The Effect of Hypertension on Renal Disease

**ROLE OF HYPERTENSION IN CHRONIC RENAL DISEASE**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Contributors to disease progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal artery stenosis or occlusion</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Atheroembolic disease</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Hypertensive nephrosclerosis</td>
<td>Tubulointerstitial disease (%)</td>
</tr>
<tr>
<td></td>
<td>Adult-onset polycystic kidney disease (%)</td>
</tr>
</tbody>
</table>

**FIGURE 6-18**

The impact of hypertension on the incidence of end-stage renal disease (ESRD) is vastly underestimated if one considers only those patients in whom systemic hypertension is the primary process resulting in loss of kidney function. The group of patients in whom ESRD is attributed to hypertension undoubtedly includes persons with renal disease of several causes. Some of these causes are occlusive disease of the main renal arteries as a result of atherosclerotic disease, atheroembolic disease of the kidneys, and hypertensive nephrosclerosis. The exact incidence of these processes within the hypertensive population with chronic renal disease is unknown. Even more commonly, poorly controlled systemic hypertension accelerates the rate of loss of kidney function in many patients in whom the primary cause of renal injury is another process altogether. This fact is particularly true in patients with glomerular diseases such as diabetic nephropathy and chronic glomerulonephritis [27,28]. Whether systemic hypertension also contributes to loss of kidney function in patients with tubulointerstitial or cystic disease of the kidney is less certain [29].

**FIGURE 6-19**

Hypertension prevalence corresponds with decreased glomerular filtration rate (GFR). Hypertension is common in glomerular, tubular, vascular, and interstitial renal disease and becomes increasingly prevalent as renal function declines. In almost 200 patients screened for the Modification of Diet in Renal Disease study, the prevalence of hypertension increased as the GFR decreased and hypertension was almost universal as the GFR approached 10 mL/min [29].

**FIGURE 6-20**

Multifactorial mechanisms for hypertension in clinical renal disease. An increased intravascular volume, owing to decreased renal excretion of sodium and water as the glomerular filtration rate declines, is probably the primary cause. Activation of sympathetic tone and involvement of the renin-angiotensin system, which is inappropriately stimulated in the setting of volume expansion, have been demonstrated in renal failure. Decreased activity of nitric oxide and other vasorelaxants and increased activity of endothelin and other endogenous vasoconstrictors also are probably contributory.
The Role of Hypertension in Progression of Chronic Renal Disease

**Figure 6-21**
Consistent relationship between hypertension and progressive renal disease. Analysis of the Modification of Diet in Renal Disease study, which involved patients with a heterogeneous miscellany of renal diagnoses, showed that the degree of elevation of the mean arterial blood pressure correlated with the decline in the glomerular filtration rate [30]. This finding has been confirmed in cohorts of patients with the same renal disease. In immunoglobulin A (IgA) nephropathy, eg, the presence of high blood pressure at diagnosis is a strong predictor for development of end-stage renal disease. In this study by Radford and coworkers [31] of 148 patients with IgA nephropathy, 69 patients with hypertension had a much higher risk of proceeding to renal failure than did the 79 patients who were normotensive.

**Figure 6-22**
Relationship between hypertension and renal failure. Johnson and Gabow [32] studied over one thousand patients with autosomal dominant polycystic kidney disease. These authors demonstrated that the time of renal survival was much shorter for patients with hypertension compared with patients whose blood pressure was normal (see Fig. 6-21). Renal survival was defined as the time period before the need for dialysis. HBP—high blood pressure; NBP—normal blood pressure.

