Cardiovascular and Renal Risk Assessment as a Guide for Treatment in Primary Hypertension

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Abstract. BP levels per se may be an unreliable indicator of risk in the individual patient. In fact, the global cardiovascular profile, including the presence and degree of target organ damage, is a better predictor of future events and, therefore, should be used to choose both treatment and BP goals. However, the prevalence of target organ damage and therefore the percentage of patients who are at risk very much depends on the diagnostic techniques used. However, as a result of the high prevalence of hypertension and its financial impact on public health systems, limiting unnecessary and extensive diagnostic tests also should be a priority. The routine search for microalbuminuria may lead to the detection of a significantly greater percentage of patients who are at high risk while contributing the optimization of the cost-effectiveness of diagnostic workup in hypertensive patients.

Hypertension is the most important modifiable risk factor for cardiovascular disease, and its prevention and treatment currently represent a public health challenge in Western countries (1). Among the large number of hypertensive patients, however, only a subgroup actually develops acute morbid complications. Early identification of those who are at risk is of paramount importance because it could set the stage for a more rational therapeutic approach by allowing direct additional measures to those who need them the most. Unfortunately, the height of BP per se is often an unreliable indicator of risk in the individual patient. In fact, it has recently been suggested that global cardiovascular risk, rather than the severity of hypertension, should be used to guide the decision of whether to begin treatment and its goals (2,3). Accordingly, several factors, such as age, gender, family history, obesity, smoking habits, lipid status, and the presence of diabetes or other comorbid conditions, should be taken into consideration together with BP load to individualize treatment. In particular, the presence and degree of subclinical target organ damage, namely left ventricular hypertrophy, carotid atherosclerosis, and renal dysfunction, may turn out to be extremely useful in guiding the choice of first drug as well as the goal BP level.

Such therapeutic strategy has proved to be beneficial in terms of cost-effectiveness. Data from the National Health and Nutrition Examination Survey, for example, indicate that, with a similar 12-mmHg reduction in systolic BP, a significantly lower number of patients had to be treated to prevent a single fatal event during a 10-yr follow-up in the subgroup of patients at high risk as compared with those at low risk (4). Thus, the higher the risk, the greater the benefit achieved from a given amount of BP reduction. It is interesting that the relationship between global risk and BP reduction holds true also in the range of normal and high-normal BP values. These considerations provide the rationale for performing a thorough evaluation of risk profile, including subclinical organ damage, before starting treatment in all hypertensive patients. However, the sensitivity of risk assessment in detecting high-risk patients very much depends on the diagnostic approach used in the clinical setting (5).

Prognostic and Therapeutic Implications of Target Organ Damage

Identifying target organ damage may vary significantly, depending on the techniques used. Noninvasive assessment of cardiac and peripheral arterial structures and function by ultrasound (US) techniques is a reliable and accurate way to detect hypertensive organ damage. Routine application of this procedure, however, is not currently recommended by international guidelines, and it is performed only on a small number of hypertensive patients. An overly restrictive diagnostic approach to risk stratification could lead to significant misclassification of patients and to underestimation of the actual absolute risk, with unfavorable practical and financial consequences.

Subclinical organ damage often precedes and predicts the development of morbid events. Thus, patients with left ventricular hypertrophy, especially the concentric type, show a higher risk of developing a coronary event or a stroke as compared with those with normal left ventricular geometry (6). Similarly, carotid atherosclerosis has been associated with a worse prognosis regardless of other traditional risk factors (7). What is even more important is that under effective antihypertensive treatment, changes in subclinical organ damage over time are paralleled by modification of risk status (8). Thus, by noninvasively detecting the presence of
left ventricular hypertrophy and/or carotid atherosclerosis, not only can we gather important information to help individualize treatment but also we are able to monitor the effectiveness of treatment. Furthermore, in the presence of renal damage (renal dysfunction or proteinuria), lower BP goals (<130/80 mmHg) are recommended.

