



**HAL**  
open science

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

Ghalib Al Badaai, Vincent Pernin, Valérie Garrigue, Valérie Monnin, Thibaut Murez, Saad Ed Dine Fadli, Nicolas Molinari, Rodolphe Thuret, François Iborra, Georges Mourad

### ► To cite this version:

Ghalib Al Badaai, Vincent Pernin, Valérie Garrigue, Valérie Monnin, Thibaut Murez, et al.. Renal graft intolerance syndrome in late graft failure patients: efficacy and safety of embolization as first-line treatment compared to surgical removal. *Transplant International*, 2017, 30 (5), pp.484 - 493. 10.1111/tri.12927 . hal-01790269

HAL Id: hal-01790269

<https://hal.umontpellier.fr/hal-01790269>

Submitted on 19 Jan 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

## ORIGINAL ARTICLE

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

Ghalib Al Badaai<sup>1</sup>, Vincent Pernin<sup>2</sup>, Valérie Garrigue<sup>2</sup>, Valérie Monnin<sup>3</sup>, Thibaut Murez<sup>1</sup>, Saad Ed Dine Fadli<sup>1</sup>, Nicolas Molinari<sup>4</sup>, Rodolphe Thuret<sup>1</sup>, François Iborra<sup>1</sup> & Georges Mourad<sup>2</sup>

1 Department of Urology and Renal Transplantation, Montpellier University Hospitals, University of Montpellier Medical School, Montpellier, France

2 Department of Nephrology, Dialysis and Transplantation, Montpellier University Hospitals, University of Montpellier Medical School, Montpellier, France

3 Department of Vascular Radiology, Montpellier University Hospitals, University of Montpellier Medical School, Montpellier, France

4 Department of Medical Information, Montpellier University Hospitals, University of Montpellier Medical School, Montpellier, France

## Correspondence

Georges Mourad MD, Department of Nephrology, Dialysis and Transplantation, Hôpital Lapeyronie, University of Montpellier Medical School, 34295 Montpellier, France.  
Tel.: +33 467 338476;  
fax +33 467 338798;  
e-mail: g-mourad@chu-montpellier.fr

## 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.

*Transplant International* 2017; 30: 484–493

## Key words

graft embolization, graft failure, graft nephrectomy, renal transplantation

Received: 18 July 2016; Revision requested: 22 August 2016; Accepted: 24 January 2017;

Published online: 5 March 2017

## 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 to *de novo* sensitization associated with surgical 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 the intervention (dialysed outside France) were excluded. We also excluded all patients with a graft-related 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 follow-up. 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.

