THE NATURAL HISTORY OF HYPERTENSION WITH MODERATE IMPAIRMENT OF RENAL FUNCTION

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SUMMARY

1. A continuing prospective study of patients with severe hypertension is now in its eighteenth year.
2. Patients with impaired renal function survive longer with present-day management if control of pressure is good and if renal structural abnormalities are not gross.
3. Since 1960 myocardial infarction, rather than cerebrovascular accident, has been the commonest cause of death.

Key words: hypertension, renal failure, proteinuria, stroke.

A continuing prospective study of patients with severe hypertension, initial diastolic blood pressure persistently 110 mmHg or more, has been in progress at the Cardio-Vascular Clinic, Sydney Hospital, since 1955 (Bauer, 1966, 1972). Of the 1700 patients investigated, we have selected the first 100, under the age of 60 years, seen in 1955, 1960, 1965 and 1970 for close follow-up study. Of the patients 98% have been followed to death or are still attending, or communicating with, the clinic.

The present study is concerned with the prognosis of patients who, on presentation, had evidence of impaired renal function, with particular reference to their length of survival and cause of death. Progressive changes in renal function at annual review tests have been analysed in terms of blood pressure control.

Impairment of renal function was initially assessed by blood urea nitrogen (BUN) levels. Since 1959 all patients had serum creatinine estimations, but for the sake of uniformity most data will be presented in terms of BUN values. A structural renal diagnosis was established by the usual clinical methods; intravenous pyelography, renal scan, arteriography, urological and other investigations were performed as indicated.

The well-known inverse relationship between a raised level of BUN and length of survival was clearly confirmed. The cumulative mortality for a group of 300 patients at 5 years ($n = 293$) was 27%, at 10 years ($n = 190$) 44% and at 15 years ($n = 93$) 63%. For the 226 patients, who

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on presentation had a normal BUN (≤ 20 mg%), the cumulative mortality values at 5, 10 and 15 years were 20%, 35% and 57%, for the seventy-four patients presenting with a BUN of ≥ 21 mg%, the respective values were 47%, 71% and 89%, a highly significant difference. Of the 226 patients with normal BUN, ninety-nine had significant proteinuria on repeated clinical testing when first examined. Survival values were not significantly different in patients with and without proteinuria, thus in this series proteinuria, in the presence of a normal BUN, was of no prognostic significance. Thirteen patients had marked elevation of BUN on first presentation, 45% or more. The longest period of survival for these patients was 7 years. More recently some

![Mortality graph](image)

**Fig. 1.** Mortality graph of patients with normal and impaired renal function. The shaded area represents the mortality curve for the entire series. ○, Normal (n = 127); ●, proteinuria (n = 99); +, BUN 21-44 mg% (n = 61); ×, BUN ≥45 mg% (n = 13).

of our patients with hypertension and severe renal failure have successfully undergone renal transplantation and may well exceed this period. Mortality curves are graphically represented in Fig. 1.

When this study commenced in 1955 the commonest cause of death among patients was a cerebrovascular accident. Since 1960 myocardial infarction has been responsible for the majority of fatalities. Of 127 deaths among clinic patients recently analysed, 36% were due to cerebrovascular accidents, 35% due to myocardial infarction and 16% due to a renal failure. Only 6% of all deaths were due to causes unrelated to hypertension. Over half the deaths occurred in hospital, 36% of all patients who died were examined at autopsy.

Patients demonstrated differences in their causes of death depending on the initial BUN level. Of seventy-six patients dying, who on presentation had a normal BUN, thirty-one died of myocardial infarction, twenty-eight of a cerebrovascular accident, four of hypertensive heart failure, three of other related causes and eight of unrelated causes. Only two patients (3%) died of renal failure, one a male with malignant hypertension who succumbed in 1955 within a few
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months to his rapidly progressive renal disease, the other a female who suffered from analgesic nephropathy, infective pyelonephritis and atheromatous renal artery occlusion, confirmed at autopsy. In contrast, of fifty-one patients dying with initial BUN of 21 mg% or more, eighteen died of cerebrovascular accidents, thirteen of myocardial infarction, two of hypertensive heart failure and eighteen (35%) of uraemia. None of these patients died of unrelated causes.

Sixty-one patients had evidence of moderate impairment of renal function when first seen, with BUN levels between 21 and 44 mg%. The total follow-up period for these sixty-one patients was 384 patient-years with a mean of 6.4 years per patient; thirty-five were males and twenty-six females. The average age at presentation has gradually decreased from 47.4 to 44.8 years in accordance with the overall trend of patients seen at our clinic.

Variation in renal function was assessed by comparing BUN and serum creatinine values on at least three annual review tests. Renal function remained stable, or showed slight improvement in twenty-three patients and deteriorated in twenty. In eighteen patients inadequate information was available, or death, from other than renal failure, occurred before the third annual review. Twice as many patients first seen in 1960 and 1965 had stable renal function compared with the 1955 patients.

Changes in renal function were correlated with response to anti-hypertensive treatment. Inadequate blood pressure control, defined as a lying diastolic pressure persistently in excess of 120 mmHg, a history of infrequent clinic attendance or evidence of non-adherence to therapy, was present in 66% of the patients with deteriorating renal function, but only in 35% of patients with stable renal function. The numbers are too small to clearly relate good blood pressure control to stability of renal function although this is a possibility. Advanced retinopathy, with grade III and IV fundal changes, was more frequent in patients with progressive renal failure, being a feature in fourteen of the twenty patients in this category.

A structural renal diagnosis was made in forty-six of the sixty-one patients with moderate impairment of renal function. Sixteen patients suffered from analgesic nephropathy; several of these also had a chronic peptic ulcer. Twelve patients suffered from infective pyelonephritis; some of these were also chronic analgesic takers. Seven patients suffered from renal calculi, seven from atheromatous renal artery stenosis and five from chronic glomerulonephritis. Other rarer diagnoses included polycystic kidneys and nephrocalcinosis. In fifteen patients no renal diagnosis could be established and these did significantly better than the rest; only one developed progressive renal failure.

In seven patients with moderate impairment of renal function autopsy revealed severe atheromatous renal artery obstruction. Sex, age, ocular fundi and serum cholesterol levels were similar in these patients when compared with the rest of the series. The one striking feature was the abrupt onset or aggravation of chronic renal failure in five of the seven patients. This may present an important additional clue for further investigations in some selected patients with no other evidence of disseminated atheroma.

This follow-up study, now in its eighteenth year, seems to demonstrate that patients with impaired renal function survive longer with present-day management and treatment especially if blood pressure control is optimum and gross structural renal abnormalities are absent.

REFERENCES