Indications for renal artery surgery: a review[1]

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The observation that experimentally-induced ischaemia of the kidney will result in high blood pressure has been known for 50 years (Goldblatt *et al.* 1934). Renovascular hypertension in man is potentially curable by surgical means and a large number of patients have undergone surgical treatment. However, the indications for surgical treatment and its long-term results remain a subject of controversy. The incidence is difficult to define, varying from 1% to 30% of hypertensive patients surveyed. These results probably reflect the bias and experience of the groups reporting the data (Smith 1956, Dustin & Page 1962). In our series the incidence of operable renal artery stenosis was 10.6% (Horvath *et al.* 1982). The true incidence in the hypertensive population is probably close to 1%. The results of a number of drug intervention trials have shown the benefit of lowering blood pressure (Australian Therapeutic Trial 1980, Hypertension Detection and Follow Up Programme 1979). No single regimen has appeared to be better than any other, and the essential criterion to achieve a good prognosis is normalization of blood pressure. Even if the lowest reported incidence of renal artery stenosis – 1% – is assumed, there are still a large number of patients with potentially surgically-curable hypertension, and it is thus appropriate to evaluate the long-term benefits of such surgery.

Indications for surgery

The commonest reason for repair of a stenosis of the renal artery has been to achieve control of blood pressure. A less common alternative indication has been the prevention or reversal of renal failure, secondary to interruption of renal blood supply by obstructed or stenosed renal arteries. This review will attempt to deal with both these issues and to try to evaluate whether any specific features of history, examination or investigation will help to determine a favourable outcome.

There have been published reports on more than 1000 patients with hypertension and demonstrable renal artery stenosis who have undergone renal artery reconstruction or, less commonly, nephrectomy, for the treatment of hypertension. Many of these patients have been re-evaluated at periods of up to 10 years following surgery, and some have been followed for as long as 20 years. Although evaluation of the patient at the time of follow up has concentrated on the level of blood pressure, other important issues such as the level of renal function, renal arterial graft patency, progression of disease in the native renal arteries, and the cause of death when remote from the time of surgery have also been evaluated.

The most appropriate way to answer the question of which patients should have renal artery surgery should be based on prospective controlled trials, comparing the best nonoperative management with surgical treatment; however, despite reports that go back more than 20 years, there has not yet been a properly designed trial that can answer this question. A recent large study reported by Whelton *et al.* (1981), supporting a non-surgical approach, relied on retrospective controls, failed to have adequate matched controls, and did not have adequate periods of follow up. There have also been extensive changes in both surgical and medical management in the 20 years under review. Thus, no appropriate prospective studies are available upon which an approach can be based. Many factors,

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such as patient selection, underlying renal disease, extent of vascular involvement and other illnesses, will affect the outcome. Despite these limitations in the studies reported, a number of observations emerge that may help us to decide which patients would benefit from renal artery reconstruction.

Patient mortality

The operative mortality for surgical reconstruction of the renal artery is less than 2%. In one large series of 505 patients (Lawrie *et al.* 1980*b*) the operative mortality was 1.8%. All these deaths were associated with complex operative procedures such as repair of aortic aneurysms. There were no deaths reported when renal artery reconstruction was the sole procedure. The operative mortality in other reported series has varied from 0% to 5%, depending on the patients and their underlying problems. Mortality is also related to the type of vascular disease and the age of the patient. In our patients (Horvath *et al.* 1981) the aetiology of the stenosis was atherosclerosis in the majority of cases (mean age 46 years) and the perioperative mortality was 3%. In contrast, Stoney *et al.* (1981) reported no perioperative mortality in 86 younger patients (mean age 35 years), most of whom had fibromuscular disease. The perioperative mortality appears to be dependent on the extent of the operative procedure and the nature of any accompanying disease; these diseases tend to be of a more serious nature in the older patient with atherosclerosis.

If long-term patient survival is examined as a function of blood pressure control, there is a direct relationship between the success in achieving control of blood pressure ($<160/100$ mmHg) and the length of patient survival. Starr *et al.* (1980) demonstrated that patients with a blood pressure of 140/90 mmHg or less had an 85% survival at 15 years, whilst those with poor blood pressure control greater than 160/100 mmHg had an expected survival of 29% at 15 years. In our series good control of blood pressure ($<140/90$ mmHg) was found to be associated with a survival of 68% at 15 years, whereas poor control of blood pressure ($>160/90$ mmHg) had a poor outlook, with a 15-year survival rate of 47% (Horvath *et al.* 1981). The most optimistic report is from Stoney *et al.* (1981) who reported 100% survival over a 16-year follow up, probably reflecting the better prognosis in the young patient with fibromuscular disease. The remote causes of death in the majority of patients were due to vascular disease (cerebrovascular accident, myocardial infarction and peripheral vascular disease), uraemia and, less commonly, apparently unrelated malignancy.

