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Preface

Hypertension and target organ damage

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1. Introduction

Although the risk of hypertension for later cardiovascular events is well established, it has also become clear that this risk is not so impressive for blood pressure levels within the "mild hypertension" range. This is even more so when other risk factors are lacking. However, better insight is necessary into the subgroups of the mildly hypertensive population where the risk is actually increased, since the potential benefits of treatment might be greatest in these groups. In daily practice, the work-up of a hypertensive patient always contains the assessment of a so-called risk-profile. Apart form blood pressure, data about other well-known cardiovascular risk-factors are also collected: smoking habits, body weight, glucose and lipids, family predisposition, sex and race. A particular place within this assessment is also the detection of eventual signs of target organ damage (TOD).

From the Framingham data the extra risk of TOD to the heart is well described. What about hypertensive TOD in other target organs such as cerebrum, kidneys, eyes and peripheral blood vessels? One of the pivotal questions in this area to be answered is whether TOD in these organs can be assessed reliably and at an early stage of the hypertension. If so, should the subgroup of patients with mild hypertension and with preclinical TOD be treated more vigorously? What would this mean in financial terms and what are the potential side-effects of more diagnostic procedures? This would also imply that the appropriate diagnostic methods for this purpose should also be available to general physicians. Another intriguing issue to be resolved and which is related to TOD is whether 24-hour ambulator blood pressure values are a better predictor of TOD than the usual clinic blood pressure values. The paper by O'Brien and Coyle in this issue of the Journal gives an excellent overview of this topic.

This issue of the Journal concerns the reports of a recent symposium on hypertensive TOD. Besides oral presentations, a panel discussion was held where the practical implications for clinicians were discussed. In short, we want to summarize here the conclusions of this discussion and the consequences for daily practice as related to the different kinds of organ damage.

2. Heart and coronary circulation

As stated above, there is no doubt that the presence of hypertensive TOD to the heart increases the risk of cardiac morbidity and mortality. In particular, the demonstration of left ven-

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tricular hypertrophy (LVH) increases this risk considerably. This makes the tracing of hypertensive subjects with LVH necessary. However, the sensitivity of the electrocardiogram (ECG) in detecting LVH is very moderate. Moreover, in the Dutch guidelines the ECG was optional, since ECG equipment is not directly available for most general physicians. Echocardiography is superior to the ECG for a number of reasons. First, it can give a quantitative answer: left ventricular mass (LVM) can be calculated and normalized for differences in body surface area. The measures of posterior wall thickness and interventricular septal thickness give also more quantitative information than the ECG. Second, the echo can deliver other specific information e.g., about systolic and/or diastolic (dys)function. The latter is often disturbed before LVH is even apparent, especially in elderly subjects. Third, since echocardiography is just as patient-friendly as the ECG, it can be repeated during follow-up by which progression or regression of LVM and the improvement or worsening of systolic and/or diastolic function can be followed. Are there then no disadvantages of echocardiography? Of course there are: for example, in 10–20% the imaging may be insufficient for calculating LVM. These problems are more prominent in obese subjects and, as known, most hypertensives are at least overweight. Other limitations are the time, costs and experience needed before accuracy becomes sufficient. Even then there remains considerable inter- and intra-doctor variation. To perform echocardiography in all hypertensive patients would mean that general physicians should send their patients at least once for echocardiography to their local cardiology departments. It is quite obvious that this would have wide implications in terms of financial costs and for the organization of this service.

What are the possible consequences of the echocardiographic findings? It may lead to better selection of hypertensives who are at greater risk, but it should be noted that prospective data are still lacking, especially for the early stages. A diagnosis of LVH may influence the individual cost–benefit balance: e.g., one will decide earlier for the addition of an extra drug, or an adverse reaction will be more easily accepted. Another potential consequence of the presence of LVH can be the choice of drug. Although in two often-cited reviews it is suggested that some classes of antihypertensive drugs are superior to others with regard to reversal of LVH, most of the studies used in the reviews were uncontrolled and/or not blinded. In this respect the paper by Fagard in this issue clearly shows that if a meta-analysis is performed with controlled studies only, no particular class of antihypertensives has the exclusive property of LVH reduction.

There are some other important aspects of the relation between hypertension and the heart: e.g., the diminished coronary flow reserve or the presence of subclinical myocardial ischaemia. Although both topics are interesting in terms of research as shown in the article by Magrini and colleagues in this issue, there have been no direct consequences so far for everyday practice.

