Results of Surgery in Hypertension Due to Renal Artery Stenosis

R. G. LUKE,* M.B., M.R.C.P., M.R.C.P.ED.; A. C. KENNEDY,† M.D., F.R.C.P.ED., F.R.C.P.GLASG.
J. D. BRIGGS,‡ M.B., M.R.C.P., M.R.C.P.ED., M.R.C.P.GLASG.; N. W. STRUTHERS,§ CH.M., F.R.C.S., F.R.C.S.ED.
J. K. WATT,|| CH.M., B.SC., F.R.C.S., F.R.C.S.GLASG.; D. W. SHORT,¶ CH.M., B.SC., F.R.C.S.ED., F.R.C.S.GLASG.
W. BARR STIRLING,** CH.M., F.R.C.S.ED., F.R.C.S.GLASG.

Brit. med. J., 1968, 2, 76-80

We have previously reported our experience on the detection of renovascular hypertension, a combination of intravenous pyelography and isotope renography being used as a screening procedure in hypertensive patients (Kennedy *et al.*, 1965; Luke *et al.*, 1966). In this paper we give an account of the effect of surgical treatment in the 27 patients with renal artery stenosis operated on up to May 1966, so that the minimum follow-up period was at least one year. These 27 patients originated from a group of 41 with functional renal artery stenosis found by screening about 1,000 patients with hypertension. We shall report separately the results of surgery in the slightly greater number of patients with unilateral chronic pyelonephritis and other forms of unilateral parenchymal renal disease originating from the same group of hypertensive patients.

Patients

Preoperative clinical details, results of renovascular investigations, and the operative procedures carried out are shown in Table I.

There were 17 males and 10 females, with a mean age of 40.5 years (range 19 to 61). Mean preoperative diastolic blood pressure was 123 mm./Hg. With the system of grading of fundi proposed by Keith *et al.* (1939) three patients had grade 4 fundi, eight grade 3, 11 grade 2, four grade 1, while in one patient (Case 10) there were no hypertensive fundal changes. In eight patients a significant abdominal bruit was heard. In 19 of the 27 patients the E.C.G. showed a left ventricular strain pattern. The mean duration of relevant symptoms or the period of elevation of blood pressure where known was 13 months (range 2 months to 12 years). One patient (Case 14) was asymptomatic, the hypertension being detected at a routine medical examination. Six of the eight female patients who had had at least one pregnancy gave a history of hypertension persisting after toxæmia of pregnancy.

In 18 of the patients there was no proteinuria. Mean preoperative blood urea was 33 mg./100 ml., the highest value being 55 mg., and the mean preoperative creatinine clearance was 95 ml./minute, the lowest value being 47 ml. In all 27 patients bacteriological examination of a midstream specimen of urine was negative.

Seventeen patients (14 males and three females) had atherosclerotic lesions, eight (five females and three males) had fibromuscular dysplasia (Harrison *et al.*, 1967) of the renal arteries, one (Case 4) had Takayasu's arteritis (Short *et al.*, 1965), and

one (Case 17) had congenital narrowing of the abdominal aorta with involvement of both renal arteries. The mean age of the patients with fibromuscular dysplasia was 31 years and that of the patients with atherosclerotic lesions 46 years.

Basis of Diagnosis of Renovascular Hypertension

In accordance with our previously described diagnostic policy (Kennedy *et al.*, 1965; Luke *et al.*, 1966) all of the patients had been selected as likely to have a functionally active renal artery stenosis as a result of screening with a "hypertensive" intravenous pyelogram (I.V.P.) and an isotope renogram. In 26 of the 27 patients the I.V.P. showed one or more changes associated with renal artery stenosis, the negative result being obtained in Case 2. The renogram was also positive in 26 of the 27 cases; the negative result was obtained in a different patient (Case 17) who had bilateral renal artery stenosis associated with congenital narrowing of the abdominal aorta. In 13 patients a C type of renogram curve was obtained, in nine a B type, and in four an A type (Luke *et al.*, 1966). Aortograms confirmed the presence of stenosis in all 27 patients. In 19 patients technically satisfactory divided renal function tests were obtained, and in 18 of these the result was positive (Kennedy *et al.*, 1965). In six patients (Cases 1, 8, 12, 20, 21, and 24) antihypertensive drug therapy before operation had failed to control the blood pressure satisfactorily.

