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ORIGINAL ARTICLE

Renal graft intolerance syndrome in late graft failure patients: efficacy and safety of embolization as first-line treatment compared to surgical removal

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SUMMARY

Although renal graft percutaneous embolization was introduced to avoid the risk associated with graft nephrectomy, there is no universal consensus about its indications and results. In order to evaluate the efficacy of graft embolization in the treatment of graft intolerance syndrome as well as its safety compared to surgical removal with respect to complications and other morbidity measures, We performed a retrospective observational study comparing two groups of patients treated for graft intolerance syndrome: Group 1: patients who had embolization as first-line treatment and Group 2: patients directly treated by surgical removal. 72 patients were included, (32 in Group 1 and 40 in Group 2); the postintervention follow-up continued for 12 months. Patients in Group 1 are older than those in Group 2. Otherwise, the two groups are similar concerning sex, manifestations of graft intolerance syndrome, diabetes and nutritional and functional status. The overall success rate of embolization in complete resolution of graft intolerance syndrome and ultimately avoidance of surgical removal was 84.37%. The surgical removal group had more serious complications, a longer hospital stay and needed more blood transfusions. We conclude that embolization of symptomatic renal grafts has considerable efficacy with less morbidity, and no serious complications compared to the standard surgical graft removal.

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Key words

graft embolization, graft failure, graft nephrectomy, renal transplantation

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Introduction

Leaving a nonfunctioning renal graft *in situ* after returning to dialysis and stopping immunosuppressive treatment can become a frustrating problem affecting the quality of life in around 40% of patients, who present the so-called graft intolerance syndrome [1]. Graft intolerance syndrome is clinically manifested by fever, malaise, local pain, gross haematuria, and/or graft tenderness. In many of these patients, investigations show a chronic inflammation represented by elevated C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR), resulting in resistance of anaemia to erythropoietin-stimulating agents (ESA) [2]. Maintenance of immunosuppressive therapy in these patients is not advisable due to associated infectious, neoplastic and cardiovascular complications [3–6]. In addition, medical treatment by nonsteroidal anti-inflammatory drugs and even sometimes the maintenance of low-dose immunosuppressive therapy is of limited long-term efficacy in symptoms resolution and reduction of chronic inflammation [3,7].

Surgical graft nephrectomy might be considered as the only or best treatment for early graft failure (especially in the first 3 months after transplantation) or in the exceptional cases of graft malignancy or localized infection. In late graft failure, the procedure is usually performed as treatment of acute rejection or graft intolerance syndrome, and it was reported to be responsible for high morbidity (17-60%) and mortality (0.7-14%) rates [8-17], because it is often performed in patients who are already on dialysis and suffering from malnutrition, anaemia and inflammation [18]. This observation made it necessary to look for other less invasive options like embolization of the nonfunctioning renal graft, firstly introduced in late 1980s by Lorenzo et al. [19]. Although its efficacy in the resolution of the graft intolerance syndrome has been demonstrated to be between 60% and 100% [1,19-30] and its morbidity to be very low [1,19-30], graft embolization has not gained widespread acceptance and there is no clear consensus as to its indications or results compared to surgery.

We hypothesized that percutaneous embolization would avoid the high risk associated with surgical removal in most late graft failure patients presenting a graft intolerance syndrome. To our knowledge, this is the first study that evaluates the efficacy of embolization in the resolution of graft intolerance syndrome and directly compares the two techniques in terms of complications and other associated morbidity and mortality events in this particular group of patients. In addition, as the nonfunctioning graft may play a role in adsorption of antibodies to the mismatched HLA donor antigens and as graft nephrectomy was associated with increased sensitization [31,32], we hypothesized that percutaneous embolization can reduce the vulnerability de novo sensitization associated with surgical to removal.