Although achieving BP targets remains the most important determinant of cardiovascular and renal protection, it has also been shown that specific classes of drugs may exert additional organ protection beyond their BP-lowering effects (2,3). A recent meta-analysis of 50 randomized, controlled trials demonstrated that angiotensin-converting enzyme inhibitors (ACEI) provide greater reduction of left ventricular mass as compared with other classes of drugs (9). More recently, results from the Losartan Intervention For Endpoint Reduction in Hypertension Study seem to add to the importance of renin-angiotensin system inhibition for cardiac protection. In fact, this study showed a significantly greater reduction of ECG-determined left ventricular hypertrophy by the use of the angiotensin receptor blocker (ARB) losartan as compared with the β-blocker atenolol, with an almost identical BP reduction in the two arms of the study (10). However, the trials completed so far, comparing the effect of various antihypertensive treatment on the regression of carotid atherosclerosis, suggest the superiority of calcium channel blockers over diuretics and β-blockers at similar BP reductions (11–14).

Finally, there is undisputed evidence that pharmacologic disruption of the renin-angiotensin system conveys superior renal protection in the hypertensive patient with renal disease and proteinuria (15). Thus, ACEI are recommended in nondiabetic patients and in those with type 1 diabetes and any degree of albuminuria, whereas ARB are considered the treatment of choice in patients with type 2 diabetes for preventing clinical nephropathy and delaying its progression to ESRD (16–18). In addition, recent preliminary data indicate that a more complete inhibition of the renin-angiotensin system obtained by the concomitant use of an ACEI and an ARB is superior to either drug alone in retarding the progression of diabetic (19) and nondiabetic renal diseases with proteinuria (20).

Usefulness of Microalbuminuria in the Treatment of Hypertensive Patients

During the past several years, an abnormal urinary albumin excretion level, below the threshold commonly used to define clinical proteinuria (i.e., microalbuminuria), has been proposed as an integrated marker of risk in patients with essential hypertension. A large number of studies have reported an association between microalbuminuria and several metabolic and nonmetabolic risk factors (increased BP load and variability, insulin resistance, lipid abnormalities, and endothelial dysfunction) (21), as well as with the presence of end organ damage, namely left ventricular hypertrophy and carotid atherosclerosis (22). Although the presence of microalbuminuria seems to be a concomitant indicator of high risk status rather than a risk factor per se, it has been shown to be a predictor of cardiovascular morbidity and mortality in patients with essential hypertension in the presence or absence of diabetes (23).

New evidence from the Losartan Intervention For Endpoint Reduction in Hypertension Study indicates that changes in urinary albumin excretion under antihypertensive treatment parallel those of ECG-determined left ventricular mass (24). Thus, given its wide availability and relatively low cost, determination of albuminuria could become a useful tool in the evaluation of global cardiovascular risk. We compared the sensitivity and costs of three different approaches to cardiovascular risk stratification in a group of 346 untreated patients with essential hypertension. The percentage of patients at high or very high risk (according to European Society of Hypertension–World Health Organization classification) as obtained by the standard approach alone, in combination with routine US-based assessment of cardiovascular organ damage, and, last, in combination with the evaluation of urinary albumin excretion varies significantly. Routine search for microalbuminuria leads to the detection of a significantly higher percentage of patients with organ damage and yields a stratification of risk almost superimposable to what is obtained by the routine use of US, although at a significantly lower cost. On the basis of these findings, we extrapolated the cost of the three different screening approaches for the general population by calculating an estimated 20% prevalence of hypertension (Figure 1). We concluded that the routine evaluation of microalbuminuria could lead to a substantial improvement in the identification of high-risk patients while optimizing the cost-effectiveness of cardiovascular risk stratification.

Conclusions

Thorough assessment of cardiovascular and renal risk, including the presence and degree of target organ damage, is a prerequisite for devising effective therapeutic strategies and for individualization of treatment goals. Clinical studies have shown that the higher the risk status of an individual patient,
the greater the benefit for a given amount of BP reduction. Thus, patients with diabetes and/or renal disease, especially those with proteinuria, should be treated to very low BP targets to achieve maximal cardiovascular and renal protection. Furthermore, the presence of target organ damage (e.g., left ventricular hypertrophy, carotid atherosclerosis, microalbuminuria) should also be taken into consideration when choosing the initial hypertensive drug.

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References