Type of Operation

Elective nephrectomy was carried out in 12 patients and reconstructive vascular surgery in 10 (Table I). In two patients secondary nephrectomy was carried out—in one (Case 27) three weeks after the first operation because of graft thrombosis, and in the other (Case 12) two years after it and three months after the routine follow-up admission because of renal vein thrombosis on the operated side. In the remaining five patients a reconstructive procedure was planned, but at operation nephrectomy had to be carried out for technical reasons, including involvement of the division of the renal artery by fibromuscular dysplasia in two (Cases 2 and 14). In 14 patients the systolic transstenotic pressure gradient was measured; it ranged from 20 to 200 mm./Hg, with a mean of 85 mm./Hg. The mean weight of the kidney in the 19 patients in whom nephrectomy was performed was 116 g. In 15 of these kidneys ischaemic tubular atrophy of varying degrees of severity was seen. In four patients, in all of whom reconstructive vascular surgery had been unsuccessfully attempted, the removed kidney showed no significant histological change.

Results

Results were assessed on the basis of regular outpatient attendances supplemented by a short admission to hospital at least one year after operation in order to obtain serial blood-

* Lecturer in Medicine, University Department of Medicine, Royal Infirmary, Glasgow C.4.

† Reader in Medicine, University Department of Medicine, Royal Infirmary, Glasgow C.4.

‡ Registrar in Medicine, University Department of Medicine, Royal Infirmary, Glasgow C.4.

§ Consultant Urological Surgeon, Department of Urology, Royal Infirmary, Glasgow C.4.

|| Consultant Surgeon, Royal Infirmary, Glasgow C.4.

¶ Senior Lecturer, University Department of Surgery, Royal Infirmary, Glasgow C.4.

** Consultant Urologist, Department of Urology, Royal Infirmary, Glasgow C.4.

TABLE I.—Preoperative Data and Type of Surgery Performed in 27 Patients with Renal Artery Stenosis

Case No.	Age and Sex	B.P. (mm. Hg.)	Length of History (mths.)	Fundi (grade)	Bruit	E.C.G.	Blood Urea (mg./100 ml.)	Creatinine Clearance (ml./min.)	Plasma Sodium (mEq/l.)	Urine Protein	I.V.P.	Renogram*	Divided Renal Function Tests	Gradient (mm. Hg.)	Weight of Kidney (g.)	Cause of Stenosis†	Operation
1	56 M	230/115	4	3	—	L.V.S.	38	90	136	Trace	+	C	+	N.D.	125	Ath.	Nephrectomy
2	26 F	170/120	36	2	—	Negative	20	114	133	—	—	C	—	200	120	F.D.	Teflon bypass
3	39 M	180/130	3	3	—	L.V.S.	28	118	138	—	+	C	+	—	—	Ath.	graft Arteriolysis
4	36 F	240/120	6	1	+	"	20	103	139	—	+	C	+	N.D.	—	Tak. art.	Nephrectomy
5	49 F	280/130	36	2	+	"	40	—	140	—	+	B	+	120	140	Ath.	"
6	44 F	195/115	6	2	—	"	34	67	140	—	—	C	+	N.D.	130	F.D.	"
7	56 M	200/120	2	4	—	Negative	24	86	141	Trace	+	A	+	130	110	Ath.	"
8	44 M	210/125	6	1	—	Isch.	48	82	138	—	+	B	+	N.D.	150	"	"
9	50 M	200/100	2	2	—	L.V.S.	45	47	136	1.8 g. 24 hr.	+	B	+	—	120	"	"
10	19 M	155/110	3	0	—	—	30	116	137	—	+	C	+	20	125	F.D.	"
11	42 M	190/125	6	2	—	Isch.	36	125	141	—	+	C	+	50	120	Ath.	"
12	49 M	210/140	9	3	—	L.V.S.	42	71	135	2.0 g. 24 hr.	+	B	+	20	—	"	Spleno-renal anastomosis
13	38 M	180/120	9	3	—	"	32	—	140	—	+	A	+	20	77	"	Nephrectomy
14	32 F	200/115	—	2	—	"	30	77	132	—	+	C	+	140	110	F.D.	"
15	31 M	230/140	4	4	+	"	27	—	134	Trace	+	B	N.D.	N.D.	130	Ath.	"
16	61 M	220/120	8	2	—	"	38	93	144	—	+	A	+	—	77	"	"
17	21 F	180/120	24	2	+	"	24	71	139	—	+	Neg.	"	37 (bilateral)	—	Con. + Ath.	Bifurcate Dacron bypass graft
18	56 M	190/110	3	3	—	"	36	136	139	—	+	B	"	120	120	Ath.	Dacron bypass graft
19	51 M	190/115	24	3	—	"	31	—	135	—	+	C	"	90	180	"	Nephrectomy
20	40 F	240/130	20	3	+	"	23	94	138	2.4 g. 24 hr.	+	B	"	N.D.	68	"	"
21	36 M	200/125	6	1	+	Negative	40	116	141	—	+	C	+	—	—	F.D.	Reimplantation
22	42 F	240/130	18	4	+	L.V.S.	55	69	138	7.8 g. 24 hr.	+	A	N.D.	—	60	Ath.	Nephrectomy
23	43 M	180/110	6	2	—	Negative	34	89	141	—	+	B	+	60	—	"	Thrombo-endarterectomy + vein patch
24	41 M	250/150	2	2	+	L.V.S.	33	103	140	—	+	C	N.D.	80	—	"	Reimplantation
25	38 F	200/125	144	2	—	"	15	93	141	Trace	+	C	+	N.D.	110	F.D.	Nephrectomy
26	20 M	200/120	12	1	—	Negative	26	134	136	—	+	B	+	—	—	"	Teflon bypass graft
27	34 F	190/130	30	3	—	L.V.S.	33	93	139	+	+	B	+	100	130	"	"