Patients and methods

Patient selection and data collection

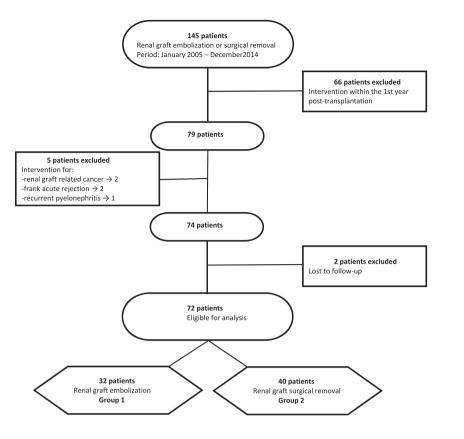
This is a single-centre retrospective observational study evaluating the difference between two groups of patients treated for renal graft intolerance syndrome by either percutaneous graft embolization as first-line treatment (Group 1) or directly by surgical graft removal (Group 2). The period of inclusion was from January 2005 until December 2014. The data were collected from our renal transplant registry with prospective database collection and from patients' medical records, papers or electronics. We have included only those patients treated after the first transplant year. Patients lost for follow-up after intervention (dialysed outside France) were the excluded. We also excluded all patients with a graftrelated condition other than graft intolerance syndrome which might have contributed to the therapeutic decision, like those with a frank acute rejection (high grade fever with remarkable swelling of the graft and/or pain needing more than weak opioids), renal graft-related cancer, recurrent pyelonephritis or pyonephrosis of the renal graft, or in whom a future renal transplantation was planned after surgical removal of one of the two iliac fossa nonfunctioning renal grafts (Fig. 1).

Patient outcome

We compared the two groups with regard to patient and renal transplantation characteristics, the duration of renal graft function and then the time between the return into dialysis and the intervention. The two groups were also compared with respect to manifestations of graft intolerance syndrome.

The main objective was to examine the efficacy of percutaneous embolization as first-line treatment in the complete resolution of graft intolerance syndrome (defined as no need for any additional medical or surgical intervention after embolization). In addition, the two groups were compared in terms of intervention-related morbidity and mortality during the 12-month followup. These complications were classified in term of severity into five grades based on Clavien–Dindo classification [33].

The higher the grade, the more severe is the complication. Grade 1 includes wound infection opened at the bed side or any complication without the need for pharmacological treatment, or surgical, endoscopic and radiological intervention. On the other hand, grade 5 means death of the patient. We aimed to evaluate the difference between the two groups concerning the incidence of serious complications, the need for blood transfusion, the duration of hospital stay, the need for readmission due to intervention-related complications and the rate of *de novo* sensitization after the intervention.



Graft embolization

All renal graft embolizations were performed through a percutaneous femoral artery approach by the insertion of microspheres of polyvinyl alcohol followed by insertion of stainless steel in the renal artery and its branches when necessary. To avoid pain, patients were given IV hydrocortisone (100 mg \times 4/day for 2–3 days) and analgesics.

Anti-HLA antibodies

The screening for the presence and identification of anti-HLA antibodies was successively performed by variable techniques including lymphocyte cytotoxicity (LCT) during the whole period, ELISA until 2009 and Luminex single antigen microbeads thereafter. We used the panel reactive antibody (PRA) percentage on LCT to compare the two groups, and we considered the appearance of *de novo* anti-HLA antibodies or an increase in PRA of >20% as a marker of sensitization.

Ethics

All patients gave written informed consent for their medical information to be collected in our Renal Transplant Registry, and we have approval of institutional review board to use these data for scientific purposes (Cohorte DIMTP, Ref: 13 334).

Figure 1 Patient flow chart.

Statistical analysis

Univariate analysis was performed for each variable. Continuous parametric data are presented as means \pm standard deviation (SD) or median [IR, interquartile range], and categorical variables as numbers and percentages. We used a chi-square test or Fisher exact test for categorical variables and Student's t-test or Mann-Whitney for quantitative variables, according to the normality of the distribution, assessed with the Shapiro-Wilk test. A multivariate analysis was conducted using a logistic regression model to determine independent risk factors of postintervention complications, in which we included all variables associated with a P value below 0.20 in the univariate analysis. Then, a stepwise procedure allowed obtaining the final multivariate model. Statistical tests were performed with R 3.2.1 software. Significance was obtained at a *P* value ≤ 0.05 .

