Transpl Int (1993) 6: 111–115

Transplant International

Renal allograft artery stenosis: results of medical treatment and intervention. A retrospective analysis

J. W. S. Merkus[1], F. T. M. Huysmans[2], A. J. Hoitsma[2], F. G. M. Buskens[3], S. H. Skotnicki[1], R. A. P. Koene[2]

[1] Clinical Vascular Laboratory, University Hospital St. Radboud, P. O. Box 9101, NL-6500 HB Nijmegen, The Netherlands
[2] Department of Nephrology, University Hospital St. Radboud, P. O. Box 9101, NL-6500 HB Nijmegen, The Netherlands
[3] Department of Surgery, University Hospital St. Radboud, P. O. Box 9101, NL-6500 HB Nijmegen, The Netherlands

Received: 26 February 1992/Accepted: 22 May 1992

Abstract. In a retrospective analysis of 1165 renal transplantations in our center, 65 cases of renal allograft artery stenosis were diagnosed angiographically (prevalence 5.5%). Hypertension was present in all cases; a bruit over the allograft and an increase in serum creatinine level were additional reasons for angiography. Shortly after diagnosis of the stenosis, two patients died and two others lost their grafts due to thrombosis. In 24 patients the decision was made not to correct the stenosis. One of these grafts was lost because the stenosis could not be corrected. Medical management of hypertension in these patients resulted in a decrease in diastolic blood pressure from 109 ± 22 to 96 ± 12 mm Hg ($P < 0.01$) 3 months after diagnosis with the use of almost twice as many antihypertensive drugs as at the time of diagnosis ($P < 0.01$). The stenosis was corrected if the angiography showed it to be so severe that it jeopardized renal allograft function or caused uncontrollable hypertension. Only three of nine percutaneous transluminal angioplasty (PTA) procedures resulted in a definitive correction of the stenosis. Surgical intervention was performed in 30 patients, including two patients whose PTAs had proved unsuccessful. Surgery led to graft loss due to thrombosis in 6 of 30 operations (20%), whereas restenosis occurred twice (7%). In three other cases (10%), the correction was not successful due to local anatomical variations or concomitant rejection. Successful correction of the stenosis by either PTA or surgical intervention ($n = 22$) resulted in a significant decrease in systolic (171 ± 31 vs 145 ± 27 mm Hg; $P < 0.01$) and diastolic (103 ± 15 vs 89 ± 14 mm Hg; $P < 0.05$) blood pressures 3 months after correction. Concomitantly, a decrease in the number of antihypertensive drugs from 2.1 ± 1.0 to 1.5 ± 1.0 ($P < 0.01$) was achieved. In conclusion, renal allograft artery stenosis could successfully be managed pharmacologically, provided that allograft perfusion was not jeopardized. Successful surgical correction of a stenosis with effective control of hypertension was achieved in 63% of the cases. PTA was less frequently successful but did not cause any graft loss.

Correspondence to: J. W. S. Merkus

Key words: Renal artery stenosis – Hypertension, renal artery stenosis – Percutaneous angioplasty, renal artery stenosis

Introduction

Hypertension is a common complication after renal transplantation. Pre-existing essential hypertension, the presence of host kidneys, original renal disease, the occurrence of rejection, and the use of cyclosporin as an immunosuppressive drug are all risk factors for hypertension [3, 8, 17]. Renal artery stenosis is another obvious cause of hypertension after renal transplantion. The reported incidence of renal artery stenosis after renal transplantation varies from 0.6% to 16% [4, 10, 13]. Due to the fact that angiographies are not routinely performed in most centers, the incidence of stenosis of the allograft artery may be underestimated. Management of this cause of hypertension consists of either pharmacological treatment or correction of the stenosis. Correction may be attempted by percutaneous transluminal angioplasty (PTA) [1, 12] or by surgical repair [15, 16]. The choice between these three treatment modalities is often difficult since data on the early and long-term results of these treatments are limited. We therefore analyzed the results of the management of stenoses of the allograft artery after renal transplantation that were diagnosed with angiography in our center.