Control of blood pressure

In most reported studies, control of blood pressure was achieved in the majority of patients who underwent surgery. Control was generally regarded as a blood pressure of less than 160/100 mmHg, but in a number of studies it was defined even more strictly, with good control being regarded as a blood pressure of less than 140/90 mmHg. Patients with a blood pressure greater than 160/100 mmHg were defined as therapeutic failures. In order properly to assess the effect of surgical correction on hypertension, the follow-up period must be of adequate length to overcome any unrelated effects of surgery and hospitalization and to try to determine if the natural history of the disease has been altered. A number of workers have attempted to follow their patients for periods of up to 20 years. Lawrie *et al.* (1980*b*) followed 505 patients for periods of 2–20 years after surgery, and found that 309 (61%) had good control of blood pressure ($<160/100$ mmHg) at the time of follow up. Dean *et al.* (1976) and Lagneau & Michel (1981) reported similar outcomes in 162 and 97 patients respectively. Significantly better results have been reported by Morin *et al.* (1980), Thevenet *et al.* (1980) and Stoney *et al.* (1981), with 93%, 89% and 98% of patients respectively having good control of blood pressure up to 16 years following surgery. In our series, on the other hand, only 47% of patients had good blood pressure control 15 years after surgery (Horvath *et al.* 1981). It is interesting to analyse these differences. In those series reporting a better outcome, the majority of the patients had fibromuscular hyperplasia and there were few patients with atherosclerosis. In our series, where the results were less favourable, the

majority of patients had atherosclerosis as a cause of the renal artery stenosis and only a minority of patients had fibromuscular disease.

Prevention of end-stage renal failure

The natural history of stenosis of the renal artery has been described by Schrieber *et al.* (1980), who demonstrated progression in the atherosclerotic stenotic lesion in 37 (44%) of 85 patients. In 14 of the 37 (38%), total occlusion of the vessel occurred with shrinkage of the kidney. In the same study, progressive lesions were found in 22 (33%) of 66 patients with fibromuscular disease. Other studies (Stewart *et al.* 1970, Wollenweber *et al.* 1968) have suggested a similar progression. Patients who have progressive bilateral renal artery stenosis may present in acute renal failure (Sheil *et al.* 1973). Repair of renal artery stenosis with the primary aim of reversing renal impairment has been reported by a number of workers. Sheil *et al.* (1973) reported 3 cases of renal failure where revascularization of occluded arteries resulted in reversal of renal failure. In a later study (May *et al.* 1976), a further 8 patients with renal impairment (serum creatinine 7.95 ± 1.81 mg/100 ml) showed improvement of renal function (serum creatinine 3.91 ± 1.21 mg/100 ml) at follow up 20 months postoperatively.

Similar encouraging results have been reported by Mackay (1981), who found that renal function improved in 9 of 11 patients studied. In an attempt to evaluate the contribution of normalization of blood pressure to improvement in renal function, Dean *et al.* (1979) studied 25 patients with hypertension and renal impairment before and after unilateral renal artery reconstruction. The creatinine clearance of the operated kidney rose significantly from 16 ± 8.9 ml/min (range 0–27) to 32 ± 16 ml/min (range 0–72) following operation, whilst renal function in the contralateral, non-operated kidney remained unaltered. Although these data are not conclusive, they suggest that re-establishing renal blood flow improves renal function, at least in the short term.

The current evidence would strongly suggest that the presence of renal impairment in patients with renovascular hypertension is an indication for surgery, as drug treatment may normalize blood pressure but will not re-establish renal blood flow. The role of angioplasty in this situation has not been adequately defined, and we await the results of adequately designed trials with long-term follow up.

Which patients do better?

Although the effect of surgery on control of blood pressure and on the preservation of renal function appears to be of benefit in the majority of patients studied, there remain considerable differences in the reported number of patients experiencing a successful outcome. In view of these differences, it would be valuable to be able to predict which patients would be more likely to have a favourable outcome.

In all reported studies the single most important prognosistic factor was age. The younger the population, the less the likelihood of perioperative death and the more likely that blood pressure would be controlled. In the 505 patients studied by Lawrie *et al.* (1980*b*), a regression analysis of the data demonstrated that age was the single most important factor predicting a favourable outcome. There was a significant ($P < 0.001$) reduction in survival at 20 years of patients undergoing surgery after the age of 50, compared with patients aged less than 50. These observations are supported by the studies of Morin *et al.* (1980) and Stoney *et al.* (1981) who reported excellent results in patients under 35 years of age. On the other hand, the older patients (average age 46 years) studied by Thevenet *et al.* (1980) and in our series (mean age 47 years; Horvath *et al.* 1981) had a worse outcome in terms of blood pressure control and patient survival. The second point made by Lawrie *et al.* (1980*b*), which was reflected in the other series, is that patients with fibromuscular disease had a better outlook than patients with atherosclerosis. Although this observation was an independent variable of age, it is clear that atherosclerosis and age are linked. It is apparent that the younger patient with fibromuscular disease has the most favourable prognosis, but

even amongst those with atherosclerosis and advancing age a favourable outcome has been reported in 30–50% of patients. Dean *et al.* (1976) found that 80% of 70 patients over the age of 50 had good blood pressure control 12 months following operation. The older patients with diffuse atherosclerosis and hypertension associated with an occlusive renal lesion should also be considered for renal artery reconstructive surgery to help blood pressure control and to try to prevent progressive renal impairment.