Results

Out of a total 145 patients who had one of these two interventions as first-line treatment for nonfunctioning renal graft in the period between January 2005 and December 2014, only 72 patients met all the inclusion and exclusion criteria (32 patients in the embolization arm and 40 patients in the surgical removal arm). 66 patients, out of whom three had embolization, were not included in the study for having the intervention performed less than 1 year after their renal transplantation. 7 patients were excluded for other reasons: two patients in whom the surgical intervention was performed for a renal graft-related cancer (renal cell carcinoma in one patient and urothelial carcinoma in the other patient), three patients in whom the clinical presentation was primarily either frank acute rejection (two patients) or recurrent graft pyelonephritis (one patient) and two patients lost to follow-up (Fig. 1). All included patients were followed up for 12 months after the intervention.

Table 1 shows the patients characteristics. Group 1 patients were older than Group 2 (55.16 \pm 12.63 vs. 46.38 \pm 18.06 years, P = 0.0340). There were no significant differences between the two groups regarding sex, prevalence of diabetes, functional status, nutrition markers or the duration of renal graft function (93.12 \pm 81.30 vs. 77.73 \pm 61.41 months P = 0.5040). In all patients, graft failure was reported at more than 1 year after transplantation. Examining the time interval between the return to dialysis and the intervention, we found no statistically significant difference between the two groups (430.97 \pm 549.24 vs. 370.67 \pm 571.55 days; P = 0.1910).

Clinical manifestations of graft intolerance syndrome were not statistically different between the two groups as illustrated in Table 2. Localized pain in the area of renal graft and fever are the two most frequent symptoms.

The overall success rate of embolization in complete resolution of graft intolerance syndrome was 84.37% (27 of 32 patients). Only five patients needed subsequent surgical graft removal, three within the first 6 weeks due to persistence of clinical symptoms, one after 5 months and one after 10 months due to recurrence of graft intolerance syndrome. This was complicated by wound infection in four patients (80%), of whom one had an abscess drained surgically under anaesthesia. Otherwise, there were no other reported complications, and none of these patients needed a postoperative blood transfusion.

Table 3a,b shows the treatment-associated morbidity and mortality. Two patients (6.25%) in the embolization group had complications compared to 14 patients (35%) in the surgical removal group: the difference is statistically significant (P = 0.0035). More importantly, the complications in the embolization group were exclusively grade 1, whereas the majority of complications in the surgical removal group were of more serious grade based on Clavien–Dindo classification: five patients (12.5%) had grade 2, five patients (12.5%) had grade 3b, and one patient (2.5%) had grade 4. In other words, no complication of grade 2 or more was observed in Group 1; in contrast, 11 patients (27.5%) in Group 2 had a complication of grade 2 or more. This is a statistically significant difference between the two groups (P = 0.0012). For complication occurrence, a logistic regression model was fitted with a stepwise procedure; only the group appears as an independent associated variable [OR = 8.08 (1.67; 38.90), P = 0.009] (Table S1).

Almost all complications occurred within the first 7 postintervention days, and no intervention-related complication was reported after month 3 during the 12-month follow-up. A significant (defined as ≥ 2 g/dl) drop in haemoglobin postoperatively was reported in eight patients in the surgical removal group and in none of the embolization group (P = 0.0073). Similarly, nine patients (22.50%) in the surgical group versus no patient in the embolization group needed a blood transfusion. Again, this difference is statistically significant (P = 0.0041).

The analysis of hospital stay demonstrates a statistically shorter hospital stay in Group 1 compared to Group 2 $(3.22 \pm 1.64 \text{ vs. } 8.37 \pm 7.65 \text{ days}; P = 0.0001)$. In addition, only two patients (6.25%) in the embolization group had a hospital stay of seven or more days compared to 16 (40%) in the surgical removal group (P = 0.0010). Although no patient was readmitted due to intervention-related complication in the embolization group, two patients in the surgical removal group needed re-admission (although this difference was not statistically significant). Table 4 shows the details of all complications reported in these patients.

