assessing lability in the setting of a busy office or clinic practice.

Labile hypertension should be suspected when the height of the casual blood pressure seems to

be out of proportion to the extent of end-organ damage. Labile hypertension often is present when the patient gives a history of long-standing hypertension but on examination exhibits no or very little evidence of end-organ damage.

HYPERLIPIDEMIA AND DIABETES MELLITUS

The association between elevated serum lipids and atherosclerosis is well established. The lipoprotein pattern has been shown to be important in determining the type of metabolic defect and for selecting appropriate treatment [17]. However, according to the Framingham data, it is the level of serum cholesterol which is the important element in estimating the risk of coronary heart disease [18]. Elevated endogenous triglyceride values were associated with increased risk only when accompanied by high cholesterol values.

Although serum cholesterol levels correlate significantly with coronary disease it is only one of several influences which appear to be playing a role. No single factor can be identified as being sufficient or required for the development of this disease. The biologic variables that have been recognized as being importantly involved are cholesterol and blood pressure. Cigarette smoking, diminished glucose tolerance, obesity and lack of physical exercise are somewhat less important but are still correlated [19-21].

The risk of developing coronary artery disease in the hypertensive patient who has an elevated cholesterol or blood sugar level is significantly higher than in one who does not. The implications as to treatment are less clear, however. There is no evidence that control of the elevated blood sugar level will influence the arterial disease seen in diabetes. Although reduction of elevated serum cholesterol and blood pressure levels seems rational and desirable on the basis of the available evidence, it must be admitted that definitive evidence of benefit in the form of controlled therapeutic trials in man is still lacking. It has not yet been demonstrated that control of blood pressure or of serum cholesterol will significantly reduce the incidence of atherosclerotic disease especially of myocardial infarction. The Veterans Administration trial, for example, showed that treatment of hypertension was associated with a significant decrease in strokes, congestive heart failure, accelerated hypertension and renal failure but not of myocardial infarction [5]. It is still possible, however, that if treatment had been started at an earlier stage of the hypertensive process and continued for a longer period than the average of 3.3 years of follow-up, a significant reduction in the incidence of coronary artery disease might have

been found. We may conclude that although the increased risk of coronary artery disease in association with high blood pressure and high cholesterol levels has been amply demonstrated, the effectiveness of treatment in reducing this risk still remains undecided.

FAMILY HISTORY

It has long been recognized that essential hypertension tends to occur in families [22]. That the familial clustering is due to genetic rather than environmental influences is suggested by observations made on identical twins with hypertension [23]. Although they may have lived apart for many years similar elevations in blood pressure generally are found in both members of each pair. Platt describes one pair of identical twins in whom malignant hypertension developed within 18 months of each other. This close similarity of blood pressure levels is seen in monozygotic twins whereas in dizygotic twins the blood pressure may differ to the same degree as is found in other siblings.

A family history of hypertension is important from two points of view: one is that it suggests essential rather than secondary hypertension, and the other is that it may have prognostic implications. A history of relatively early death in a parent or sibling from a hypertensive complication such as a stroke, renal failure or congestive heart failure makes it more likely that the patient with borderline or mild hypertension will progress to a more severe stage. In Platt's series a middle-aged sibling of a patient with severe essential hypertension had about eight times the chance of having a diastolic pressure of 100 mm Hg or over as a person selected at random [23].

TARGET ORGAN DAMAGE

The importance of target organ damage in estimating the prognosis in hypertension is obvious. The mortality over a 5 or 10 year period in untreated hypertension is directly related to the extent of cardiovascular disease present at the initial examination [9,24]. Even minimal damage in either the optic fundi, heart or kidneys is associated with some increase in mortality. In the Veterans Administration study the untreated patients with initial diastolic blood pressures between 90 and 114 mm Hg were subdivided into two groups: those who exhibited any cardiac, central nervous system or renal abnormality prior to entry and those who did not. Over an average follow-up of 3.3 years the incidence of major complications was two and a half times higher in the patients with evidence of end-organ damage prior to randomization [25].

Symptoms, physical signs and laboratory data all are useful in evaluating the presence of cardiovascular damage. In the history the complaint of morning occipital headaches often accompanies severe hypertension but not mild or moderate hypertension. Cerebral vascular atherosclerosis may be suggested by unsteady gait, memory defects or transient ischemic attacks. A history of substernal pain aggravated by exercise or emotion and relieved by rest suggests the presence of coronary artery disease. A recent decrease in exercise tolerance with dyspnea on mild exertion, ankle edema in the evening and nocturia is consistent with the presence of early or incipient congestive heart failure. Intermittent claudication indicates the presence of atherosclerosis of the aorta or vessels of the lower extremities.

A most important aspect of the physical examination is the observation of the optic fundi. Aside from the obvious hemorrhages, exudates and papilledema that are associated only with severe hypertension, the fundusoscopic changes seen in less severe forms of hypertension should be interpreted with some caution. There is a considerable overlapping of normal with hypertensive patients with respect to arteriolar narrowing, tortuosity, irregularity and other changes that are supposedly related specifically to hypertension. Even arteriovenous nicking can be seen in vessel crossings near the optic disc in some normal subjects. The presence of nicking at arteriovenous crossings that are more than two disc diameters away from the optic disc, however, does provide a reliable sign of arteriolar sclerosis.

A fourth heart sound is commonly heard in hypertensive patients. It probably reflects decreased compliance of the left ventricular wall which in turn may be due to left ventricular hypertrophy. The latter, however, is more reliably indicated by the electrocardiogram. The presence of a third heart sound or diastolic gallop should alert the examiner to the presence of left ventricular failure. Finally, palpation of the peripheral pulses including the carotid and femoral arteries, and auscultation over the major vessels for the presence of bruits will give some indication of the degree of atherosclerosis of the large arteries.

As a prognostic guide the value of the chest roentgenogram is somewhat limited. Left ventricular hypertrophy even when considerable may not be apparent on the roentgenogram. Dilatation may be difficult to evaluate because the transverse diameter of the heart is greatly influenced by the depth of inspiration as well as the phase of the cardiac cycle. A gross increase in cardiac diameter, however, is good evidence of compromised

left ventricular function. An additional useful sign in the chest roentgenogram is the degree of aortic dilatation or unfolding that is present. These latter signs reflect organic changes in the wall of the aorta secondary to the hypertension.

The electrocardiogram provides one of the most useful prognostic indices in hypertension. Left ventricular hypertrophy is indicated by voltage and/or ST-T changes and the degree of such changes appears to correlate directly with mortality risk [9]. In addition, other changes in the electrocardiogram such as heart blocks or ischemia may indicate the presence of damage secondary to associated coronary artery disease.

Significant renal damage usually is not seen in the presence of mild hypertension. Renal damage is difficult to detect in the early stages of its development using the currently available clinical tests. Serum creatinine appears to be somewhat more specific and sensitive as an indicator of renal damage than blood urea nitrogen. Proteinuria also is indicative of renal damage, although when present in younger patients it suggests the presence of an underlying primary renal disease. Such a suspicion is strengthened if, in addition, the urinary sediment contains cells and casts. Whatever its cause, however, the prognosis is worse than it would be if proteinuria were absent.

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