Controversies in management

Occluded renal arteries

There remains some considerable doubt about the correct approach to management of the patient who has a totally occluded renal artery. The principle of trying to preserve renal tissue at all cost is balanced by the risk of vascularizing a permanently damaged ischaemic kidney. If a stenosis has progressed slowly over many years, finally leading to occlusion, the kidney may be well supplied with collateral and capsular blood vessels; the results of revascularizing such a kidney are surprisingly good. Sheil *et al.* (1973) reported improved renal function and blood pressure control in 3 patients who presented with hypertension and renal impairment (serum creatinine 2.8–8.8 mg/100 ml): postoperative renal function improved in all 3 patients (1.8–2.0 mg/100 ml). Subsequently May *et al.* (1976) reported normal control of blood pressure at follow up in 13 of 14 patients, and improvement of previously impaired renal function in 8 of these. Similar results were achieved by Lawrie *et al.* (1980*a*) who assessed 40 patients with occluded renal vessels: 21 were considered suitable for reconstruction rather than nephrectomy, and good control of blood pressure was achieved in 15 (71%). It appears from the data in these studies that total occlusion of a renal artery is not a contraindication to attempting to restore the blood supply and salvage the renal parenchyma.

Renal pathology

The role of renal biopsy in the decision-making process related to revascularization remains unclear. Our own group (May *et al.* 1976) has found little benefit from intraoperative biopsy in predicting either control of blood pressure or improvement in renal function – a view shared by Lawrie *et al.* (1980*a*), who placed most value on the kidney size and mass, rather than the histological features. On the other hand, Libertino *et al.* (1980) and Ekestrom *et al.* (1979) both found that knowledge of the renal histology was useful in deciding whether renal artery reconstruction was worthwhile. At present there is insufficient evidence on which to base a firm conclusion regarding the role of examining renal pathology in this situation.

Renal vein renin measurement

It is difficult to imagine that the measurement of renal vein renin ratios (RVRR) could still be a matter of controversy. In unilateral renal artery stenosis, the use of RVRR as a way of determining unilateral functional ischaemia is widely reported (Fry 1979). There is, however, surprisingly little data correlating RVRR, the long-term results of surgery, and control of blood pressure. Ekestrom *et al.* (1979) found that 14 of 19 patients with no evidence of excess renin secretion from the affected side preoperatively had persistent hypertension following surgery. In our series, 14 patients who failed to demonstrate excess renin production from the affected side underwent repair of the stenosis on the renal artery, and 12 remained hypertensive (Horvath *et al.* 1981).

It appears that failure to demonstrate excess renin production from the affected side means that the likelihood of curing the hypertension is reduced. Thus, the failure to demonstrate a significant ratio, particularly in older, high-risk patients, would suggest that medical management should be pursued.

Persisting hypertension

There remains in all the studies, including those with positive renin studies, a group of patients who remain hypertensive following surgery. It has been suggested that thrombosis

or stenosis of the graft may be a contributing factor. However, in the review by Ekestrom *et al.* (1979) of 24 patients with persisting hypertension following surgery, only 6 patients had an anatomical abnormality that could account for the persisting hypertension. Other studies (Thevenet *et al.* 1980, Stoney *et al.* 1981) have demonstrated a small incidence of graft occlusion or progression of underlying pathology. It appears that, in the majority of patients with persisting hypertension following surgery, occlusion of the graft or progression of underlying vascular disease in the vessels distal to the graft or on the contralateral side is not the cause of the failure to control blood pressure. Other possible explanations are irreversible parenchymal damage to one or both kidneys due to hypertension, repair of a unilateral renal artery stenosis where the stenosis was not causing the high blood pressure, or coexistent non-hypertensive renal disease.

Percutaneous transluminal angioplasty (PTA)

The relatively recent introduction of PTA for the treatment of the hypertensive patient with renal artery stenosis has been greeted with a great deal of enthusiasm. The complication rate for the procedure has been reported to be between 5 and 10% (Grim 1981, Mahler *et al.* 1982), the most common complication being the necessity to redilate the artery to achieve a radiographically satisfactory result. PTA has been reported as having a successful outcome in 70–80% of patients with fibromuscular hyperplasia (Mahler *et al.* 1982, Grim 1981, Saddekni *et al.* 1980), but the follow-up period for most of the patients was less than 24 months.

Patients with atherosclerosis who have been treated with PTA appear to have a less favourable outcome (Grim 1981). Slater (1980) has attempted to compare the results of PTA with surgical repair, and correctly concludes that until a properly-designed, controlled trial comparing the two modes of therapy is carried out, the role of PTA will remain undefined.

Conclusion

The surgical management of the patient with renovascular hypertension will achieve a blood pressure of less than 160/100 mmHg in about 60% of patients 10 or more years following surgery. It appears that young patients with fibromuscular disease, free from associated disease processes, will have a better prognosis than older patients with atherosclerosis or renal impairment.

Despite the information available, only a properly-designed, prospective trial comparing current surgical management with current medical management will properly define the role of surgery in the management of renovascular hypertension. The recent enthusiasm for angioplasty will mean that any trial of therapy must include this approach.

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