Concerning the rate of sensitization, as the majority of patients were already sensitized before the intervention (26 of 40 patients (65%) in the surgical removal group and 22 of 32 (68.75%) in the embolization group; P = 0.6315), we were not able to show any significant difference between both groups. Four versus two patients developed *de novo* sensitization and two versus three an increase of >20% in PRA in the graft nephrectomy versus embolization groups, respectively.

Discussion

Our study clearly shows that graft embolization results in complete resolution of symptoms in >80% of cases

| | Group 1 Embolization of graft (N = 32) | Group 2 Surgical nephrectomy of graft (N = 40) | P value |
|---|---|---|---------|
| Sex: n (%) | | | |
| Male | 18 (56.25) | 27 (67.50) | 0.3272 |
| Female | 14 (43.75) | 13 (32.50) | |
| Age (years) | | | |
| Mean \pm SD | 55.16 ± 12.63 | 46.38 ± 18.06 | 0.0340 |
| Median [IR] | 58 [49; 65] | 49.5 [31; 61.25] | |
| Duration of graft function (months) | | | |
| Mean \pm SD | 93.12 ± 81.30 | 77.73 ± 61.41 | 0.5040 |
| Median [IR] | 74 [38.75; 100.75] | 62.5 [32.75; 109.25] | |
| Time between return to dialysis and | intervention (days) | | |
| Mean \pm SD | 430.97 ± 549.24 | 370.67 ± 571.55 | 0.1910 |
| Median [IR] | 279 [143; 415.75] | 218 [116.25; 338.25] | |
| Time between transplantation and ir | ntervention (months) | | |
| Mean \pm SD | 107.22 ± 88.38 | 89.88 ± 67.87 | 0.3963 |
| Median [IR] | 84.5 [53.75; 116.5] | 72.5 [43; 115] | |
| Albumin (g/l) | | | |
| Mean \pm SD | 33.66 ± 5.56 | 35.38 ± 5.53 | 0.1507 |
| Median [IR] | 32.5 [30; 38.25] | 35 [33,38] | |
| Albumin (g/l), subgroups: n (%) | | | |
| <30 | 7 (21.87) | 5 (12.50) | 0.349 |
| ≥30 | 25 (78.12) | 35 (87.50) | |
| BMI (kg/m ²) | | | |
| Mean \pm SD | 23.37 ± 4.24 | 21.66 ± 2.87 | 0.0599 |
| Median [IR] | 21.95 [20.6; 26.47] | 20.81 [19.46; 22.49] | |
| BMI (kg/m ²), subgroups: <i>n</i> (%) | | | |
| <18.5 | 2 (6.25) | 1 (2.50) | 0.581 |
| 18.5–30 | 30 (93.75) | 39 (97.50) | |
| ASA risk score: <i>n</i> (%) | | | |
| 2 | 7 (21.87) | 11 (27.50) | 0.784 |
| 3 | 25 (78.12) | 29 (72.25) | |
| Diabetes mellitus: n (%) | | | |
| No | 27 (84.37) | 35 (87.50) | 0.877 |
| Yes, before renal transplantation | 2 (6.25) | 3 (7.50) | |
| Yes, after renal transplantation | 3 (9.37) | 2 (5.00) | |
| Haemoglobin (g/dl) | | | |
| Mean \pm SD | 10.58 ± 1.51 | 10.55 ± 1.52 | 0.8471 |
| Median [IR] | 10.7 [9.5; 12.03] | 10.25 [9.93; 11.5] | |
| Period of the intervention: n (%) | | | |
| <2010 | 13 (40.62) | 19 (47.50) | 0.73 |
| ≥2010 | 19 (59.37) | 21 (52.50) | |

Table 1. Patient demographics at the time of intervention (Statistically significant differences are in bold).

BMI, body mass index; ASA, American Society of Anesthesiologists; SD, standard deviation; IR, interquartile range.

and that this procedure is associated with significantly less complications than surgical graft removal in patients with graft intolerance syndrome. In fact, despite including older patients, Group 1 had significantly less complications, shorter hospital stay and no need for blood transfusion compared to Group 2. Moreover, in the multivariate analysis, the Group was the only significant factor associated with complication occurrence.

