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Treatment of renal allograft with clinical intolerance: percutaneous renal artery embolization *versus* graft nephrectomy

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ABSTRACT

Background: The aim of this study was to assess the effectiveness of graft embolization as an alternative treatment to graft nephrectomy in patients with graft intolerance syndrome

Patients and Methods: We considered 21 cases of clinical intolerance between January 1990 and January 2001. Seven were treated by graft embolization and 14 by graft removal. Variables considered were age, sex, renal aetiology, time with functioning renal graft, type of dialysis, aetiology of graft loss, time of hospital stay, mortality and biochemical parameters six months after the procedure (albumin, haemoglobin, rate of resistance to erythropoietin (RRE), and cholesterol). We compared patients treated only by embolization versus those treated only by graft nephrectomy.

Results: A patient required nephrectomy after the embolization, which was considered as failure of the embolization technique (14%). Duration of graft function was 49.5±34.1 months for embolization *versus* 57.5±27.8 months for nephrectomy. Latency time between graft failure and embolization was 4.8±2.7 months and 4.4±2.1 months between graft failure and nephrectomy. The mean time of hospital stay was 6.33±5.5 days for embolization versus 12.7±5.8 days for nephrectomy. The accumulated days of hospital stay during the year following the technique were 4.7±3.6 days for embolization versus 12.7±5.8 days for nephrectomy. Serum albumin 6 months after was 3.7±0.37 for embolization and 3.1±0.25 for nephrectomy; cholesterol was 193±20 for embolization and 158±26.6 for nephrectomy and RRE was 7.5±5.2 *versus* 13.8±7.5.

Conclusions: The results suggest that graft embolization is a safer and more effective technique for treating renal graft intolerance than graft nephrectomy and that graft embolization should be the first treatment option in the case of graft failure more than six months after the transplant.

Key-Words:
Embolization; graft intolerance; nephrectomy; renal transplant.

INTRODUCTION

Patients returning to dialysis after failure of their kidney transplant can suffer from high morbidity and mortality rates. It is common practice to keep failed renal graft in place, decrease the dose of immunosuppressive drugs and completely withdraw them after 6 months[1]. Graft intolerance syndrome (GIS) can

occur in some failed renal grafts when the immunological treatment is completely withdrawn. These patients may develop fever, haematuria and pain in the graft zone[1,2].

Transplantectomy is the conventional technique for managing symptomatic failed renal allografts but it is associated with high morbidity and mortality rates[3]. While renal vascular embolization is now suggested as a possible alternative treatment, it is not fully accepted[4] and there are no reports comparing both techniques.

This study consequently analyses graft embolization in failed renal grafts that were not tolerated *versus* transplantectomy after a 6 month period in order to compare both.

PATIENTS AND METHODS

Patient population

We performed a retrospective, observational cohort study of 60 transplant kidneys in 59 patients who returned to dialysis therapy between January 1990 and January 2001.

We excluded 18 cases where graft failed in the first six months and 21 cases that showed clinical tolerance and the renal graft was not removed.

The diagnosis of GIS was based on clinical evidence in the absence of concomitant infections such as fever, haematuria, malaise, pain or tenderness in the graft zone. Routine screening for antiviral antibodies, blood and urine cultures and chest radiography were performed in all patients to exclude infection. In cases with an unclear clinical diagnosis, imaging procedures (doppler ultrasound or arteriography) were used to verify the persistence of arterial flow in the nonfunctioning graft. Steroids were used to successfully treat all cases of clinical manifestations of GIS.

Twenty one cases in 21 patients with clinical intolerance were treated by percutaneous renal artery embolization (n=7) and the others by graft removal (n=14).

Demographic and laboratory data were collected on all patients and the following variables were considered: age, gender, renal aetiology, time with functioning renal graft, type of dialysis, aetiology of graft loss, time of hospital stay. In order to evaluate a possible inflammatory state after the techniques had been performed, mortality and morbidity data and biochemical parameters (albumin, haemoglobin, rate of resistance to erythropoietin (RRE) and cholesterol) were registered six months after the technical procedure. The RRE was obtained by dividing the total weekly erythropoietin dose first by the patient's body weight in kilograms and then by the patient's haemoglobin level in g/dl and was expressed as units/wk per Kg per g/dl[1].

We compared patients treated by embolization only *versus* those treated by graft nephrectomy only.

Statistical analysis

Data are mean ± SD. Statistical analysis employed the chi square and Mann-Whitney U test. A p-value ‹0.05 was considered to be statistically significant.

RESULTS

The incidence of GIS after immunosuppresion withdrawal was 50%(21/42).

Twenty one patients with GIS after 6 months of return to dialysis were studied. Seven patients were treated by renal embolization and 14 by transplantectomy. The mean age in the transplantectomy group

Table I

Demographic characteristics

	Transplantectomy (n=14)	Embolization (n=7)
Age (years)	54 ±13.8	48±12
Gender (male/female)	8/6	2/5
Haemodialysis/Peritoneal Dialysis	11/3*	2/5*
Aetiology of renal failure	GN(52%), DN(20%), CTN(17%), unknown(11%)	GN(42%), CTN(27%), DN(22%), unknown(9%)

GN – glomerulonephritis; **DN** – diabetic nephropathy; **CTN** – chronic tubulointerstitial nephropathy-
*p‹0.05

was 54±13.8 yr and in the embolization group was 48±12 yr. The original causes of end-stage kidney failure in the embolization group were chronic glomerulonephritis (42%), chronic tubulointerstitial nephropathy (CTN) (27%) diabetic nephropathy (DN) (22%) and unknown in the rest. In the transplantectomy group the causes were chronic glomerulonephritis (52%), CTN (17%), DN(20%) and unknown in the rest (table I).