Patients and methods

Patients with an angiographically diagnosed allograft artery stenosis were identified by a computer search of all renal transplantations performed in our center between 1968 and 1991. The hospital charts of these patients were manually searched for the reason for angiography, the severity of the stenosis, the therapy initiated after diagnosis, and the result of that therapy. Moreover, clinical data on patients shortly before angiography and 3 months after the diagnosis or intervention, as well as at the end of the observation period, were registered. Data from 3 months after diagnosis of the artery stenosis or after the intervention were analyzed with regard to several known

risk factors for hypertension, such as the presence of host kidneys, the original disease, the number of previous rejections, and the steroid dose.

Transplantation was performed using standard surgical techniques with end-to-side anastomosis of the renal allograft artery to the external iliac artery. When a stenosis was suspected, angiography was performed by contrast injection through a catheter introduced into the contralateral femoral artery. When necessary, oblique views were used to identify stenoses. PTA or surgery was undertaken when a significant stenosis (> 75% narrowing of the arterial lumen) was found that was considered to be the main cause of deterioration of renal function or of hypertension. The decision to perform a correction and the way in which to do so was usually the result of a discussion between the radiologist, the vascular surgeon, and the nephrologist. PTA was only performed after 1981 in cases of a short stenosis, distal from the anastomotic site. PTA dilatation was performed with a balloon equal in size to the renal artery in a nonstenotic segment of the artery. After the procedure, angiographic inspection was done to establish the immediate result of angioplasty. Surgical correction was performed using a lateral retroperitoneal approach of the renal artery and the iliac artery. Arterial reconstruction was performed by resection of the stenotic segment and end-to-side reimplantation of the renal allograft artery in the iliac artery, using interposition grafting, if necessary, or by vein patch angioplasty of the stenotic arterial segment, or by construction of a bypass graft between the iliac artery and the renal artery distal to the stenotic segment, without occlusion of the stenotic renal artery.

All values are expressed as means ± SD. Statistical analysis was done with the Wilcoxon test or Student's t-test for paired observations, when appropriate.

Results

During the observation period, 1165 renal transplantations were performed in our center. Among those, 65 cases of renal artery stenosis were diagnosed with angiography, thus rendering the prevalence of identified renal transplant artery stenosis in our center approximately 5.5%. In all patients the reason for angiography was persistent hypertension; a bruit over the allograft (50%) and a rise in serum creatinine level (76%) were additional reasons. The mean age of the patients (37 males, 28 females) was 45.3 years. Six of the 65 stenoses (9%) were found in the allograft artery of a kidney from a living related donor, while 101 of the 1165 (9%) transplantations were performed with grafts from living related donors. In 18 patients with a renal artery stenosis, the native kidneys had been removed before transplantation. There were no differences in blood pressure or number of antihypertensive drugs at the time of angiography between patients with and without host kidneys. Immunosuppression was achieved with azathioprine and prednisone in all patients at the time of angiography.

In two patients the angiography was made shortly after transplantation and showed a very severe stenosis and almost no perfusion of the allograft. During subsequent transplantectomy, complete thrombosis of the renal artery was, in fact, found and the allografts were removed. Two other patients died in the week after angiography, both of pneumonia. Thus, 61 patients remained for evaluation of the therapy for stenosis. Of these 61 patients, 6 underwent angiography during their first hospital admission because their renal function did not reach a satisfactory level and hypertension was present. In the other 55 patients, the diagnosis of renal artery stenosis was made during a subsequent hospital admission 1 month to 12 years (median 5 months) after the transplantation. In these 55 patients, the systolic and diastolic blood pressures increased from 149 ± 18 mm Hg and 90 ± 12 mm Hg at the time of the first discharge after transplantation to 173 ± 30 mm Hg ($P < 0.01$) and 104 ± 18 mm Hg ($P < 0.01$) at the time of angiography. During this period, their serum creatinine level rose from 137 ± 67 μmol/l at discharge to 213 ± 146 μmol/l ($P < 0.05$) at the time just prior to angiography.

