Risk Factors of Early Kidney Graft Transplantectomy

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ABSTRACT

Background. Kidney allograft explant in the first month after transplant is a major concern for medicosurgical teams specialized in kidney transplantation and unacceptable graft loss in the current shortage. The aim of our study was to evaluate the risk factors of early kidney graft explant.

Methods. We retrospectively analyzed all adult kidney transplantations performed at our center from January 2006 to December 2011. Recipient, donor, and transplant characteristics were collected, as well as operating data and early postoperative complications. Univariate and multivariate logistic regression models were used to determine risk factors of early renal allograft explant.

Results. From a total of 707 kidney transplantations, 28 transplantectomies were performed in the first month following transplantation (3.96%). The average delay in days ± SD was 7.6 ± 10. Eighty-six percent of transplantectomies were due to vascular complications. In multivariate analysis, obesity (odds ratio [OR] = 9.6; 95% confidence interval [CI], 1.63-56.5; $P = .0007$), range of transplantation (OR = 36.89; 95%CI, 5.5-245; $P = .0006$), intraoperative complications (OR = 3.99; 95%CI, 1.22-13; $P = .026$), and early postoperative vascular complications (OR = 85.15; 95%CI, 23.6-306; $P < .0001$) were independent risk factors. Neither donors nor graft characteristics were significant.

Conclusions. Early renal graft transplantectomies are rare but account for 50% of renal graft loss in the first year. Because obesity, perioperative complications, and early vascular complications are independent factors associated with early transplantectomies, their prevention should be based on meticulous surgery during organ procurement, implantation of the kidney, and on the rehabilitation of future recipients.

KIDNEY transplantation (KT) is the ideal treatment of terminal chronic renal failure. Patients with kidney transplants have better 5-year survival [1], a longer life expectancy [2], and a better quality of life [3] than those who remain on dialysis. The economic benefit has already been shown in France and the United States [4].

Despite the promotion of living donations and the extension of the criteria for deceased donors, graft shortage is still problematic. For example, in France, the number of candidates for grafts keeps increasing; it was 4.9 in 2016 whereas it was 3.5 in 2008. In this context, early graft loss is detrimental. The causes of these failures are difficult to establish and can be the result of donor or recipient characteristics or perioperative factors. Many studies have reported the incidence and the risk factors for late complications [5–7], but only a few studies have focused on complications occurring immediately after the surgery [8,9].

The purpose of this study was to assess the incidence of early kidney graft transplantectomy and to identify the risk factors associated.

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MATERIALS AND METHODS

Study Population

We conducted a retrospective cohort study including all adult patients who underwent KT between January 2006 and December 2011 in our regional university transplant center. Patients < 18 years old and those with multiorgan transplantations were excluded.

All transplants were performed by senior or junior surgeons sufficiently trained according to the standard surgical techniques for transplantation, with an extraperitoneal approach, using a Gibson incision. Graft vessels were anastomosed end-to-side to the recipient external or common iliac vessels, with polypropylene 5-0 or 6-0 suture. Urinary anastomosis techniques depended on the surgeon's preference, Lich-Gregoire or Leadbetter techniques with or without a double-J stent, were performed. The bladder catheter was removed 7 to 10 days after the transplantation, and when it was used, a double-J stent was removed 6 weeks later. Doppler ultrasound was systematically performed at day 1 to verify vascular anastomosis and graft flow. In the postoperative period, recipients were hospitalized in the intensive care urology unit for 2 or 3 days, then in the nephrology department.

Data Collection

Recipient and donor characteristics, as well as preoperative and postoperative data were prospectively collected in the transplant database and in the medical file at the time of transplantation. All data collected were confidential and anonymized. All patients gave their consent for data collection and analyses, and the conduct of this study was approved by the institutional review board.

The primary endpoint was the identification of factors associated with early transplantectomies in our population of adult patients who received transplants. An early transplantectomy was defined as the need to remove the kidney within the first month following the graft. All transplantectomies were included regardless of the cause of the malfunction. The parameters evaluated in this study were: (1) recipient characteristics: age, sex, weight, body mass index (BMI), cause of kidney failure, dialysis modality, time on dialysis, previous transplant, comorbidities (diabetes, smoking, dyslipidemia), previous abdominal surgery, iliac vessel atherosclerosis evaluated by abdominal tomodensitometry; (2) donor characteristics: age, sex, cadaveric or living, cause of death, renal function by serum creatinine, number of renal arteries and veins on transplant, and atherosclerosis of graft vessels evaluated during the procurement; (3) perioperative data: duration of intervention, cold ischemia time, graft revascularization time, type of vascular anastomosis (with patch or not), type of urinary anastomosis, vascular complication (difficult bench surgery, vascular injury or thrombosis, repair of anastomoses), blood loss, and medical perioperative complication including hemodynamic instability and respiratory problems; and (4) postoperative factors: serum creatinine, delayed graft function (defined as the need for dialysis in the first week), acute rejection, duration of hospitalization, vascular complications (arterial or venous thrombosis, hemorrhage, other: Doppler anomalies, artery kinking, vascular thrombosis at another place), urinary complications (urinary leaks, hematuria, infection), wound complications (hematoma, dehiscence, abscess), surgical revision, and kidney graft explantation.