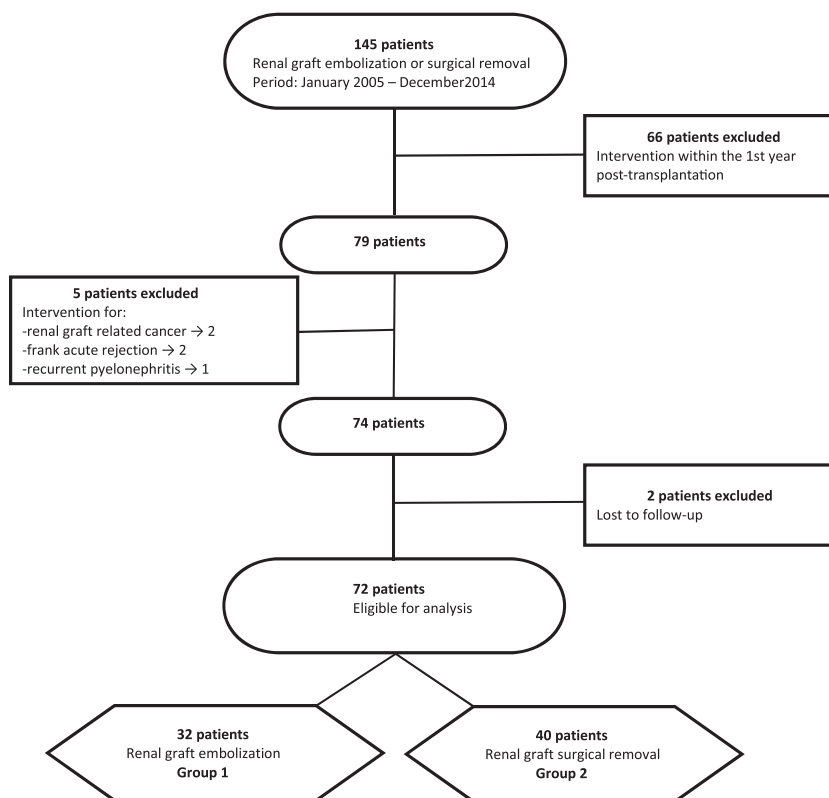


Figure 1 Patient flow chart.

### 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 × 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).

### Statistical analysis

Univariate analysis was performed for each variable. Continuous parametric data are presented as means ± 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  $\geq 2$  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 ( $3.22 \pm 1.64$  vs.  $8.37 \pm 7.65$  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

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

	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 ± SD	55.16 ± 12.63	46.38 ± 18.06	<b>0.0340</b>
Median [IR]	58 [49; 65]	49.5 [31; 61.25]	
Duration of graft function (months)			
Mean ± 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 ± 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 intervention (months)			
Mean ± 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 ± 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 <sup>2</sup> )			
Mean ± 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 <sup>2</sup> ), subgroups: n (%)			
<18.5	2 (6.25)	1 (2.50)	0.581
18.5–30	30 (93.75)	39 (97.50)	
ASA risk score: n (%)			
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 ± 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)	

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].



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

	Group 1 Embolization of graft (N = 32)	Group 2 Surgical nephrectomy of graft (N = 40)	P 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 ± 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), subgroups: 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)	
>100	5 (15.62)	6 (15.00)	
WBC count before intervention: n (%)			
>11.0 and ≤16.0 × 10 <sup>9</sup> /l	5 (15.62%)	3 (7.50)	0.4527
>16.0 × 10 <sup>9</sup> /l	0 (0.00)	0 (0.00)	

CRP, C-reactive protein, WBC, white blood cell; SD, standard deviation; IR, interquartile range.

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 low-dose 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

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

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

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



**Table 4.** Details of complications.

	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 site reopened to control renal pedicle bleeding	–	2
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 and re-anastomosis	–	1 (2.5%)
Entero-cutaneous fistula treated medically	–	1 (2.5%)
Acute lower limb ischaemia managed by urgent surgical thrombectomy	–	1 (2.5%)
Acute coronary syndrome	–	1 (2.5%)
Incisional hernia	–	1 (2.5%)
Disseminated intravascular coagulation	–	1 (2.5%)
Intensive care unit hospitalization	–	1 (2.5%)

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 site-related 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.

## Funding

The authors have declared no funding.