L.V.S. = Left ventricular strain. Isch. = Myocardial ischaemia. N.D. = Not done. *A = Flat curve. B = Flattening of phase 2 and delay of phase 3. C = Delay of phase 3. †Ath. = Atherosclerosis. F.D. = Fibromuscular dysplasia. Tak. art. = Takayasu's arteritis. Con. = Congenital narrowing of aorta.

pressure readings, fundoscopic assessment, chest x-ray picture, E.C.G., blood urea and electrolytes, chemical, microscopic, and bacteriological examination of urine, endogenous creatinine clearance, I.V.P., and isotope renogram. This short admission was possible in all the patients surviving for at least one year after operation except in two (Cases 26 and 27), who now reside in England. In Case 27 a reasonably satisfactory assessment was obtained by postal inquiry from her medical attendants.

The condition of the other patient when last seen by us nine months postoperatively is used in the assessment; he is known to have been alive until March 1967, but details of his blood pressure are not available.

Follow-up data are shown in Table II. The duration of follow-up was taken as the time interval between operation and the short admission study period, and ranged from 12 to 47 months, with a mean of 25 months. In assessing the effects of renovascular surgery on the blood pressure three terms are employed: (1) correction—diastolic blood pressure of 90 mm. Hg or less; (2) improvement—fall in diastolic blood pressure of 20 mm. or more without hypotensive therapy; and (3) failures—others. We have avoided the word "cure," since, especially with an atherosclerotic lesion, correction of the hypertension may do no more than slow the rate of progression of the underlying diffuse atherosclerotic disease process.

The results of surgery in the 27 operated cases are summarized in Table III. There was one operative death due to thrombosis in an extremely atherosclerotic aorta 48 hours after an attempt at reconstructive vascular surgery (Case 18). One patient (Case 17) with extensive congenital narrowing of the aorta died of haemorrhage from the junction of a bilateral bypass graft four months after surgery, and another (Case 19) died of haemorrhage six months after reconstructive surgery which had been complicated by subphrenic abscess. In both instances outpatient supervision showed that the blood pressure had been corrected (B.P. 120/80 and 130/80 respectively) in the period between surgery and death. In 23 of the remaining 24 patients blood pressure was corrected or improved. In the seven patients in whom the blood pressure was improved the mean fall in diastolic was 27 mm. Hg, with a range of 20–45 mm. Hg. Two other patients have died since the short admission study for reasons unrelated to their previous nephrectomy—one (Case 11) died after a myocardial infarction 28 months after surgery, and another (Case 14) died from anaplastic bronchial carcinoma 23 months after surgery. In both patients hypertension had been corrected.

Three vascular incidents related to extrarenal atherosclerosis have occurred. In Case 8 a left hemiparesis developed, sub-

TABLE II.—Postoperative Data and Results of Surgery in 27 Patients with Renal Artery Stenosis