Statistical Analysis

A descriptive analysis of the collected data was conducted in addition to a logistic regression model. Both univariate and multivariate analyses were used to assess the significance of multiple risk factors for early transplantectomy. In univariate analysis, the significant threshold was reached for $P < .05$. For multivariate analysis, we included in a descending stepwise logistic regression model, candidate variables identified when P was less than .02 in the univariate analysis. Statistical analysis was performed using SAS version 9.3 software (SAS Institute, Cary, NC, United States).

RESULTS

Of 748 KTs reported, 707 adult patients were included in the analysis, 25 minors, and 16 multiorgan transplants were removed. The mean age of donors and recipients in years ± SD was 50 ± 16 and 51 ± 13, respectively. Forty six (6.5%) of them were living donors, 179 (45%) of the grafts had atherosclerosis, and 148 (21%) of them had multiple arteries. The rest of the population characteristics are presented in Table 1.

Concerning the perioperative data, mean revascularization time in minutes ± SD was 58 ± 21, and vascular complications occurred in 81 cases (11.5%) (Table 2).

In the postoperative period, 1 or more surgical complications occurred in 253 of the 707 patients (35%). Table 3 presents the details of the postoperative factors for the whole cohort. Early transplantectomy was necessary for 28 patients (3.96%), with a mean time after surgery in days ± SD of 7.6 ± 10.5. Three (10.7%) transplantectomies occurred during the initial surgery and 21 (75%) during the first week. Twenty-four (86%) kidneys were explanted for vascular complications: 11 vein thromboses, 8 renal artery thromboses, 4 hemorrhagic complications, and 1 poststenotic aneurysm. Two kidneys (7%) were explanted for sepsis, including 1 secondary to a urinary leak. The last 2 transplantectomies occurred for acute rejection, and a hepatic malignant tumor was discovered in the donor.

In a multivariate analysis, recipients who were overweight (25 < BMI < 30) or obese (BMI > 30) were significantly associated with early transplantectomy, multiplying the risk by 10 compared to patients with a BMI under 25 (odds ratio [OR] = 9.6, 95% confidence interval [CI], 1.63-56.5). Patients with 1 previous KT were more than 4 times as likely to undergo transplantectomy (OR = 4.52, 95%CI, 1.15-17.8), and the risk was increased by 36 for recipients who received their third kidney or more (OR = 36.89, 95%CI, 5.5-245). Both perioperative complications (OR = 3.99, 95%CI, 1.22-13) and vascular postoperative complications (OR = 85.15. 95%CI, 23.6-306), including arterial or venous thrombosis and hemorrhage, were related to the transplantectomy (Table 4).

None of the recipients from a living donor had early transplantectomy and there were fewer grafts with multiple arteries in the group who underwent transplantectomy. Graft vessel atherosclerosis was significantly associated with early transplantectomy in the univariate analysis only. Concerning the recipients, age, diabetes, smoking, dyslipidemia, previous dialysis or atherosclerosis were not associated with transplantectomy.

Table 1. Clinical Data of Donors, Grafts, and Recipients

Variable	Values
Donors Characteristics	
Mean age (y) ± SD	49.5 ± 15.5
Living donors, n (%)	46 (6.5)
Cause of death: cerebrovascular/traumatic, n (%)	392 (59)/138 (21)
Cardiac arrest, n (%)	164 (26.5)
Graft Characteristics	
Right kidney, n (%)	305 (43.5)
Vessels atherosclerosis, n (%)	179 (45)
Multiple renal arteries, n (%)	148 (21.2)
Mean cold ischemia time (h) ± SD	16.49 ± 7.9
Recipients Characteristics	
Mean age (y) ± SD	50.72 ± 13
Male, n (%)	472 (67)
Mean BMI (kg/m^2) ± SD	24.43 ± 4.23
Smoking, n (%)	282 (40.75)
Dyslipidemia, n (%)	243 (35.12)
Diabetes, n (%)	86 (12.43)
Previous transplant: Second graft/> 2 grafts, n (%)	100 (14.16)/24 (3.39)
Type of dialysis: none/hemodialysis/peritoneal dialysis, n (%)	50 (7.23)/583 (82)/40(6)
Mean waiting time (mo) ± SD	20.47 ± 25
Initial nephropathy: glomerular/polycystic/vascular, n (%)	268 (37.9)/118 (16.7)/60 (8.5)
Vessel atherosclerosis, n (%)	389 (59.4)
Previous abdominal surgery, n (%)	466 (66.5)

Abbreviation: BMI, body mass index.

