Fifteen year survival of patients presenting with hypertension to a hospital clinic

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Summary: The survival has been determined for the 404 patients who presented to the Hammersmith Hospital Hypertension Clinic during the years 1962 to 1966 and in whom the untreated blood pressure was known. The fifteen year survival ranged from 72% for young men aged 30–49 at presentation to 27% for men aged 60–69. Sixty-eight percent of the deaths were cardiovascular or renal, 33% of all deaths were from ischaemic heart disease (IHD), 17% from stroke and 3% from renal causes. Death from any cause was predicted with statistical significance by age, the presence of accelerated or malignant hypertension, impaired renal function, smoking at presentation and systolic blood pressure. Death was not predicted by hypokalaemia, hyperuricaemia (after adjusting for renal function) and obesity.

Introduction

The drug treatment of moderate or severe hypertension is usually for life and it is important to determine the long term survival of such patients. Survival was determined for the patients who presented to the Hammersmith Hospital Hypertension Clinic between the years 1962 to 1966. These years were selected as marking the beginning of an era of more modern anti-hypertensive treatment, the use of ganglion blocking drugs having been discontinued and the beta-adrenoceptor blocking drugs having been introduced towards the end of that 5 year period. This report describes the characteristics of this cohort of patients and their survival according to age, sex, untreated and treated blood pressure, smoking habits, renal function, plasma potassium, serum cholesterol and uric acid.

Methods

The records of the Hammersmith Hospital Hypertension Clinic include the names of 404 patients who first attended the clinic for treatment in the years 1962 to 1966 and who had an untreated diastolic blood pressure known to be equal to or greater than 90 mm Hg. The patients were registered with the Office of Population Censuses and Surveys (OPCS) in

order to receive a copy of any death certificate prior to July 1981. Outcome could not be determined in 34 patients. Information concerning visits up to July 1977 was extracted from the clinic notes and included the following data: age, sex, race, untreated blood pressure, smoking habits, family history of hypertension, retinal appearance, weight and biochemical results at presentation. This information was not available for all patients and the completeness of data is indicated in the tables. Information on follow-up was also retrieved and included blood pressure measurements during treatment, measurements of plasma urea and potassium, serum cholesterol and uric acid. The methods of study have been described previously and certain results for 205 patients who received methyl-dopa have been reported (Dollery *et al.*, 1984).

Statistical methods

The survival of the patients was analysed using standard life table techniques (Berkson & Gage, 1950). When different groups were compared for survival the nonparametric test of Lee & Desu (1972) was employed. When different groups were compared for characteristics other than survival, unpaired *t* tests, analysis of variance and chi-squared techniques were employed as appropriate. In order to determine the independent effects of the different variables on survival, the fact of death was employed as the Y variable in multiple regression equations.

Life tables were also calculated separately for a death from ischaemic heart disease (IHD), stroke and

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renal disease and cancer. The end point in each instance was a mention of the cause of death on the death certificate. Patients who died from another cause of death, other than the cause mentioned, were censored (assumed lost to follow-up) at the date of death.

Results

The characteristics of the patients at presentation

Table I gives the characteristics of the patients at presentation. Their average age was 50 years with a range from 13 to 84. By 1985 standards they were a severely hypertensive group, average untreated lying pressure being 210 mm Hg systolic and 122 mm Hg diastolic. Over 4% had malignant hypertension and 21% accelerated hypertension (cotton wool spots or haemorrhages in the retina without papilloedema). Sixty-three percent of the men and 31% of the women smoked.

Characteristics of the patients during follow-up

Table I also gives the characteristics of the patients during follow-up including the average treated blood pressure for all patients alive and attending the clinic at the time of the second and fifth year of follow-up and the average biochemical results during follow-up. Blood pressure control tended to be better in men than in women.

Causes of death

The underlying cause of death for the 158 patients who died was determined from the death certificates. Sixty-eight percent of the deaths were cardiovascular or renal. Smoking related diseases such as lung cancer tended to be more common in males. Thirty two percent of deaths were from ischaemic heart disease in men and 34% in women (ICD 8th revision codes 410–414), 13% of deaths were from stroke in men and 23% in women (ICD 430–438), 3% from renal causes in both men and women (ICD 580–599) and 16% of

Table I Characteristics of patients at presentation and information extracted from the records during follow-up