Case No.	Time of Follow-up (months)	B.P. (mm. Hg.)	Fundi (grade)	E.C.G.	Blood Urea (mg./100 ml.)	Creatinine Clearance (ml./min.)	Plasma Sodium (mEq/l.)	Urine Protein	Result
1	47	190/95	1	L.V.S. (1)*	38	80	137	—	Improved
2	44	140/80	1	—	28	102	142	—	Corrected
3	42	145/90	1	—	32	N.D.	142	—	"
4	40	160/100	1	—	23	80	140	—	Improved
5	33	190/90†	2	—	36	57	143	—	Failed
6	32	130/85	1	L.V.S. (1)	36	67	142	—	Corrected
7	26	190/90	0	—	35	64	144	—	"
8	30	150/100	1	Isch.	50	65	139	—	Improved
9	26	150/90	1	N.D.	25	N.D.	138	—	Corrected
10	25	115/80	0	—	32	82	142	—	"
11	24	120/70	2	Isch.	32	N.D.	—	—	"
12	21	140/90	1	—	32	67	141	0.3 g.	"
13	20	140/80	0	—	34	65	140	—	"
14	19	140/90	0	—	34	55	141	—	"
15	18	140/90	0	—	29	78	140	—	"
16	15	140/95	1	L.V.S.	40	56	140	0.5 g.	Improved
17	4 (died)	120/80	—	N.D.	25	N.D.	—	—	—
18	Died	—	—	—	—	—	—	—	—
19	6 (died)	130/80	—	"	35	"	—	—	—
20	16	150/95	1	L.V.S. (1)	28	—	141	—	Improved
21	12	140/80	1	—	43	95	138	—	Corrected
22	14	120/80	2	—	56	36	141	—	"
23	12	140/90	1	—	38	104	143	—	"
24	12	170/105	2	—	30	92	143	—	Improved
25	12	130/90	0	—	24	N.D.	142	—	Corrected
26	9	160/100	1	N.D.	30	—	—	N.D.	Improved
27	36	130/90	—	"	33‡	95§	—	—	Corrected

N.D. = Not done.
*L.V.S. (1) = Left ventricular strain (improved, as compared with preoperative E.C.G.).
†On methylglutamate.
‡Estimation 18 months after operation.
§Estimation one month after operation.

sequently followed by a myocardial infarction; however, the patient made a fair recovery and was working again. Blood-pressure levels were unaltered. In one patient (Case 5), in whom there was no response to nephrectomy, symptoms of peripheral vascular disease developed. In all the other patients assessment remained, at the time of writing, as at the admission period except for one (Case 12), in whom renal vein thrombosis on the operated side led to redevelopment of hypertension; thereafter nephrectomy improved the blood pressure. In summary the blood pressure was initially corrected or improved in 93% of patients, but because of the two late "operative" deaths the final figure for correction or improvement of blood pressure is 85%.

TABLE III.—Summary of Results of Surgery

	No. of Cases	Percentage
B.P. corrected	16	59.2†
B.P. improved	7	25.9
No effect on B.P.	1	3.7
Immediate operative death	1	3.7
Late operative deaths	2*	7.4
Total	27	99.9

* Cases 17 and 19. These patients died four and six months respectively after surgery, the B.P. having been corrected in the interim period.

† Includes two patients who subsequently died: Case 14 from bronchial carcinoma 23 months after surgery; Case 11 from myocardial infarction 28 months after surgery.

Because of the relation between plasma renin and serum sodium levels (Brown *et al.*, 1965) and the possible relation between renovascular hypertension and the renin-angiotensin system, the preoperative and follow-up admission plasma sodium levels were compared. There was a significant rise in plasma sodium levels after operation (Table IV).

TABLE IV.—Renal Function, Plasma Sodium, and P.C.V. Before and After Renovascular Surgery

	Before*	After†	n‡	t Test§
Blood urea (mg./100 ml.)	32.7	33.8	25	N.S.
Creatinine clearance (ml./min.)	94.7	74.4	14	P < 0.001
Plasma sodium (mEq/l.)	138.2	140.9	21	P < 0.001
P.C.V. (%)	43.0	43.7	21	N.S.

* Mean of all patients preoperatively.

† Mean of all patients at time of follow-up admission.

‡ Number of patients having estimations both before and after surgery.

§ Student's *t* test on mean difference in this group (n).

N.S. = Not significant.

No significant alteration was observed in the mean blood urea levels before and after surgery, but there was a significant fall in creatinine clearance (Table IV). The mean postoperative creatinine clearance in all patients was 74.4 ml./min. For the patients who had nephrectomy the mean postoperative creatinine clearance was 69.4 ml./min.

Serial isotope renograms were carried out in patients who underwent reconstructive vascular surgery. In Cases 3, 4, 21, and 24 the renogram became normal, and in Case 12 it became normal until renal vein thrombosis occurred on the affected side 24 months after the initial operation. In Case 27 the renogram indicated no function 20 days after the original operation, when hypertension had increased to frankly malignant levels; at operation the graft was found thrombosed and nephrectomy was performed. In Case 26 there was a slight delay in the third phase of the curve—which had previously been a B type—when the patient was last seen, associated with a still not normal B.P., which, especially in a young patient, suggests a degree of residual renal ischaemia. In those patients with normal renograms the I.V.P. had also become normal, while in Case 26 slight delay in excretion and increased density of the dye were still present.