Loss of renal allograft function challenges the transplant physician with three important questions: time of return to dialysis, cessation of immunosuppression and indication of transplant nephrectomy [34]. Usually, graft nephrectomy is indicated in early failure [8– 10,13,16,35–38], whereas the nonfunctioning grafts are usually left *in situ* when failure occurs after the first year. In recent years, some authors have questioned this strategy, as a registry analysis showed that survival was longer in dialysis patients who had surgical graft nephrectomy after graft loss versus those who retained their graft [16].

| | Group 1 Embolization of graft ($N = 32$) | Group 2 Surgical nephrectomy of graft (N = 40) | <i>P</i> value |
|--|---|---|----------------|
| Fever: n (%) | 20 (62.50) | 18 (45.00) | 0.1394 |
| Localized pain on area of graft: n (%) | 28 (87.50) | 39 (97.50) | 0.3166 |
| Graft tenderness: n (%) | 7 (21.87) | 15 (37.50) | 0.1527 |
| Macroscopic haematuria: n (%) | 16 (50.00) | 14 (35.00) | 0.1995 |
| CRP before intervention (mg/l) | | | |
| Mean \pm SD | 57.3 ± 41.45 | 50.6 ± 45.74 | 0.2816 |
| Median [IR] | 43 [33.75;70.5] | 37.55 [18.9;68.45] | |
| CRP before intervention (mg/l), subgrou | ps: n (%) | | |
| ≤10 | 3 (9.37) | 6 (15.00) | 0.4673 |
| >10 and <40 | 9 (28.12) | 16 (40.00) | |
| ≥40 and ≤100 | 15 (46.87) | 12 (30.00) | |
| >10 | 5 (15.62) | 6 (15.00) | |
| WBC count before intervention: n (%) | | | |
| >11.0 and <16.0 × 10 ⁹ /l | 5 (15.62%) | 3 (7.50) | 0.4527 |
| >16.0 × 10 ⁹ /l | 0 (0.00) | 0 (0.00) | |

Table 2. Graft intolerance syndrome: manifestations of the disease.

One of the main indications for surgical graft removal is graft intolerance syndrome. Due to increased infectious and cardiovascular risks associated with continuing immunosuppressive therapy [3,4], the usual practice in our hospital is to minimize the maintenance double or triple therapy dosing in the predialysis period, to stop antiproliferative agents as early as patients return to dialysis in order to avoid anaemia and/or leucopenia and to maintain calcineurin inhibitors (CNI) for 3-6 months. In patients receiving lowdose steroids, progressive withdrawal is undertaken over 3-6 months. Nevertheless, after stopping or even under low-dose immunosuppressive therapy, some patients demonstrate symptoms of graft intolerance syndrome. Although surgical nephrectomy has been the standard treatment of such a problem, its high associated risk encouraged us to try the less invasive percutaneous embolization. Our literature review found very few comparative studies, and most studies are small number, nonrandomized series, including both early and late failure patients.

In our study, we aimed to have a direct comparison between allograft embolization and surgical removal in terms of complications and other associated morbidity and mortality. We included only those interventions performed at more than 1 year after transplantation. As mentioned above, one of the reasons for our selection is that surgical graft nephrectomy might theoretically be considered as the only or the best treatment for early graft failure especially in the first 3 months after transplantation. Previous studies have shown that the earlier the graft loses its function, the greater the likelihood of its surgical removal [8-10,13,16,35-38]. Secondly, the morbidity and mortality profile is more hazardous when surgical removal is performed in patients with late graft failure who often suffer from chronic inflammation, anaemia and malnutrition [3,4,8]. We therefore considered that late graft failure patients might be the best candidates for percutaneous embolization to avoid the high risk associated with surgical removal. Even when intervention is performed later than 1 year after transplantation, we have chosen only those patients in whom percutaneous embolization might be a valid option, thus excluding patients with overt acute graft rejection, cancer or infection.