In 24 of the 61 patients with a renal artery stenosis, correction of the stenosis was not attempted because the stenosis was assessed as not being severe enough to jeopardize renal allograft perfusion ($n = 11$) or because there were multiple stenoses ($n = 9$) that were considered unsuitable for correction. In 4 patients, even though there was a significant stenosis, a correction was not attempted because the anatomical situation was judged unsuitable for any correctional therapy. The clinical data at the time of angiography and 3 months thereafter of the 24 patients in whom no correction was performed and in whom hypertension was treated pharmacologically are shown in Table 1. Diastolic blood pressures decreased significantly 3 months after angiography, while there was an increase in the number of antihypertensive drugs prescribed. There were no differences in the changes in blood pressures or in the number of antihypertensive drugs between patients with moderate, severe, and multiple stenoses on angiography.

An analysis of risk factors for hypertension showed a difference in the number of antihypertensive drugs after 3 months in patients with ($n = 15$) and without ($n = 9$) host kidneys (2.67 ± 0.78 vs 1.75 ± 1.17; $P < 0.05$). No significant influence of the other known risk factors for the occurrence of hypertension could be found in this relatively small group of patients.

At the time of this analysis (median follow-up 116 months; range 2–219 months), five grafts had been

Table 1. Results of medical management of transplant renal artery stenosis ($n = 24$)

	Angiography		P-value
	Before	After 3 months	
Systolic BP (mm Hg)	177 ± 34	160 ± 30	NS
Diastolic BP (mm Hg)	109 ± 22	96 ± 12	< 0.01
Serum creatinine (μmol/l)	173 ± 77	167 ± 94	NS
Proteinuria (g/l)	0.6 ± 1.1	0.6 ± 1.2	NS
Antihypertensive drugs (number)	1.4 ± 1.4	2.2 ± 1.1	< 0.01

Table 2. Results of correctional intervention for renal artery stenosis ($n = 22$)

	Correction		P-value
	Before	After 3 months	
Systolic BP (mm Hg)	171 ± 31	145 ± 27	< 0.01
Diastolic BP (mm Hg)	103 ± 15	89 ± 14	< 0.01
Serum creatinine (μmol/l)	194 ± 122	144 ± 93	< 0.01
Proteinuria (g/l)	0.9 ± 2.9	1.0 ± 2.4	NS
Antihypertensive drugs (number)	2.1 ± 1.0	1.5 ± 1.0	< 0.01

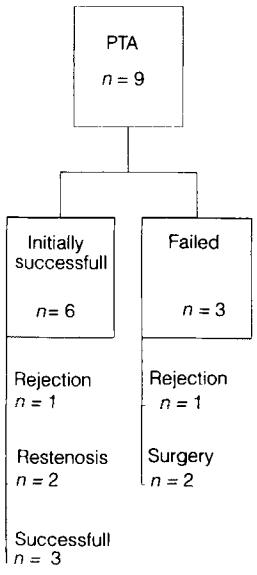

Fig. 1. Overview of the outcome of percutaneous transluminal angioplasty (PTA) of renal allograft artery stenosis. The *bottom line* shows all eventually successful corrections. Note that in two patients an unsuccessful PTA procedure was followed by surgical intervention

lost due to chronic rejection between 6 months and 3 years after diagnosis of the stenosis. One graft with severe artery stenosis was lost due to the fact that the stenosis could not be corrected. The remaining 18 patients with functioning grafts at the time of the last follow-up had systolic and diastolic blood pressures of 155 ± 22 mm Hg and 92 ± 8 mm Hg, respectively. This was still significantly lower ($P < 0.01$ and $P < 0.01$) than blood pressures before angiography. The number of antihypertensive drugs had also decreased to 1.74 ± 1.28, which was no longer significantly higher than the number administered before angiography.

Figure 1 schematically shows the outcome of percutaneous transluminal angioplasty (PTA). A PTA was performed in nine patients. In six patients this procedure was initially successful; however, in two of them, restenosis was diagnosed 4 months and 1 year later. In another of these six patients, streptokinase was successfully used to resolve PTA-induced thrombosis of the dilated artery. Eventually, this graft was lost, 3 months after PTA, due to rejection, as was another graft in which PTA did not correct the stenosis; no further therapy was initiated because of concomitant rejection. In two other cases, surgical intervention was necessary after initial PTA. Immediate surgical intervention for arterial thrombosis after PTA was necessary in one patient. In another, the PTA procedure did not correct the stenosis, as judged by angiographic inspection, and surgical correction was done 5 days later, due to persistent hypertension.