	Percentage patients in whom information available	Males	Females
Number of patients		193	211
Average age (years)		49.7 ± 11.4†	50.4 ± 13.0
Range		21–81	13–84
<i>Mention in the records of</i>			
Current smoking (%)	87	63	31
Positive family history (%)	100	17	27
Malignant hypertension (%)	100	7	3
Accelerated hypertension (%)	100	30	13
<i>Average result at presentation</i>			
Untreated lying pressure			
systolic (mm Hg)	100	209 ± 33	211 ± 32
diastolic (mm Hg)	100	125 ± 19	119 ± 16
weight (kg)	90	74.7 ± 19	67.2 ± 20
plasma urea (mmol/l)	92	6.7 ± 6.4	6.0 ± 5.5
serum uric acid (μmol/l)	72	381 ± 83	317 ± 101
<i>Average systolic blood pressure at end of:</i>			
second year of follow-up	60	153 ± 26.4	161 ± 24.5
fifth year of follow-up	44	147 ± 25.0	154 ± 26.5
<i>Average diastolic blood pressure at end of:</i>			
second year of follow-up	60	95 ± 14.9	97 ± 12.4
fifth year of follow-up	44	90 ± 13.0	93 ± 12.3
<i>Average result during follow-up</i>			
Plasma urea (mmol/l)	99	8.4 ± 8.5	6.7 ± 5.9
Plasma potassium (mmol/l)	87	3.9 ± 0.42	3.8 ± 0.40
Serum cholesterol (mmol/l)	81	6.3 ± 1.2	6.7 ± 1.3
Serum uric acid (μmol/l)	82	402.1 ± 83.9	339.4 ± 91.8

†Standard deviation

Table II Characteristics of those patients who lived, those who died and those who died with IHD, stroke and cancer recorded as the underlying cause of death $\pm$ s.e.m.

	Alive	Dead	Underlying cause of death		
			IHD	Stroke	Cancer
Number patients	213	158	52	27	23
% males	41	56	54	41	65
Average age (years)	47.2 $\pm$ 0.77	55.0 $\pm$ 0.91	56.9 $\pm$ 1.12	52.94 $\pm$ 2.55	58.1 $\pm$ 0.21
Lying blood pressure (mm Hg)					
Untreated systolic	202.4 $\pm$ 2.09	219.9 $\pm$ 2.48	222.2 $\pm$ 4.44	229.6 $\pm$ 6.35	224.3 $\pm$ 4.47
Untreated diastolic	117.7 $\pm$ 1.08	126.8 $\pm$ 1.45	126.5 $\pm$ 2.11	128.7 $\pm$ 3.22	127.0 $\pm$ 4.08
Average treated systolic (first five years)	155.1 $\pm$ 1.19	167.0 $\pm$ 1.60	166.4 $\pm$ 3.11	169.5 $\pm$ 3.14	167.9 $\pm$ 3.88
Average treated diastolic (first five years)	96.2 $\pm$ 0.57	100.2 $\pm$ 0.77	98.5 $\pm$ 1.13	102.8 $\pm$ 1.72	97.5 $\pm$ 1.60
% Accelerated or malignant hypertension	12.7	24.7	25.0	22.2	17.4
% Smoker at presentation	39.8	57.3	58.8	52.4	50.0
% Family history hypertension	24.9	17.1	7.7	25.9	26.1
Average height (cm)	164.9 $\pm$ 1.32	165.0 $\pm$ 2.03	164.9 $\pm$ 4.19	162.0 $\pm$ 3.52	167.9 $\pm$ 9.73
Average weight (kg)	71.7 $\pm$ 1.30	69.4 $\pm$ 1.85	70.3 $\pm$ 3.09	76.0 $\pm$ 4.03	67.9 $\pm$ 2.50
Plasma urea at presentation (mmol/l)	5.52 $\pm$ 0.20	7.22 $\pm$ 0.63	6.16 $\pm$ 0.34	4.89 $\pm$ 0.26	6.05 $\pm$ 0.40
Plasma urea during follow-up (mmol/l)	6.14 $\pm$ 0.17	9.23 $\pm$ 0.77	6.93 $\pm$ 0.27	6.73 $\pm$ 0.50	6.06 $\pm$ 0.31
Serum uric acid at presentation (μ mol/l)	344.9 $\pm$ 8.3	349.8 $\pm$ 8.6	330.9 $\pm$ 11.6	319.6 $\pm$ 23.7	372.3 $\pm$ 18.3
Serum uric acid during follow-up (μ mol/l)	360.7 $\pm$ 6.8	382.1 $\pm$ 8.3	366.8 $\pm$ 12.2	360.9 $\pm$ 20.4	379.0 $\pm$ 17.1
Plasma potassium during follow-up (mmol/l)	3.85 $\pm$ 0.029	3.93 $\pm$ 0.036	3.93 $\pm$ 0.048	3.87 $\pm$ 0.078	3.79 $\pm$ 0.082
Serum cholesterol at presentation (mmol/l)	6.87 $\pm$ 0.145	6.82 $\pm$ 0.151	7.16 $\pm$ 0.258	6.82 $\pm$ 0.343	6.78 $\pm$ 0.378
Serum cholesterol during follow-up (mmol/l)	6.58 $\pm$ 0.095	6.39 $\pm$ 0.113	6.71 $\pm$ 0.197	6.85 $\pm$ 0.259	6.10 $\pm$ 0.234

men and 13% of women died from other cardiovascular causes (remainder of 390–459). Cancer deaths excluding lung cancer accounted for 10% of the deaths both men and women. Lung cancer deaths accounted for 7% and 1% respectively.