**Figure 6-23**
Hypertension accelerates progression of renal failure in children and adults. For 2 years, Wingen and coworkers [33] followed almost 200 children and adolescents with renal disease, aged 2 to 18 years. Here, renal survival is defined as stability of the creatinine clearance rate. Compared with patients with systolic blood pressures lower than 120 mm Hg, those with systolic blood pressures higher than 120 mm Hg had more rapid development of renal death. Renal death was defined as a decrease in the creatinine clearance rate by 10 mL/min/1.73 m².
Hypertension and the Kidney

Hypertension to later development of renal failure. In over 300,000 men screened for the Multiple Risk Factor Intervention Trial, Klag and coworkers [34] showed that a single blood pressure measurement was strongly correlated with the risk of end-stage renal disease (ESRD) later in life. Even men with high-normal blood pressures (defined as a systolic pressure of 130 to 139 mm Hg or a diastolic blood pressure of 85 to 89 mm Hg) were at a statistically significant greater risk for ESRD than were men with blood pressures under 120/80 mm Hg. This risk increases sequentially with the higher stage of hypertension. This study used definitions of hypertension discussed in the Fifth Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC-5). Stage I hypertension is defined as a systolic pressure of 140 to 159 mm Hg and a diastolic pressure of 90 to 99 mm Hg. Stage II hypertension is defined as a systolic pressure of 160 to 179 mm Hg and a diastolic pressure of 100 to 109 mm Hg. Stage III hypertension is a systolic pressure of 180 to 209 mm Hg and a diastolic pressure of 110 to 119 mm Hg. Stage IV hypertension is a systolic pressure of 210 mm Hg or higher and a diastolic blood pressure of 120 mm Hg or greater. The highest relative risk for renal failure was among persons with stage III or IV hypertension.

FIGURE 6-24
There has long been controversy over whether hypertension alone, without renal disease, can cause renal failure, especially in whites. Recent convincing epidemiologic evidence, however, links hypertension to later development of renal failure. In over 300,000 men screened for the Multiple Risk Factor Intervention Trial, Klag and coworkers [34] showed that a single blood pressure measurement was strongly correlated with the risk of end-stage renal disease (ESRD) later in life. Even men with high-normal blood pressures (defined as a systolic pressure of 130 to 139 mm Hg or a diastolic blood pressure of 85 to 89 mm Hg) were at a statistically significant greater risk for ESRD than were men with blood pressures under 120/80 mm Hg. This risk increases sequentially with the higher stage of hypertension. This study used definitions of hypertension discussed in the Fifth Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC-5). Stage I hypertension is defined as a systolic pressure of 140 to 159 mm Hg and a diastolic pressure of 90 to 99 mm Hg. Stage II hypertension is defined as a systolic pressure of 160 to 179 mm Hg and a diastolic pressure of 100 to 109 mm Hg. Stage III hypertension is a systolic pressure of 180 to 209 mm Hg and a diastolic pressure of 110 to 119 mm Hg. Stage IV hypertension is a systolic pressure of 210 mm Hg or higher and a diastolic blood pressure of 120 mm Hg or greater. The highest relative risk for renal failure was among persons with stage III or IV hypertension.

FIGURE 6-25
Hypertension and impact on progression of renal disease caused by hypertension. In a study of 94 patients with essential hypertension and an initially normal serum creatinine concentration, Rostand and coworkers [35] showed that hypertension control apparently had little impact on progression of renal disease. When patients were divided into those with diastolic blood pressures higher and lower than 90 mm Hg, the percentage whose renal function deteriorated was equivalent in both groups. Blacks were at especially high risk; 23% of black patients with diastolic blood pressures below 90 mm Hg had worsened renal function over time, compared with 11% of white patients with diastolic blood pressures lower than 90 mm Hg.

FIGURE 6-26
Lower-than-usual blood pressure (BP) target. The Modification of Diet in Renal Disease study [36] also prospectively examined the effect of a lower-than-usual BP target in a larger cohort of patients with renal insufficiency. Patients were randomized to two target BPs: a usual mean arterial pressure (MAP) target of 107 mm Hg, corresponding to a BP of 140/90 mm Hg; or a low MAP target of 92 mm Hg, corresponding to a BP of 125/75 mm Hg. The changes in the glomerular filtration rate (GFR) in the two groups over a 3-year follow-up period are depicted. (The y-axis depicts the changes in GFR, and the x-axis represents months. For example, F36 means 36 months after initiation of the study.) Patients in the two groups had statistically equivalent declines in GFR. Over the last 6 months of the study, however, a trend toward greater stabilization in renal function occurred in the group randomized to the lower target.