Surgical intervention was initially planned in 28 cases; as mentioned earlier, it was also performed in two patients after unsuccessful PTA. Figure 2 shows the outcome of surgical correction in these 30 patients. In one of these patients a correction was not actually performed since, during surgery, it appeared that the arteries of the patient were too brittle for reconstruction. In another patient the graft (originating from a 3-year-old donor) was removed because it had grown around the arterial anastomosis, making correction impossible. Thus, a total of 28 surgical corrections were performed. In ten patients an arterial reimplantation was performed after resection of the stenotic segment. In four of these ten cases, interposition grafting was necessary. Ten corrections (including the two performed after PTA) were performed with vein patch angioplasty of the stenotic segment, and in eight patients a part of the greater saphenous vein was used as a bypass graft.

Of the ten arterial reimplantations, eight operations were successful. In one patient a mild restenosis occurred in the end-to-end anastomosis of the interposition graft. One graft was lost due to thrombosis shortly after the operation. Of the ten patients (eight initially planned and two after unsuccessful PTA) in whom a vein patch angioplasty was performed, two patients lost their grafts as an immediate result of the operation, both due to thrombosis. In one, this occurred after reintervention for postoperative bleeding and interposition of a part of the greater saphenous vein. One graft was eventually lost due to concomitant rejection. In eight patients a part of the greater saphenous vein was used as a bypass graft. In three of these patients, a reintervention for postoperative complications was necessary, two times because of postoperative bleeding and once because of uncontrollable hypertension that improved after revision of the bypass. One of these patients lost the graft despite reintervention; two others lost their grafts due to thrombosis of the bypass. Restenosis in the venous bypass graft was diagnosed in one patient 1 month after the operation.

In all, a successful correction of the arterial stenosis was performed on 22 patients, either by PTA, PTA followed by surgical correction, or surgical correction alone (Figs. 1, 2). Blood pressure and antihypertensive medication, as well as serum creatinine levels of these patients at the time of angiography and 3 months after correction, are shown in Table 2. Systolic and diastolic blood pressure decreased significantly 3 months after successful correction of the stenosis and fewer antihypertensive drugs were necessary to control blood pressures. Renal function, as determined

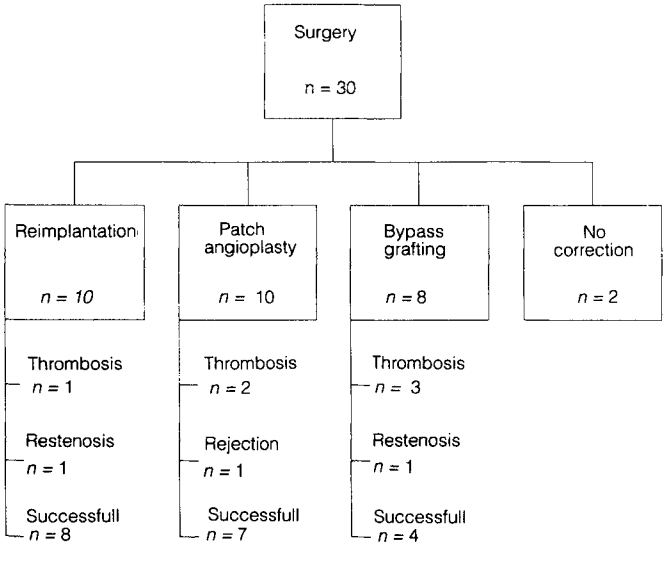

Fig. 2. Overview of the outcome of surgical correction of renal allograft artery stenosis. The *bottom line* shows all eventually successful corrections

by serum creatinine levels, also improved after correction of the renal allograft artery stenosis.

During the follow-up period (median 64 months; range 3–218 months), six grafts were lost due to rejection between 3 months and 7 years after the correction. The remaining 16 patients had systolic and diastolic blood pressures of 139 ± 22 and 88 ± 10 mm Hg, respectively, at the time of the last follow-up. The number of antihypertensive drugs decreased to 1.2 ± 1.2. All of these values are still significantly lower ($P < 0.01$) than the values before correction.