Determinants of survival

Table II gives certain results according to whether the patients lived or died. The results are not adjusted for age and other variables but they are so adjusted in Section 7 below. Table II is available for both sexes separately on application to the authors.

1. *Blood pressure, presence of accelerated or malignant hypertension*

Patients who died had higher average untreated systolic and diastolic pressures than those who survived, higher average treated systolic and diastolic pressures and were more likely to have had accelerated or malignant hypertension ($P < 0.01$ for all comparisons). These associations were true after adjusting for age (Section 7). Patients dying from a stroke had the highest untreated and treated levels of systolic and diastolic pressure.

2. *Renal function at presentation*

Patients who died had a higher average plasma urea at presentation ($P < 0.01$) and during follow-up ($P < 0.001$). This was true even when deaths from renal causes were excluded and after adjusting for age.

3. *Serum uric acid*

The average serum uric acid tended to be higher during follow-up in patients who died. This association was not present after adjusting for plasma urea.

4. *Plasma potassium*

The average plasma potassium tended to be higher in those who died but this appeared to be due to deterioration in renal function in a proportion of these patients. After adjusting for renal function or excluding those with renal failure neither a low nor a high serum potassium was associated with death. The table of average plasma potassium according to outcome and 4 categories of plasma urea is available from the authors.

5. *Serum cholesterol and weight*

For total mortality, the serum cholesterol either at presentation or during follow-up, was not an important predictor of death. However, serum cholesterol during follow-up was higher in men who died from cardiovascular diseases than those who died from cancer ($P < 0.01$). Neither over- nor under-weight were important predictors of survival.

6. *Smoker at presentation*

Smoking cigarettes at presentation was more common among those who died than those who lived

($P < 0.01$). This was also statistically significant when deaths from ischaemic heart disease were considered on their own ($P < 0.05$).

7. *Prediction of death after adjusting for age and other variables*

After adjusting for age and sex the important predictors were, ranked in order of the partial correlation coefficients, average urea during follow-up ($r = 0.25$, $P < 0.001$), untreated diastolic pressure ($r = 0.22$, $P < 0.001$), five year average treated systolic pressure ($r = 0.20$, $P < 0.001$), untreated systolic pressure ($r = 0.19$, $P < 0.001$), presenting plasma urea ($r = 0.18$, $P < 0.01$), five year average treated diastolic pressure ($r = 0.16$, $P < 0.01$), presence of accelerated or malignant hypertension ($r = 0.15$, $P < 0.01$), and smoking at presentation ($r = 0.13$, $P = 0.01$). Partial correlations within the range $+0.05$ and -0.05 were observed for uric acid and cholesterol at presentation and a family history of hypertension. Death was predicted on the basis of all the following variables in a multiple regression equation (β = partial regression coefficient): age ($\beta = 0.014$, $P < 0.001$), smoking ($\beta = 0.14$, $P < 0.01$), average urea during follow up ($\beta = 0.013$, $P < 0.01$) and untreated diastolic pressure ($\beta = 0.0051$, $P < 0.001$), constant = -0.217 . Being male or having malignant or accelerated hypertension did not make any important additional contribution to this equation ($t = 0.8$ and 0.1 to enter, respectively).

8. *Time of death from renal failure, stroke, IHD and cancer*

When considering deaths in the first year, 4 of the 5 renal deaths occurred during this period. The probability of a renal death in the first year was 0.0009 when computed from the life table analysis. Eleven stroke deaths occurred during the first 5 years of follow-up (average probability 0.0006/year) and 15 in the next 10 years (average probability 0.0005/year). Deaths from IHD were also constant over time. Ten IHD deaths occurred in men in the first 5 years (average probability 0.0011/year) and 17 in the next 10 years (average probability 0.0012/year). Eighteen IHD deaths occurred in women in the first 5 years (average probability 0.0007/year) and 14 in the next ten years (average probability also 0.0007/year).