Five years later, 14 of the 28 patients were transplanted again, and 9 were on hemodialysis since the transplantectomy.

DISCUSSION

In our study, we found 10% of surgical revisions, 11% of vascular complications, and 19% of wound complications; these results are in concordance with the literature [7,10]. Many studies have analyzed the risk factors for surgical complications [8] or for each type of complication [7], but only 1 had already studied the early transplantectomies and their risk factors [9]. A few studies only presented the rate of transplantectomy within the set of surgical complications, rates varying from 1.8% to 4.3% [7,8]. Englesbe et al [10] found 14 (2%) early transplantectomies in the 2 weeks following the graft within a cohort of 714 KTs. The risk factors were diabetes of the recipients and older donors. They didn't find any connection with cold ischemia time, multiple renal arteries, or previous transplantation. Even if the risk factors were not the same in our study, the rate of explanted grafts seemed coherent. Ariyarathenam et al found 4.15% of early transplantectomies, here again, closer to our result, but the risk factors were not considered [11].

However, all these studies highlight a close link between allograft explantations and vascular complications, similar to our results. In the cohort by Samhan et al [12], all the transplantectomies occurred after artery or venous thrombosis; this represented 10 of the 12 transplantectomies in

Table 2. Perioperative Factors

Variable	Values
Mean revascularization time (min) ± SD	57.9 ± 21
Lich-Gregoir urinary anastomosis, n (%)	392 (69)
Double-J stent, n (%)	531 (80)
Mean blood loss (mL) ± SD	270.45 ± 253
Transfusion, n (%)	26 (3.68)
Vascular complication, n (%)	81 (11.45)
Medical complication, n (%)	10 (1.41)
Transplantectomy, n (%)	3 (0.42)

Table 3. Posttransplant Factors

Variable	Values
Mean Hospitalization time (d) ± SD	17 ± 10
Reintervention, n (%)	70 (9.97)
Transplantectomy, n (%)	28 (3.96)
Wound complications, n (%)	137 (19.49)
Perigraft hematoma	88 (12)
Vascular complications, n (%)	79 (11.17)
Renal artery thrombosis	13 (1.8)
Vein thrombosis	13 (1.8)
Hemorrhage	4 (.,6)
Other	49 (7)
Urinary leak, n (%)	14 (2)
Medical complications, n (%)	322 (45)
Delayed graft function, n (%)	227 (32.5)
Acute rejection, n (%)	75 (10.7)
Death, n (%)	4 (0.5)

Posttransplant factors within the first month.

Table 4. Risk Factors for Early Transplantectomy

Risk Factor	Univariate Analysis			Multivariate Analysis	
	Patients With Transplantectomy, n (%) n = 28	Patients With Functional Graft, n (%) n = 679	*P* Value	OR (95% CI)	*P* Value
BMI (kg/m^2)			.013		.0007
< 25	9 (32)	416 (61)		1	
25-30	15 (54)	202 (30)		10.43 (3.07-35.4)	
> 30	4 (14)	61 (9)		9.6 (1.63-56.5)	
Previous transplant			.044		.0006
None	18 (64)	564 (83)		1	
Second	6 (21)	94 (14)		4.52 (1.15-17.8)	
> 2	4 (14)	21 (3)		36.9 (5.55-245)	
Atherosclerosis renal artery	15 (68)	264 (41)	.014	-	NS
Perioperative complication	11 (39)	77 (11)	.001	3.99 (1.2-213)	.02
Postoperative complications					
Hematoma	9 (36)	79 (12)	.0008	-	NS
Wound complication	11 (44)	126 (19)	.003	-	NS
Vascular complication	21 (84)	59 (9)	.0001	85 (23.6-306)	.0001

Abbreviations: BMI, body mass index; CI, confidence interval; NS, not significant; OR, odds ratio.

the cohort of Terrier et al [8] and 13 of the 14 transplantectomies in the cohort of Englesbe et al [9]. In our study, the occurrence of postoperative vascular complication was an independent factor associated with early transplantectomy, although it was more of an etiology than a risk factor.