## 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 occurrence of complications.

## REFERENCES

- Delgado P, Díaz F, González A, et al. Intolerance syndrome in failed renal allografts: incidents and efficacy of percutaneous embolization. *Am J Kidney Dis* 2005; **46**: 339.
- López-Gómez JM, Pérez-Flores I, Jofré R, et al. Presence of a failed kidney transplant in patients who are on hemodialysis is associated with chronic inflammatory state and erythropoietin resistance. *J Am Soc Nephrol* 2004; **15**: 2494.
- Smak-Gregoor PJH, Zietse R, van Saase JLCM, et al. Immunosuppression should be stopped in patients with renal allograft failure. *Clin Transplant* 2001; **15**: 397.
- Smak-Gregoor PJH, Kramer P, Weimr W, van Saase JL. Infection after renal allograft failure in patients with or without low-dose maintenance immunosuppression. *Transplantation* 1997; **63**: 1528.
- Pham PT, Pham PC. Immunosuppressive management of dialysis patients with recently failed transplants. *Semin Dial* 2011; **24**: 307.
- Dantal J, Hourmant M, Cantarovich D, et al. Effect of long-term immunosuppression in kidney-graft recipients on cancer incidence: randomised comparison of two cyclosporin regimens. *Lancet* 1998; **351**: 623.
- Naini AE, Harandi AA, Daemi P, Kosari R, Gharavi M. Outcome of patients without any immunosuppressive therapy after renal allograft failure. *Saudi J Kidney Dis Transpl* 2008; **19**: 59.
- Mazzucchi E, Nahas WC, Antonopoulos IM, Piovesan AC, Ianhez LE, Arap S. Surgical complications of graft nephrectomy in the modern transplant era. *J Urol* 2003; **170**: 734.
- Zerouali F, Levchenko EN, Feitz WF, Cornelissen EA, Monnens LA. Renal transplant nephrectomy in children: can an aggressive approach be recommended? *Pediatr Transplant* 2004; **8**: 561.
- Secin FP, Rovegno AR, Del Rosario Brunet M, Marrugat RE, Dávalos Michel M, Fernandez H. Cumulative incidence, indications, morbidity and mortality of transplant nephrectomy and the most appropriate time for graft removal: only nonfunctioning transplants that cause intractable complications should be excised. *J Urol* 2003; **169**: 1242.
- Zomorrodi A, Buhluli A. Debulking transplant nephrectomy leaving an intact ureter and instillation of betadine intracapsular is safe nephrectomy: fifteen years' experience. *Transplant Proc* 2008; **40**: 205.
- Sharma DK, Pandey AP, Nath V, Gopalakrishnan G. Allograft nephrectomy – a 16-year experience. *Br J Urol* 1989; **64**: 122.
- O'Sullivan DC, Murphy DM, McLean P, Donovan MG. Transplant nephrectomy over 20 years: factors involved in associated morbidity and mortality. *J Urol* 1994; **151**: 855.
- Berthouix F, Jones E, Gellert R, Mendel S, Saker L, Briggs D. Epidemiological data of treated end-stage renal failure in the European Union (EU) during the year 1995: report of the European Renal Association Registry and the National Registries. *Nephrol Dial Transplant* 1999; **14**: 2332.
- Grochowicki T, Szmidi J, Galazka Z, et al. Influence of timing of transplant nephrectomy on surgical complications. *Transplant Proc* 2000; **32**: 1381.
- Ayus JC, Achinger SG, Lee S, Sayegh MH, Go AS. Transplant nephrectomy improves survival following a failed renal allograft. *J Am Soc Nephrol* 2010; **21**: 374.
- Lund Hansen B, Rohr N, Starklint H, Svendsen V, Birkeland SA. Indications for and timing of removal of non-functioning kidney transplant. *Scand J Urol Nephrol* 1986; **20**: 217.
- Mourad G, Minguet J, Pernin V, et al. Similar patient survival following kidney allograft failure compared with non-transplanted patients. *Kidney Int* 2014; **86**: 191.
- Lorenzo V, Díaz F, Pérez L, Dominguez ML, et al. Ablation of irreversibly rejected renal allograft by embolization with absolute ethanol: a new clinical application. *Am J Kidney Dis* 1993; **22**: 592.
- Cofan F, Vilardell J, Guierrez R, et al. Efficacy of renal vascular embolization versus surgical nephrectomy in the treatment of non-functioning renal allograft. *Transplant Proc* 1999; **31**: 2244.
- González-Satué C, Riera L, Franco E, Escalante E, Dominguez J, Serrallach N. Percutaneous embolization of the failed renal allograft in patients with graft intolerance syndrome. *BJU Int* 2000; **86**: 610.
- Cofan F, Riera MI, Vilardell J, Montanya X, et al. Percutaneous renal artery embolization of non-functioning renal allograft with clinical intolerance. *Transpl Int* 2002; **15**: 149.
- Delgado P, Diaz F, Gonzalez A, Hernández E, Hidalgo R, et al. Transvascular ethanol embolization: first option for the management of symptomatic nonfunctioning renal allograft in situ. *Transplant Proc* 2003; **35**: 1684.
- Capocasale E, Larini P, Mazzoni MP, Marcato C, et al. Percutaneous renal artery embolization of nonfunctioning allograft: preliminary experience. *Transplant Proc* 2005; **37**: 2523.
- Pérez Martínez J, Gallego E, Julià E, et al. Embolization of non-functioning renal allograft: efficacy and control of systemic inflammation. *Nefrologia* 2005; **25**: 422.
- Solinas A, De Giorgi F, Frongia M. Ablation of non-functioning renal allograft by embolization: a valid alternative to graft nephrectomy? *Arch Ital Urol Androl* 2005; **77**: 99.