9. *Length of survival and the effect of treatment*

Table III reports the 15 year survival of patients from presentation in three age groups. For comparative purposes the survival for the general population in England and Wales is reported for the same period of time. The 15 year survival of all patients ranged from 72% for men aged 30–49 at presentation to 27% for men aged 60–69. The younger patients, both men and women, had the

Table III Five, ten and fifteen year survival from presentation (%) in male and female patients in 3 age groups and the corresponding figures for the general population of England and Wales (cohort analysis for age 42, 53 and 63 at start)

	Men		Women	
	(1)	General population (2)	(1)	General population (2)
Age 30–49				
<i>n</i>	79		80	
5 year survival	85	98	85	99
10 year survival	77	97	82	98
15 year survival	72	92	70	95
SE (15 year)	5.5		5.5	
Relative risk (15 year)	3.5		6.0	
Attributable risk (/100/15 years)	20		25	
Age 50–59				
<i>n</i>	66		74	
5 year survival	84	93	96	97
10 year survival	68	80	85	91
15 year survival	50	65	75	81
SE (15 years)	6.4		5.1	
Relative risk (15 years)	1.4		1.3	
Attributable risk (/100/15 years)	15		6	
Age 60–69				
<i>n</i>	35		30	
5 year survival	66	80	66	90
10 year survival	46	57	55	75
15 year survival	27	33	47	54
SE (15 years)	7.7		9.4	
Relative risk (15 years)	1.1		1.2	
Attributable risk (/100/15 years)	6		7	

$$\text{Relative risk at 15 years} = \frac{100 - (1)}{100 - (2)}$$

Risk attributable to hypertension = (2) – (1)/100/15 years

SE (15 years) = standard error of cumulative % surviving at 15 years.

highest relative and attributable risks from presenting with hypertension.

Discussion

The treatment of hypertension in these patients presenting in the 1960s did not confer the same expectation of life as in the general population. During the fifteen years the relative risk of dying for both male and female patients under 60 years of age ranged from 1.3 to 6.0. It may be argued that the relative risk is a poor indicator as the general population of England and Wales may not be an appropriate comparison group for patients referred to the Hammersmith Hypertension Clinic, and moreover, the relative risk must approach unity in the elderly when many die over 15 years. However, both relative risk and the risk attributable to being a patient was markedly increased in men and women under the age of 50, compared with the mortality rate in the general population. An excess

of between 20% and 25% of those under the age of 50 died over the 15 years of observation.

In the 1950s mortality was even greater as 54% of patients attending the Hammersmith Clinic presented with accelerated or malignant hypertension and 44% died from uraemia (Breckenridge *et al.*, 1970). In the present study from the 1960s, 37% of men and 16% of women had malignant or accelerated hypertension at presentation, but only 3% of males and females died of renal disease during 15 years of follow-up. The decline in uraemic deaths must be partly due to dialysis and transplantation, but the large decrease in the proportion presenting with accelerated and malignant hypertension suggests that these conditions were becoming rarer in the general population, either due to a change in the severity or nature of the underlying disease, or to early and preventive treatment.

Despite fears that diuretic treatment may increase IHD rates (Multiple Risk Factor Intervention Trial Research Group, 1982), the death rate for IHD was not observed to increase with time and was fairly

stable year by year. The present study does not suggest any worsening in the survival of hypertensive patients during long-term follow-up and the recent reports from the European Working Party on High Blood Pressure in the Elderly (Amery *et al.*, 1985) and Medical Research Council Working Party (1985) trials do not suggest an excessive IHD risk from diuretic treatment. The patients in the present study were far more severely hypertensive than in either of these trials. Both trials showed a 40% or greater reduction in stroke events, but owing to the high incidence of stroke in the elderly, only 90 patients had to be treated for one year to save one stroke event in the EWPHE trial (incidence in placebo group 2.9%/year) against 850 for one year in the MRC trial (placebo incidence 0.3%/year). The corresponding number of patients to prevent one death from stroke were 170 and 5,000 patients treated for one year in the EWPHE and MRC trials respectively.

The average age of the patients in the present study was comparable with that in the MRC trial. However, the stroke death rate on active treatment in our study was much higher, suggesting that the number of stroke deaths prevented by every year of treatment may be greater than in the MRC trial.

The data support the present strategy of rigorous anti-smoking advice, but provide less cause for concern with respect to other potential risk factors such as

obesity, hypokalaemia and hyperuricaemia. Patients with hypokalaemia appeared to survive as long as those who did not have this condition. Hyperuricaemia also did not appear to be a predictor of death once renal function had been taken into account. The patients who died were not more obese than the survivors.

Serum cholesterol was higher in those men dying from cardiovascular causes than those dying of cancer. Overall total mortality was not related to serum cholesterol, a finding reported in patients presenting in the 1970s (Bulpitt *et al.*, 1979).

The severely hypertensive group of patients who began treatment in the early 1960s achieved a remarkably long survival but they still suffered a substantial excess of cardiovascular mortality. The patients who died had more severe hypertension, more cigarette smokers, a greater degree of renal damage, were older and more likely to be of male sex. Early treatment of moderately severe hypertension should reduce the degree of vascular damage that occurs before the treatment is begun but there is still much to be done if a goal of normal life expectancy is to be attained.

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