3. Cerebral and peripheral circulation

After cardiac events, cerebrovascular events come second in frequency. Therefore, research on the cerebral circulation in hypertension was started long ago. The review by Strangaard and Paulson in this issue gives an actual impression by the most experienced investigators in this field. However, their method of measuring cerebral blood flow cannot be used in large-scale studies. A number of new non-invasive techniques for this purpose are now being developed: newer CT-scans, MRI or MR-angiography, and near-infrared spectroscopy (NIRS) etc. A development already more close to clinical practice is that developed by and described in this issue by Reneman and Hoeks. It has been developed for the study of the distensibility and compliance of the carotid artery, e.g. in hypertension. Interesting observations demonstrate differences between different drugs with regard to the properties of the carotid artery wall, but no studies with objective end-points are presently available. Though promising for clinical and fundamental research in specialized centres, the method is not available for general daily practice.

Two papers in this issue by Forette et al. about vascular dementia and by Lees about stroke should motivate all doctors to take an active attitude to prevention and to undertake more clinical research in this field.

Since the carotid arteries can also be considered as part of the peripheral circulation, the above-mentioned technique of Reneman and Hoeks is applicable to other arteries, as is also shown by Safavian et al. in this issue. Both groups have developed an extensive expertise in this field of research and although promising for research or use in specialized centres or special patient categories, this non-invasive technique is not yet available for general clinical practice. This method can give new insights into both vascular physiology and pharmacology, but its prognostic value as a tool for early diagnosis of hypertensive TOD has still to be determined.

4. Renal organ damage due to hypertension

The kidney can be the cause of hypertension but also the target for damage by hypertension. The improvement of antihypertensive treatment protects patients from dying from major cerebral and cardiac events. Thus an increasing number of elderly subjects remain at risk for damage in other target organs, e.g. the kidney. The ever increasing life expectancy in most western countries is an additive factor. These factors explain that over the last decennium the percentage of patients coming to dialysis after longstanding primary hypertension has risen. Most clinicians will follow the course of the kidney function and eventual proteinuria at regular intervals in their hypertensive patients, but once these parameters deteriorate we are too late. In diabetic patients the determination of microalbuminuria is an early sign of renal damage. For hypertension, with its slower deterioration of kidney function, there are no data so far that demonstrate that regular nephelometric determination of urinary albumin excretion has any prognostic value. There may be a subgroup where there are indeed arguments that it is a cost-effective diagnostic procedure. Generally speaking, no strong advice can be given at present as to whether or not it is useful to determine microalbuminuria. Some studies are currently underway. The paper by de Leeuw and Birkenhäger in this issue gives the pathophysiological background and also discusses the influence of antihypertensive drugs both as a cause of renal function disturbances and as therapy for renal damage.

5. Hypertensive retinal damage

The retina is the place where atherosclerosis can be observed and followed easily with (almost) non-invasive methods. Although the significance of fundoscopy for accelerated or malignant hypertension is beyond doubt, the use of retinal inspection in subjects who have no malignant or accelerated hypertension is questionable. Several practical difficulties limit the wide-scale application of retinoscopy in all hypertensive subjects: it costs time, experience is needed, the more qualitative rather than quantitative scoring and the disadvantage of mydriasis for the outclinic patient. Recently there have been some developments with alternative methods measuring retinal atherosclerosis and remodelling in hypertension and/or diabetes using standardized retinal photographs.

6. Conclusions for the clinician

The heart, kidney and cerebral blood vessels are still the major target organs for damage by hypertension. The assessment and follow-up of TOD of these organs should be improved. It seems that detection of subgroups of patients with only mild hypertension but with subclinical or early TOD would be beneficial. More vigorous treatment of these subjects might improve the clinical outcome in the long term. However, prospective studies in this area of extension of diagnostic procedures and treatment intensification are mandatory in order to justify the unevitable increments in side-effects and financial costs. At present, for the clinician measurement of renal function and protein excretion and the

ECG will keep their place despite limitations. The implementation of echocardiography for all hypertensives will probably be the next development for the reasons mentioned above. The value of measurements of microalbuminuria, cerebral blood flow, coronary blood flow reserve, retinal imaging and assessment of the properties of the large arteries in the daily care of the general hypertensive population remains to be determined.