One patient required nephrectomy after the embolization, which was considered as failure of the embolization technique (14%). This patient has not been included in the transplantectomy group. There were no deaths associated with any technique.

Epidemiological results are shown in table II. There was no statistical difference in duration of graft function between the two groups: 49.5±34.1 months for embolization and 57.5±27.8 months for nephrectomy. Latency time between graft failure and embolization was 4.8±2.7 months and 4.4±2.1 months between graft failure and nephrectomy.

Table II

Epidemiological results

	Transplantectomy (n=14)	Embolization (n=7)
Latency time between graft failure and the technique (months)	4.4 ±2.1	4.8±2.7
Mean time of hospital stay (days)	12.7±5.8*	6.3±5.5
Accumulated days of hospital stay during the year following the technique	12.7 ±5.8*	4.7±3.6*

*p<0.05

The mean time of hospital stay was 6.33±5.5 days for embolization *versus* 12.7±5.8 days for nephrectomy (p<0.05). The accumulated days of hospital stay during the year following the technique were 4.7±3.6 days for embolization *versus* 12.7±5.8 days for nephrectomy (p<0.05).

Laboratory data are shown in table III. Serum albumin 6 months after was 3.7±0.37 for embolization *versus* 3.1±0.25 for nephrectomy (p<0.05); cholesterol was 193±20 for embolization and 158±26.6 for nephrectomy (p<0.05) and RRE was 7.5±5.2 *versus* 13.8±7.5 (p<0.05). The other variables were similar for both groups.

Table III

Laboratory results six months after the technique

	Post Embolization (n=7)	Post Transplantectomy (n=14)
Haemoglobin	12.05±1.21	10.8±1.5
RRE	7.5 ±5.2*	11.8±6.5*
Albumin	3.7±0.37*	3.3 ±0.44*
Cholesterol	193±20*	158±26.6*

RRE — Rate of resistance to erythropoietin
*p<0.05

DISCUSSION

GSI is not uncommon although is variable: 37%[4], 86%[14], 30%[12]. The magnitude of this problem is considerable and it seems reasonable to suppose that this problem will increase worldwide as the number of transplantation increases annually. In our study it is approximately 50%.

Clinical manifestations and their reversal with steroids are often sufficient to allow for the diagnosis of graft intolerance syndrome but imaging techniques may be useful in diagnosis (doppler ultrasound, scintigraphy and more recently indium 111-labeled platelets)[4]. In our study the diagnosis of graft intolerance syndrome was based on clinical manifestations and in cases in which clinical presentation was unclear, imaging procedures (doppler ultrasound or arteriography) were used to verify the persistence of arterial flow in the nonfunctioning graft.

While nephrectomy for failed renal transplant was defended for many years[3,5,8], some clinicians argue that subsequent complications could be avoided and that early graft removal is accompanied by less morbidity and mortality. The complications of graft nephrectomy cannot be ignored, however: infection of surgical incision, haematoma, manipulation of peritoneum, sepsis, shock, exitus...[7,8]. Graft embolization has been suggested as a possible alternative with less complications and low morbility[9-13], but there is a risk of subclinical inflammation state. The duration of admission in the hospital due to nephrectomy was longer than with embolization (12.7±5.8 *vs.* 6.3±5.5 days), suggesting less per-operation morbidity. The technique was not only sure but also effective. In 86% of the cases GSI disappeared, and cor-

ticoids were completely withdrawn. Only in one case was transplantectomy necessary for recovery from graft intolerance syndrome (14%).

The accumulated days of hospital stay during the year following the technique were 4.7±3.6 days for embolization *versus* 12.7±5.8 days for nephrectomy. The causes of hospitalization in both groups were principally infections (75%) and cardiovascular events (20%)

In order to evaluate the possible subclinical inflammatory syndrome, biochemical parameters are compared and a clear increase of haemoglobin is observed as well as a decrease of RRE and increased levels of cholesterol and albumin. This means that the patients who underwent embolization present an improvement in the nutritional condition as well as the inflammatory state as opposed to the patients who underwent transplantectomy. Similar information is observed in other studies[6,9,10].

Embolization was performed more in peritoneal dialysis patients (62%) than haemodialysis patients (38%) $p<0.05$. This might be due to the physicians' choices, designed to avoid later damage peritoneal.

In conclusion, graft embolization is a simple, safe, effective and simpler technique for the treatment of nonfunctioning renal allografts and involves less morbidity than transplantectomy. Our data suggest embolization as first-line treatment for patients with symptomatic failed renal allografts after 6 months and transplantectomy for those patients in whom the embolization fails.

Conflict of interest statement. None declared.

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