However, this study has several limitations. It is a retrospective, single-centre study which may introduce several biases including a selection bias due to lack of randomization. This would explain why Group 1 patients are older than group 2. Nevertheless, in our study as in other previous studies, we clearly showed that there were no serious intervention-related complications reported with percutaneous embolization compared with surgical removal after a follow-up of at least 12 months. Apart from the expected self-limited postembolization syndrome (fever and/or local pain for 2–3 days) observed in many patients, a mild puncture site haematoma, although not frequently observed, is the main complication of this procedure. Similar results

| | Group 1 Embolization of graft (N = 32) | Group 2 Surgical nephrectomy of graft ($N = 40$) | <i>P</i> value |
|---|--|--|----------------|
| (a) | | | |
| Complications: n (%) | | | |
| All complications | 2 (06.25) | 14 (35.00) | 0.0035 |
| Clavien–Dindo classification | | | 0.0064 |
| Grade 1 | 2 (06.25) | 3 (7.50) | |
| Grade 2 | 0 (0.00) | 5 (12.50) | |
| Grade 3 | - () | | |
| За | 0 (0.00) | 0 (0.00) | |
| 3b | 0 (0.00) | 5 (12.50) | |
| Grade 4 | 0 (0.00) | 1 (2.50) | |
| Grade 5 | 0 (0.00) | 0 (0.00) | 0.0040 |
| Grade 2 and more | 0 (0.00) | 11 (27.50) | 0.0012 |
| Time of complications | 1 (50) | | 0.25 |
| Within first 7 days after intervention | 1 (50) | 12 (85.71) | 0.35 |
| After 7 days | 1 (50) | 2 (14.29) | |
| (b) $(1)^2 = \alpha drop in part op L(b) + \alpha (0/2)$ | 0 (0.00) | 8 (20.00) | 0.0073 |
| ≥ 2 g drop in post-op Hb: n (%) Post-op blood transfusion | 0 (0.00) | 8 (20.00) | 0.0075 |
| Need for post-op transfusion: n (%) | 0 (0.00) | 9 (22.50) | 0.0041 |
| Number of units of packed Red | 0 (0.00) | 3(22.50) 3.11 + 2.09 | 0.0041 |
| blood cells needed: mean \pm SD | — | 5.11 ± 2.09 | — |
| Hospital stay | | | |
| Number of days: mean \pm SD | 3.22 ± 1.64 | 8.37 ± 7.65 | 0.0001 |
| \geq 7 days: n (%) | 2 (6.25) | 16 (40.00) | 0.0010 |
| Need for readmission due to | 0 (0.00) | 2 (5.00) | 0.9999 |
| intervention-related complication: <i>n</i> (%) | 0 (0.00) | _ (0.00) | 0.0000 |
| Patients already sensitized | 22 (68.75) | 26 (65.00) | 0.6315 |
| before intervention: n (%) | | | |
| De novo sensitization after | 2 (6.25) | 4 (10.00) | 0.2865 |
| intervention: n (%) | | · · / | |
| Patients with an increase in | 3 (9.37) | 2 (5.00) | 0.3246 |
| PRA >20%: n (%) | | | |

Table 3. (a) Intervention-related complications. (b) Other intervention-related morbidity events (Statistically significant differences are in bold).

PRA, panel reactive antibody.

were reported in previous studies [1,19–30]. Other very rare previously reported complications include emphysematous pyelonephritis, pseudoaneurysm, and graft and groin abscesses [19,30,39,40].

Surgical graft nephrectomy was associated with a morbidity rate of 35% (14 patients) that is comparable to previous studies [8–17]; more importantly, most of the complications were of grade 2 or higher based on Clavien–Dindo classification, whereas no death was observed in our series. Our study shows also a significantly shorter hospital stay and a higher number of patients discharged from the hospital at less than 7 days postoperatively in the embolization group. The previously reported mortality rate associated with surgical graft removal in all patients who return to dialysis is

between 7% and 14% [8–17]. Almost a quarter of patients in the surgical removal group needed a blood transfusion postoperatively compared to none of the patients in the embolization group. This significant difference would furthermore demonstrate the risk associated with surgical removal.