Discussion

The British literature on the results of surgical treatment of renal artery stenosis is relatively sparse. Brown *et al.* (1960)

gave a detailed account of the experience of the St. Mary's group with especial regard to the clinical features and diagnosis; and Owen (1967) reported 69 operated cases with a blood pressure correction rate of 43%, a combined correction or improvement rate of 72%, and six operative deaths. Thirty-one of these patients had nephrectomy, 22 being primary and 9 secondary procedures. Fenton *et al.* (1966) described the results of surgery in 15 patients with renal artery stenosis, 11 of whom had fibromuscular dysplasia; blood pressure was corrected in eight and improved in two by nephrectomy. Other British workers reporting smaller series of cases have sounded a more pessimistic note (Chamberlain and Gleeson, 1965; Parsons *et al.*, 1965; Groden *et al.*, 1966).

The American literature is more extensive and more enthusiastic. De Bakey and his colleagues (Morris *et al.*, 1966) report a series of 432 operated patients, 93% of whom had reconstructive vascular surgery. Blood pressure was corrected or improved in 81% one year after operation, the operative mortality (up to 30 days) being 7%. Several reviews of the American literature made in conjunction with the reports of personal series (Kaufman, 1965; Maxwell, 1966; Genest *et al.*, 1966) show that in approximately 1,000 patients correction rates varied from 37 to 66%, improvement rates from 16 to 45%, correction plus improvement rates from 65 to 95%, and mortality rates from 0 to 18%.

Precise comparison of results between different centres is difficult, but these American overall results are similar to our own, where blood pressure was corrected or improved in 85% of patients. It is our view that if good results are to be attained, and moreover improved on, then both a satisfactory selection of patients for surgery and expert vascular surgery are required, and these can be obtained only by experienced medical and surgical teams working in close co-operation.

Case Selection

Renal artery stenosis possibly suitable for renovascular surgery is uncommon, probably representing only 3 to 5% of the hypertensive population (Kennedy *et al.*, 1965). It can mimic all degrees of severity of "essential" hypertension and can occur in all age groups. Clinical features which may be of value in diagnosis are a renal bruit and recent onset or abrupt change in the character or rapid progression of hypertension, but these are seldom decisive. We have been impressed by the relative frequency of a history of hypertension dating back to a toxæmia of pregnancy or of a history of recurrent toxæmia of pregnancy in young females with renovascular hypertension. Polycythaemia is a rare association with renovascular hypertension due to renal artery stenosis (Luke *et al.*, 1965). In this series the length of history or duration of hypertension, where known, was relatively short at 13 months. Maxwell (1966) found a significantly longer duration of hypertension in those failing to respond than in those responding to renovascular surgery; but contrary views are expressed by Owen (1967), and in our experience the presence of hypertension for a considerable period, especially in a young patient, by no means precludes correction of hypertension by surgery, as, for example, in Case 25, where hypertension was known to have been present for 12 years.

A safe, reasonably practical, and yet reliable screening procedure for renovascular hypertension is clearly mandatory (Lancet, 1966; Brit med. J., 1967) so that the more elaborate and potentially harmful investigations are confined to a small selected group. We continue to hold the view that the combination of the I.V.P. and the renogram offers such a screening process, though we believe that the screening procedure may be improved in the future by the addition of a humoral assay on peripheral blood.

It is important to decide at the outset whether the patient's hypertension is significant enough to merit investigation and whether a surgical approach would be feasible. Some patients are sensibly excluded from even the initial screening procedure by their age, relative insignificance of the hypertension, or the presence of coincidental disease such as severe atherosclerosis of the brain, heart, or peripheral vessels, severe chronic respiratory disease, or because of significantly impaired renal function. Though Morris *et al.* (1966) and Gifford and Poutasse (1965) claim that azotaemia itself may offer an indication for operation in renal artery stenosis with renal atrophy, we believe that a search for renovascular hypertension is unlikely to be justified if the blood urea is above 70 mg./100 ml. and the creatinine clearance below about 45 ml./minute, especially where the patient does not have accelerated hypertension. In malignant hypertension, where some of the renal impairment may be due to potentially remediable acute hypertensive vascular changes, it is perhaps more justifiable to attempt renovascular surgery at the lower limits of these values. Thus in Case 22 malignant hypertension, poorly controlled by drugs, was dramatically corrected (B.P. 120/80) by removal of a contracted kidney (60 g.).