Discussion

Stenosis of a renal artery after renal transplantation can cause hypertension and a decline in renal function. Pharmacological treatment is sufficient if blood pressure can be controlled and if the stenosis does not actually endanger allograft perfusion. In this retrospective analysis, the selection of patients for correction of a stenosis or for pharmacological management of the accompanying hypertension was done on the basis of angiography and the clinical course of renal function and hypertension. The severity of the stenosis and an appraisal of the possibility for safe correction were also taken into account.

In the 24 patients in whom antihypertensive drug treatment was extended, diastolic blood pressure decreased 3 months after diagnosis of the stenosis. In only one of these patients was the graft actually lost due to the vascular complication. Four other grafts were lost due to chronic rejection that may very well have been responsible for the hypertension of their hosts [11]. In the other patients, both blood pressure and the number of antihypertensive drugs decreased with time. This phenomenon of a decrease in blood pressure with time after renal transplantation has been demonstrated before [8]. Patients with native kidneys in situ needed a higher number of antihypertensive drugs 3 months after diagnosis than those without their own kidneys. This suggests that the presence of host kidneys at least partly contributed to the hypertension of these patients [3, 8, 17]. It also supports the view that a stenosis that is diagnosed with angiography is not necessarily the cause of hypertension. A renal allograft artery stenosis may be present without causing hypertension [7, 9]. Another explanation is that some patients may have had a false-positive angiography [14] showing a stenosis, while the hypertension, which was the reason for angiography, may have been caused by the presence of host kidneys or the consequence of damage to the allograft following rejection episodes. Correction of the stenosis in those patients probably would not have improved the hypertension but only have exposed them to the risks of intervention.

In six patients PTA initially improved the stenosis; however, restenosis occurred in two of them 4 months and 1 year after PTA. Although the number of patients undergoing PTA in our study was relatively small, the results of PTA were rather disappointing. Other studies report incidences of serious complications of PTA, such as dissection and thrombosis in 7%–28% of all cases [1, 5, 12, 14]. Failure to correct the stenosis is reported to range from 19% [12] to 50% [14]. Graft loss as an immediate result of PTA is also widely reported, ranging from 0% [12] to 20% [14]. These varying results may be due to differences in the position of the stenosis. Stenoses that are located distally from the anastomosis may be more suitable for correction by PTA than those located at the anastomotic site [2, 6]. In our series patients were selected on the basis of the angiography for either PTA or surgical correction. PTA was only performed when there was a short stenosis that was not located at the anastomotic site. This never led to graft loss and six stenoses (66%) were initially improved by PTA. Restenosis and thrombosis, however, appeared as a complication rather frequently.

After resection and reimplantation, thrombosis occurred only once. Surgical correction with vein patch angioplasty twice resulted in graft loss due to thrombosis. Restenosis occurred once. In the eight patients in whom a venous bypass graft was used, postoperative bleeding or thrombosis necessitating reoperation was a frequent complication. Eventually, three of these grafts were lost to thrombosis of the graft. As in other studies, the number of complications and graft losses was relatively high in patients in whom a venous bypass graft was used [10]. Although the three surgical procedures used are not real alternatives and the local anatomical situation may necessitate bypass grafting, we suggest that this type of correction be avoided, if possible. Reimplantation, with or without interposition grafting, or vein patch angioplasty, when appropriate, seems to be the treatment of first choice in cases where either of these methods can be used.

Of the seven grafts lost after surgery, one was lost due to rejection, thus rendering the incidence of graft loss as a result of surgery itself 20% (6/30). Others have reported the incidence of graft loss after surgery as varying from 0% [14] to 20% [6]. In some of these series, no venous bypasses were used, which may partly explain our comparatively high incidence. After successful correction of a renal artery stenosis, blood pressure and the number of antihypertensive drugs necessary to control blood pressure decreased significantly. Renal function, as determined by serum creatinine levels, also improved and blood pressure decreased slightly more with time.

