Review Article

Global Cardiovascular Risk Assessment in the Management of Primary Hypertension: The Role of the Kidney

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The knowledge of each patient’s global risk profile is a prerequisite for effective therapeutic strategies in primary hypertension. Detecting the presence of subclinical organ damage at the cardiac, vascular, and renal levels is key for stratifying cardiovascular risk and may also be helpful in choosing antihypertensive agents and in monitoring the effectiveness of treatment. A systematic, in-depth search for subclinical organ damage, however, may be difficult to carry out because of logistic and economic problems related to the high prevalence of hypertension in the population. Renal abnormalities such as microalbuminuria and reduction in glomerular filtration rate have proven to be powerful predictors of cardiovascular and renal outcome. Thanks to their relatively low cost and wide applicability, more widespread use of these tests in the diagnostic workup will help detect subsets of patients at greater risk for whom additional preventive and therapeutic treatment is advisable.

1. Introduction

The prevalence and incidence of hypertension, arguably the most important modifiable risk factor for cardiac and cerebrovascular diseases, are going to increase dramatically worldwide over the next decade [1]. Prevention and treatment of high blood pressure (BP) already represent a public health challenge in many areas of the world and will likely require even more economic resources in the future. Not all hypertensive patients share the same adverse outcome, however. While, on the average, increased BP values are known to entail an unfavourable outcome whose magnitude is proportional to the severity of hypertension, for the majority of patients the long term risk of developing a cardiovascular (CV) event depends more on their overall risk profile than on their BP levels per se [2]. Given the overwhelming number of hypertensive subjects, early identification of those at greater risk for CV complications is of paramount importance because it could set the stage for directing additional measures to those who need them the most. Thus, besides taking into account traditional risk factors like age, gender, family history, obesity, smoking habits, lipid status, and diabetes, other conditions such as the presence of subclinical organ damage are currently used to identify high-risk patients and tailor treatment [3, 4].

2. Prognostic and Therapeutic Implications of Target Organ Damage

Subclinical organ damage at the cardiac, vascular, and renal levels often precedes and predicts the development of morbid events [5]. Thus, patients with left ventricular hypertrophy, especially the concentric type, show a higher risk of developing a coronary event or a stroke as compared to those with normal left ventricular geometry [6]. Similarly, carotid atherosclerosis has been associated with a worse prognosis regardless of other traditional risk factors. Non-invasive, ultrasound-detected left ventricular hypertrophy and/or asymptomatic signs of extracardiac atherosclerosis (i.e., intima media thickness at the carotid and femoral levels) are often used to identify subsets of patients at increased risk [7]. It has been shown that a systematic in-depth search for multiple risk factors or organ damage significantly increases the likelihood of identifying high-risk individuals.
It is generally agreed upon that this abnormality signals the coexistence of functional and structural abnormalities of the systemic vasculature secondary to atherosclerosis and hypertension. The resulting state of widespread increased permeability, which is revealed at the kidney level by an abnormal amount of urine albumin, possibly the end product of both increased glomerular permeability and reduced tubular reabsorption, is a forerunner and a risk factor for major CV events. A recent meta-analysis clearly showed that the risk for CV morbidity and mortality is linearly related to urinary albumin excretion and that the relationship becomes significant at relatively low values of albuminuria and shows no recognizable threshold or plateau [9, 22]. Furthermore, a reduction of albuminuria under antihypertensive treatment is paralleled by changes in CV risk [23, 24]. These results have led some investigators to claim that reducing albuminuria might become a therapeutic goal in itself.

Another subclinical renal abnormality, that is, a slight

### Table 1: ESH-ESC Guidelines 2013.

| Marker                                | Predictive power (CV disease) | Feasibility | Cost effectiveness |
|---------------------------------------|------------------------------|-------------|--------------------|
| Electrocardiography                   | +++                          | ++++        | +++                |
| Echocardiography                      | ++++                         | +++         | +++                |
| Carotid intima-media thickness        | +++                          | ++          | +                  |
| Arterial compliance (pulse wave velocity) | +++               | ++          | +                  |
| Ankle-brachial index                  | +++                          | +++         | +                  |
| Coronary calcium score                | ++                           | +           | +                  |
| Endothelial dysfunction               | +                            | +           | +                  |
| Cerebral lacune/white matter disease  | +                            | +           | +                  |
| Estimated GFR                         | +++                          | +++         | +++                |
| Microalbuminuria                      | +++                          | +++         | +++                |

The table shows how renal abnormalities, that is, increased albuminuria and reduced eGFR, are best suited for the initial routine assessment of cardiovascular profile in patients with primary hypertension (modified from [2]).
the detection of a significantly higher percentage of patients with organ damage and yield a stratification of risk that is almost superimposable to what is obtained by the routine use of US, although at a significantly lower cost. This, in turn, may lead to a substantial improvement in identifying high-risk patients while optimizing the cost effectiveness of CV risk stratification [27]. Screening for the presence of these abnormalities is a relatively low-cost and therefore widely applicable way to implement a more thorough risk assessment of the hypertensive patient and gain useful information for therapeutic management. A rational, cost-effective search for organ damage must start from low-cost, easy-to-perform tests and proceed to more expensive ones only in patients resulting at relatively low overall risk on the basis of previous risk stratification (modified from [27]).

Unfortunately, the powerful predictive power of renal abnormalities is not yet fully exploited in clinical practice, at least in Europe, as confirmed by a recent survey carried out by the ESH [29].

4. Conclusions

Thorough assessment of CV risk, including the presence and degree of target organ damage, is a prerequisite for devising effective therapeutic strategies and for tailoring treatment goals in primary hypertension. 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. The presence of target organ damage may also be helpful when choosing antihypertensive agents and in monitoring the effectiveness of treatment. Due to the high prevalence of high BP in the general population, logistic and economic reasons may limit a liberal approach to the evaluation of organ damage aimed at risk assessment. Subclinical renal abnormalities such as microalbuminuria or a slight reduction in eGFR provide a useful and easily applicable way to detect subsets of patients at greater risk for whom additional preventive and therapeutic treatment is advisable. A more widespread use of these tests in the assessment of CV risk in patients with hypertension is advisable.

Acronyms

BP: Blood pressure  
CV: Cardiovascular  
eGFR: Estimated glomerular filtration rate.

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