Preoperative Tests

When screening tests suggest functionally significant renal artery stenosis there is disagreement over which further tests are required in order to allow a decision on surgical intervention. An aortogram is essential in order to demonstrate the anatomical relations of the lesion to the surgeon. No matter which plan of investigation is used there is now wide agreement that merely anatomical renal artery stenosis (Eyer *et al.*, 1962; Holley *et al.*, 1964) is not an indication for surgery aimed at correcting hypertension. Though the exact pathogenesis of renovascular hypertension is not yet known there is certainly a close relation between the alteration in renal plasma flow, glomerular filtration rate, and tubular sodium and water reabsorption distal to functional stenosis and hypertension (Stamey, 1966).

Some authors (Stamey, 1965; Peart, 1966) insist on divided renal function tests as a routine before operation, but we believe that divided renal function tests are not essential provided the clinical features, I.V.P., renogram, and aortogram are all in agreement, since the I.V.P. and renogram are altered by functional renal artery stenosis for the same reasons as are divided renal function tests (Luke *et al.*, 1966). Similarly, if the preoperative assessment is of clear-cut functional unilateral renal artery stenosis then we and others (Gifford and Poutasse, 1965) do not believe that demonstration of a definite transstenotic gradient is essential; pressure measurements may sometimes be difficult to obtain for technical reasons, and, moreover, the results may be affected by a fall in blood pressure under anaesthesia. Nevertheless, pressure gradients should be measured during operation wherever possible, both before and after revascularization.

Biopsy of the ipsilateral kidney to study the juxtaglomerular apparatus and the arterioles, and of the contralateral kidney for small vessel changes, have been advocated, and Vertes *et al.* (1965) claimed that vascular changes in the contralateral kidney would prevent a response to operation. We have not done preoperative renal biopsies and believe that contralateral kidney biopsy could be hazardous, as that kidney is a potentially solitary one if surgery is performed. There is increasing evidence that the changes in the juxtaglomerular apparatus are not more helpful than other tests in deciding on operation, and that it is impossible to prognosticate from percutaneous renal biopsy whether changes in the contralateral kidney will preclude a response to surgery (Stamey, 1965; Kincaid-Smith, 1966; Owen, 1967; Maxwell *et al.*, 1967). Stamey (1965) believes that measurement of renal plasma flow in the contralateral

kidney is of value when deciding on surgery, cases with para-aminohippuric acid clearance rates of less than 200 ml./min. being unlikely to respond to operation. Our policy has been not to recommend operation unless the renogram and I.V.P. and nephrogram phase of aortogram on the contralateral kidney were normal, except occasionally in the case of malignant or accelerated hypertension as noted above. Stamey (1965) also recognizes this latter possibility of response to surgery despite lower plasma flow values in the contralateral kidney where malignant hypertension is present.

If the renin angiotensin mechanism is important in the pathogenesis of renovascular hypertension, assay of renin levels either in the peripheral blood or in the renal vein should, in theory at least, be valuable in deciding on surgery; and indeed this view has been expressed, based on retrospective studies (Genest *et al.*, 1966). However, other workers have found a scatter of values between essential and renovascular hypertension (Brown *et al.*, 1966; Creditor and Loschky, 1967), and renin values are often high in malignant hypertension due to any cause (Brown *et al.*, 1966). Peart (1966) goes no further than to state that "a patient with a low renin value is unlikely to have renovascular hypertension." The dramatic fall in blood pressure after operation in some patients (as in Case 22) is suggestive of a humoral mechanism. The mean rise in plasma sodium in our patients after surgery is of interest, in view of the reciprocal relation between plasma sodium and renin (Brown *et al.*, 1965). However, the plasma sodium level would not have proved useful in deciding on surgery in any individual patient. Studies of renin levels in renovascular patients submitted to surgery should certainly continue.

Our own preoperative investigation consisting of I.V.P., renogram, and aortogram, with divided renal function tests only in some cases, is a relatively simple one, but the blood pressure response to surgery seen in 25 out of 26 patients suggests that it is reasonably adequate, at the present stage of our knowledge, for the selection of patients for surgery.

Nature of Surgery

There is no evidence that reconstructive vascular surgery is more likely to be associated with a good blood-pressure response than nephrectomy (Maxwell, 1966), but we would agree with Peart (1966) that every effort should be made to conserve functioning renal tissue and that reconstructive vascular surgery should be carried out wherever possible; and there is no doubt that increasing experience leads to a greater percentage of successful reconstructions. Reconstructive procedures, however, are often of necessity protracted, and, especially in the older patient, may carry a significant morbidity and mortality. We believe that in some patients nephrectomy may be the only step consistent with a reasonable risk. Furthermore, reconstructive surgery is not possible in a significant proportion of patients with fibromuscular dysplasia because of involvement of the distal renal artery by the disease process (Fenton *et al.*, 1966; Hunt *et al.*, 1967). Again, where the kidney on the stenotic side is small and shrunken it is unlikely that reconstructive vascular surgery will correct hypertension, probably because of the severe histological changes on that side (Kaufman, 1965; Maxwell *et al.*, 1967). We have found the pattern of renogram curve over the affected kidney of value in making the choice between nephrectomy and reconstructive vascular surgery.