27. Krause I, Cleper R, Belenky A, Atar E, Bar-Nathan N, Davidovits M. Graft intolerance syndrome in children with failed kidney allografts: clinical presentation, treatment options and outcome. *Nephrol Dial Transplant* 2008; **23**: 4036.
28. Chong X, Han Zhong L, Zhi Gang J, Yi X, Jing Chao H. Safety and effectiveness of percutaneous embolization for late failed renal allograft in patients with graft intolerance syndrome. *Acta Acad Med Sin* 2011; **33**: 76.
29. Riera L, Vigués F, Franco E, *et al*. Embolization of non-functioning kidney graft: alternative to surgical removal with clinical intolerance. *Transpl Int* 1994; **7**(Suppl.): S301.
30. Atar E, Belenky A, Neuman-Levin M, Yussim A, Bar-Nathan N, Bachar GN. Nonfunctioning renal allograft embolization as alternative to graft nephrectomy: report on seven years' experience. *Cardiovasc Intervent Radiol* 2003; **26**: 37.
31. Adeyi OA, Girmata AL, Howe J, *et al*. Serum analysis after transplant nephrectomy reveals restricted antibody specificity patterns against structurally defined HLA class I mismatches. *Transpl Immunol* 2005; **14**: 53.
32. Rosenberg JC, Berri R, Jackowski M, Levis D, Nehlsen-Cannarella S, Oh H. Multi-array antibody screening in detecting antibodies to mismatched HLA in patients awaiting a second transplant. *Transplant Proc* 2006; **38**: 3393.
33. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205.
34. Pham PT, Everly M, Faravardeh A, Pham PC. Management of patients with a failed kidney transplant. *World J Nephrol* 2015; **4**: 148.
35. Bond M, Pitt M, Akoh J, Moxham T, Hoyle M, Anderson R. The effectiveness and cost-effectiveness of methods of storing donated kidneys from deceased donors: a systematic review and economic model. *Health Technol Assess* 2009; **13**: 35.
36. Johnston O, Rose C, Landsberg D, Gourlay WA, Gill JS. Nephrectomy after transplant failure: current practice and outcomes. *Am J Transplant* 2007; **7**: 1961.
37. Eng MM, Power RE, Hickey DP, Little DM. Vascular complications of allograft nephrectomy. *Eur J Vasc Endovasc Surg* 2006; **32**: 212.
38. Goldstein SL, Mattoo TK, Morgenstern B, Martz K, Stablein D, Talley L. Anemia and growth status in pediatric patients receiving maintenance dialysis after a failed renal transplant course: an NAPRTCS report. *Pediatr Transplant* 2007; **11**: 201.
39. Ortiz A, Petkov V, Urbano J, Contreras J, *et al*. Emphysematous pyelonephritis in dialysis patient after embolization of failed allograft. *Urology* 2007; **70**: 372.
40. Marco Pérez LM, Riera Canals L, Romera Villegas A, Iborra E, González Satué C, *et al*. Iliac pseudoaneurysm in non-functioning renal graft 10 years after embolization. *Actas Urol Esp* 2001; **25**: 683.
41. Neschis DG, Gutta R, Al-Qudah HS, *et al*. Intraoperative coil embolization reduces transplant nephrectomy transfusion requirement. *Vasc Endovascular Surg* 2007; **41**: 335.
42. AL-Geizawi SM, Singh RP, Zuckerman JM, Requarth JA, *et al*. Role of allograft nephrectomy following kidney graft failure: preliminary experience with preoperative angiographic kidney embolization. *J Nephrol* 2015; **28**: 379.