In addition, postintervention *de novo* sensitization or the increase in PRA level was similar between the two procedures. This finding has several caveats. First, many of the patients included in the study were already sensitized before the procedure. Second, due to inclusion of patients before the availability of Luminex techniques in our HLA laboratory, the technique used for comparison of anti-HLA antibodies was LCT, a low-sensitivity technique, unable to precisely determine the specificity and

| | Group 1 Embolization of graft (N = 32) | Group 2 Surgical nephrectomy of graft ($N = 40$) |
|--|--|--|
| Wound infection: superficial/deep | _ | 6 (15%) |
| Opened at bed side | _ | 5 |
| Opened surgically under anaesthesia | _ | 1 |
| Haemorrhage | _ | 9 (22.5%) |
| Needed blood transfusion in postoperative period | _ | 7 |
| Massive bleeding: needed surgical | _ | 2 |
| site reopened to control renal pedicle bleeding | | |
| Haematoma | 2 (6.25%) | 4 (10%) |
| With drop in haemoglobin of more than 2 g | _ | 2 |
| Without drop in haemoglobin of more than 2 g | 2 | 2 |
| Pulmonary infection | - | 5 (12.5%) |
| Without major respiratory distress | _ | 2 |
| With respiratory distress | - | 3 |
| Bowel injury with need for resection | - | 1 (2.5%) |
| and re-anastomosis | | |
| Entero-cutaneous fistula treated medically | - | 1 (2.5%) |
| Acute lower limb ischaemia managed | - | 1 (2.5%) |
| by urgent surgical thrombectomy | | |
| Acute coronary syndrome | - | 1 (2.5%) |
| Incisional hernia | — | 1 (2.5%) |
| Disseminated intravascular coagulation | - | 1 (2.5%) |
| Intensive care unit hospitalization | - | 1 (2.5%) |

Table 4. Details of complications.

to quantify the intensity of antidonor antibodies. With these limitations in mind, it appears that sensitization is probably related to graft loss and cessation of immunosuppression rather than to surgical graft removal or embolization.

Regarding the efficacy of percutaneous embolization, our study shows that complete resolution of graft intolerance syndrome was observed in 27 of 32 patients (84.37%) which is comparable to previous studies [1,19-30]. Several relevant points need to be discussed here. First, this high rate of success is probably related to the good clinical selection of patients, as we excluded patients with overt acute rejection. Second, repeat embolization for incomplete embolization or presence of collateral arteries may improve the success rate. None of our patients have had a repeat imaging technique (Doppler ultrasound, scintigraphy or arteriography) to verify the persistence of renal vascularization and then evaluate the need for a repeat embolization. Delgado et al. [1] had a series of embolization in which 8 of 48 patients needed a second embolization, which increased the success rate from 65% to 78%. Third, it is interesting to ask whether embolization modified negatively or positively the risk of subsequent surgical removal. Neschis et al. [41] compared retrospectively two groups

of 13 patients each, with or without intra-operative embolization of renal graft prior to graft removal. Embolization significantly reduced intra-operative blood loss and transfusion requirements while slightly reducing operative time. The same finding was reproduced by Al-Geizawi *et al.* [42]. In our study, although it was reported in four of five patients (80%), wound siterelated infection was the only complication after subsequent surgical removal, of which the evolution was generally favourable with drainage and local care. However, no firm conclusion can be drawn due to the small number of patients.

Conclusion

Our preliminary study suggests that given a good selection of patients and exclusion of those presenting with frank acute rejection, graft intolerance syndrome in late failure patients can successfully be treated initially by percutaneous embolization. This procedure is highly successful (>80% of patients) and does not jeopardize secondary surgical removal in cases of technical failure. In addition, it is associated with a significantly lower rate and severity of postoperative complications, less need for blood transfusions and shorter hospital stay. Careful surveillance after the procedure is necessary, and systematic US Doppler verification of persistence of allograft vascularization may help to decide the need for repeat embolization in nonresponders. A well-conducted prospective study is mandated to address the limitations to our study.

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Conflict of interest

The authors have declared no conflicts of interest.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. Multivariate analysis of risk factors for occurence of complications.

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