Drug Therapy

Drug therapy offers an obvious alternative to surgery in renovascular hypertension (Sheps *et al.*, 1965; Dustan *et al.*, 1966). There is a potential hazard that blood-pressure reduction by hypotensive drugs might precipitate vascular occlusion on the affected side, but this does not seem to have been an

undue problem (Dustan *et al.*, 1966), though some cases have been reported (Sheps *et al.*, 1965; Gifford and Poutasse, 1965; Owen, 1967). Valid comparisons between the results of treatment in medically and surgically treated cases are not so far available, mainly because medical treatment in the reported series was being given to renovascular patients selected because they were older, had bilateral renal vascular lesions, had extensive vascular disease, or were less fully studied than the operated cases (Dunstan *et al.*, 1966; Owen, 1967). Fourteen of our patients with renal artery stenosis were not operated on for such reasons.

It is our view that where renovascular investigations reveal a functional unilateral renal artery stenosis with well-maintained function in the opposite kidney, surgery by an experienced group should in general be offered as the treatment of choice to the young patient with significant hypertension and to the older patient with accelerated hypertension and in whom operation does not constitute an undue hazard. Where bilateral functional stenosis is present, as in Case 17, surgery is difficult and drugs are the first line of approach, but the otherwise gloomy prognosis if drugs fail to control the blood pressure may necessitate an attempt at bilateral revascularization.

Conclusions

As a result of our experiences in the detection of renovascular hypertension and the selection of such cases for surgery, we suggest the following policy.

- (1) Assess the significance of the hypertension, total renal function, and fitness for possible surgery.
- (2) In suitable cases proceed to I.V.P. and renogram.
- (3) If the I.V.P. and renogram suggest unilateral renal artery stenosis with renal ischaemia, if the opposite kidney is normal, and if the patient is young with significant hypertension or has accelerated hypertension, proceed to aortography. If the clinical features and tests are in agreement, and if there is no contra-indication, renovascular surgery is indicated; if there is uncertainty, divided renal function tests may also be required before the decision about surgery.
- (4) In the older patient with less severe hypertension a trial of drugs should be carried out even if renal artery stenosis is suspected on screening tests (I.V.P. and renogram). If the blood pressure is poorly controlled or the side-effects of drugs are intolerable, or if hypertension becomes accelerated, reconsider a surgical approach.
- (5) Reconstructive vascular surgery is preferred where feasible, but nephrectomy is likely to be the operation of choice if the kidney is small, if the longer operation means an undue risk, or if the distal renal artery is diseased.
- (6) Postoperative isotope renograms provide a useful guide to the function of a reconstructed renal artery.

Summary

Renovascular surgery has been carried out in 27 patients with functionally significant renal artery stenosis. These 27 originated from a group of 41 patients with functional renal artery stenosis found by studying approximately 1,000 hypertensive patients. Reconstructive vascular surgery was performed in 10 and nephrectomy in 17 patients. There was one immediate postoperative death, and two late deaths occurred at four and six months for reasons related to reconstructive surgery; in both of these cases the blood pressure was corrected between surgery and death. Of the remaining 24 patients assessed at least one year after surgery, with a mean assessment time of 25 months, the blood pressure was corrected (less than

90 mm. Hg diastolic) in 16 and improved (fall of diastolic by at least 20 mm. Hg without hypotensive drugs; mean fall 27 mm. Hg) in seven.

It is suggested that the I.V.P. and renogram offer a suitable screening procedure for hypertensive patients, that aortography is necessary before surgery in all cases, but that differential renal function tests are not necessarily required before surgery.

In the older patient with less severe hypertension, even if the screening tests suggest renal artery stenosis, drugs should be given a trial before proceeding to more complicated tests.

Reconstructive vascular surgery should be aimed at wherever possible, but nephrectomy is more appropriate in those unfit for a prolonged operation or with a contracted ipsilateral kidney or with distal disease of the affected renal artery.

Many of the patients in this series were referred to us by members of the Hypertension Unit, Department of Cardiology, by the physicians in Glasgow Royal Infirmary, and by physicians in other hospitals in Glasgow and the West of Scotland; we are grateful to them for their co-operation. We would also like to thank Professor W. A. Mackey, Department of Surgery, Royal Infirmary, who, with Mr. D. W. Short, operated on two patients (Cases 4 and 17); Dr. W. P. Duguid, of the Department of Pathology, Royal Infirmary; and those radiologists who carried out some of the investigations before referral.