In conclusion, in patients with a mild to moderate stenosis of the renal allograft artery, it is possible to control blood pressure with antihypertensive drugs. Moreover, a stenosis on angiography may not always be the cause of hypertension and, thus, correctional intervention may subject some patients to complications of intervention without any chance of improving their hypertension. As in other renal transplant recipients, in patients with allograft artery stenoses that do not actually endanger renal allograft perfusion, blood pressure decreases with time after transplantation, warranting an anticipatory policy in these cases.

As we did not encounter any graft losses as an immediate result of PTA, this can be the therapy of first choice, if technically possible, when a correction is indicated. Complications, however, are not rare and surgical rescue therapy should be anticipated. After PTA patients should be carefully monitored for recurrence of the stenosis. When

PTA is not possible or does not sufficiently dilate the stenosis and surgical correction is indicated, it seems best, if possible, to perform arterial reimplantation or vein patch angioplasty rather than to bypass the stenosis with a venous bypass graft.

References

1. Carr D, Quin RO, Hamilton DNH, Briggs JD, Hunor BJR, Semple PF (1980) Transluminal dilatation of transplant renal artery stenosis. BMJ 281: 196–197
2. Chandrasoma P, Aberle AM (1986) Anastomotic line renal artery stenosis after transplantation. J Urol 135: 1159–1162
3. Curtis JJ (1986) Hypertension and kidney transplantation. Am J Kidney Dis 7: 181–196
4. Glassock RJ, Feinstein EI, Campese VM, Finck E, Silberman H, Chandrasoma P (1984) Hypertension in a renal transplant recipient. Am J Nephrol 4: 262–271
5. Greenstein SM, Verstandig A, McLean GK, Dafoe DC, Burke DR, Meranze SB, Naji A, Grossman RA, Perloff LJ, Barker CF (1987) Percutaneous transluminal angioplasty: the procedure of choice in the hypertensive renal allograft recipient with renal artery stenosis. Transplantation 43: 29–32
6. Grossman RA, Dafoe DC, Schoenfeld RB, Ring EJ, McLean GK, Oleaga JA, Freiman DB, Naji A, Perloff LJ, Barker CF (1982) Percutaneous transluminal angioplasty treatment of renal transplant artery stenosis. Transplantation 34: 339–343
7. Henrikson C, Nilson A, Thoren OKA (1975) Artery stenosis in renal transplantation. Scand J Urol Nephrol 29: 89–93
8. Huysmans FTM, Hoitsma AJ, Koene RAP (1987) Factors determining the prevalence of hypertension after renal transplantation. Nephrol Dial Transplant 2: 34–38
9. Lacombe M (1975) Arterial stenosis complicating renal allotransplantation in man. Ann Surg 181: 283–288
10. Munda R, Alexander JW, Miler S, First RM, Fidler JP (1977) Renal allograft artery stenosis. Am J Surg 134: 400–403
11. Pollini J, Guttmann RD, Beaudoin JG, Morehouse DD, Klassen J, Knaak J (1979) Late hypertension following renal allotransplantation. Clin Nephrol 11: 202–212
12. Raynaud A, Bedrossian J, Remy P, Brisset JM, Angel CY, Gaux JC (1986) Percutaneous transluminal angioplasty of renal transplant arterial stenoses. Am J Radiol 146: 853–857
13. Rijksen JFWB, Koolen MI, Walaszewski JE, Terpstra JL, Vink M (1982) Vascular complications in 400 consecutive renal allotransplants. J Cardiovasc Surg 23: 91–98
14. Roberts JP, Ascher NL, Fryd DS, Hunter DW, Dunn DL, Payne WD, Sutherland DER, Dastaneda-Zuniga W, Najarian JS (1989) Transplant renal artery stenosis. Transplantation 48: 580–583
15. Smith RB, Cosimi AB, Lordon R (1976) Diagnosis and management of arterial stenosis causing hypertension after successful renal transplantation. J Urol 115: 639–644
16. Tilney NL, Rocha A, Strom TB, Kirkman RL (1984) Renal artery stenosis in transplant patients. Ann Surg 199: 454–460
17. Waltzer WC, Turner S, Frohnert P, Rapaport FT (1986) Etiology and pathogenesis of hypertension following renal transplantation. Nephron 42: 102–109