REFERENCES

- Brit. med. J.*, 1967, 2, 4.
 Brown, J. J., Davies, D. L., Lever, A. F., and Robertson, J. I. S. (1965). *Brit. med. J.*, 2, 144.
 Brown, J. J., Lever, A. F., Davies, D. L., and Robertson, J. I. S. (1966). *Postgrad. med. J.*, 42, 153.
 Brown, J. J., Owen, K., Peart, W. S., Robertson, J. I. S., and Sutton, D. (1960). *Brit. med. J.*, 2, 327.
 Chamberlain, M. J., and Gleeson, J. A. (1965). *Lancet*, 1, 619.
 Creditor, M. C., and Loschky, U. K. (1967). *Amer. J. Med.*, 43, 371.
 Dustan, H. P., Meaney, T. F., and Page, I. H. (1966). In *Antihypertensive Therapy*, edited by F. Gross, p. 544. Berlin.
 Byler, W. R., Clark, M. D., Garman, J. E., Rian, R. L., and Meininger, D. E. (1962). *Radiology*, 78, 879.
 Fenton, S. S. A., Lytle, J. A., and Pantridge, J. F. (1966). *Lancet*, 2, 117.
 Genest, J., *et al.* (1966). In *Antihypertensive Therapy*, edited by F. Gross, p. 518. Berlin.
 Gifford, R. W., and Poutasse, E. F. (1965). *Progr. cardiovasc. Dis.*, 8, 141.
 Groden, B. M., James, W. B., and Davidson, J. K. (1966). *Postgrad. med. J.*, 42, 177.
 Harrison, E. G., Hunt, J. C., and Bernatz, P. E. (1967). *Amer. J. Med.*, 43, 97.
 Holley, K. E., Hunt, J. C., Brown, A. L., jun., Kincaid, O. W., and Sheps, S. G. (1964). *Amer. J. Med.*, 37, 14.
 Hunt, J. C., Bernatz, P. E., and Harrison, E. G. (1967). *Circulat. Res.*, Suppl. No. 2, vol. 21, p. 211.
 Kaufman, J. J. (1965). *J. Urol.*, 94, 211.
 Keith, N. M., Wagener, H. P., and Barker, N. W. (1939). *Amer. J. med. Sci.*, 197, 332.
 Kennedy, A. C., Luke, R. G., Briggs, J. D., and Stirling, W. B. (1965). *Lancet*, 2, 963.
 Kincaid-Smith, P. (1966). In *Antihypertensive Therapy*, edited by F. Gross, p. 485. Berlin.
Lancet, 1966, 2, 94.
 Luke, R. G., Briggs, J. D., Kennedy, A. C., and Stirling, W. B. (1966). *Quart. J. Med.*, 35, 237.
 Luke, R. G., Kennedy, A. C., Stirling, W. B., and McDonald, G. A. (1965). *Brit. med. J.*, 1, 164.
 Maxwell, M. H. (1966). *Proc. 3rd Int. Congr. Nephrol.*, 3, 131.
 Maxwell, M. H., Lupu, A. N., and Franklin, S. S. (1967). *Circulat. Res.*, Suppl. No. 2, vol. 21, p. 201.
 Morris, G. C., De Bakey, M. E., Crawford, E. S., Cooley, D. A., and Zauger, L. C. C. (1966). *Surg. Gynec. Obstet.*, 122, 1255.
 Owen, K. (1967). XIV Kongress der internationalen Gesellschaft für urologie, p. 311. Paris.
 Parsons, V., Cameron, J. S., and Gray, B. (1965). *Guy's Hosp. Rep.*, 114, 114.
 Peart, W. S. (1966). In *Antihypertensive Therapy*, edited by F. Gross, p. 468. Berlin.
 Sheps, S. G., Osmundson, P. G., Hunt, J. C., Schirger, A., and Fairbairn, J. F. (1965). *Clin. Pharmacol. Ther.*, 6, 700.
 Short, D. W., Kennedy, A. C., Luke, R. G., and Mackey, W. A. (1965). *Brit. J. Surg.*, 52, 963.
 Stamey, T. A. (1965). *Amer. J. Med.*, 38, 829.
 Stamey, T. A. (1966). In *Antihypertensive Therapy*, edited by F. Gross, p. 555. Berlin.
 Vertes, V., Grauel, J. A., and Goldblatt, H. (1965). *New Engl. J. Med.*, 272, 186.