One of the first risk factors for vascular complication was atherosclerosis of the recipient, as shown by Hernàndez et al or Terrier et al, for example [7,8]. This factor was not found in the studies mentioned previously and is not significant in our study, even if only 28% patients in the early-transplantectomy group had good vascular status against 41% in the allograft-in-place group.

Secondly, allografts with multiple renal arteries have been controversial. Even if surgeons have long thought that it complicated the surgery [13], recent studies don't confirm this trend, finding no difference in terms of allograft survival and vascular complications [14-16]. Keller et al concluded their review by saying that multiple renal arteries are a historical risk factor that is negated by the surgeon's experience [17]. In our study, multiple renal arteries did not increase the risk of transplantectomy, and there were more allografts with multiple renal arteries in the group with allograft in place than in the group of early transplantectomy (21.6% vs 10.7%). Going from Keller's point of view, in our university hospital, KT with multiple arteries grafts were willingly seniorized to overcome any surgical difficulties.

Right kidneys are known to be at risk of venous thrombosis but also of artery thrombosis [18]. In our study, there were more right kidneys in the early-transplantectomy group that in the other group (60% vs 41%), but the difference was not significant.

Regarding vascular complications, many possible risk factors have been raised in several studies; risk factors commonly accepted are diabetes and thrombophilia of the recipient, hemodynamic instability, and perioperative surgical difficulties, right kidneys, and older donors [17]. These data are not significant in our study even if we noted a few trends, as for the right kidneys and atherosclerosis. In all cases, these factors are more and more frequent especially because of the aging of the population, and right kidneys or with atherosclerotic vessels can't be rejected in the shortage context. Considering the appalling prognosis of vascular complications, it is necessary to prevent them as much as possible. This requires global and optimized support, including: (1) meticulous surgical techniques during organ removal, with preparation on the back table, and during the graft; (2) reduction of cold ischemia time and use of perfusion machines; (3) preservation of vascular health of the patients on the waiting list (smoking cessation, balanced diet) and evaluation of vascular status and thrombophilia before performing transplantation; (4) hemodynamic stability during the surgery and 48 hours postoperatively; (5) use of anticoagulant or antiplatelet treatment, according to the comorbidities of the recipient; and (6) systematic Doppler ultrasound for early diagnostics of vascular complications in the postoperative period.

All these approaches aim to reduce the rate of vascular complications and, therefore, the rate of early transplantectomy, while adapting to available grafts in the current shortage context.

An interesting finding in our study is the significant association between early transplantectomy and BMI, particularly in the overweight or obese category. This relationship was not found in the study of Englesbe et al [9]. It has been previously established that obesity is a risk factor of surgical complications after adult KT, especially wound complications, surgical site infections [8] [19], delayed graft function, and lower graft survival [20]. Despite this increased risk of surgical complications, the benefit of survival for obese patients with KT has been proved. Glanton et al showed that KT on obese patients reduced the risk of death by 61% as compared to obese patients on dialysis [21]. In regular

practice, it is difficult to appreciate the threshold of BMI beyond which the surgical complications would become higher than the expected benefits of KT. At the moment, no scholarly society has established this and practices are heterogeneous in the world. In France, the threshold BMI of 35 kg/m^2 seems to be usually used, even if the European association of transplantation suggests a threshold of 30 kg/m^2 in the European Renal Best Practice [22]. Different values have been mentioned in the literature; 35 kg/m^2 by Holley, 40 kg/m^2 by Gill [23], and 41 kg/m^2 by Glanton [21], yet, there is still no consensus on a cut-off of BMI before KT.

Here again, multidisciplinary management in the pretransplant of obese recipients is essential and must contain the patient's education, dietary recommendations, exercise programs, and behavioral therapy. In case of failure, the use of bariatric surgery before transplantation is an alternative for patients with BMI up to 40 kg/m^2, even if studies are missing [24]. The use of a robotic technique could yield low complication rates in the obese population, especially wound complications [25,26].

Concerning the retransplantations, which are an independent risk factor in our analysis, it is not an established risk factor of surgical or vascular complication. However, Tisserand et al found 54% of surgical complications after the second transplantation vs 46% after the first, but without significant difference [6]. In research by Ojo et al, retransplantations were a risk factor of graft thrombosis [27]. A French report from the biomedicine agency found previous transplantations to be predictive factors of failure at 1 year. In cases of retransplantation, the surgery is more difficult because the choice of the implantation site is more restricted and the recipient likely has a deteriorated vascular status. If a perioperative vascular complication occurs, backup solutions are less available.

All these practical applications can explain the significance of this factor in our study but, in all cases, the range of transplantation is an unchangeable criterion that cannot contraindicate being added to the waiting list in view of the expected benefits of the KT.

This is a retrospective and monocenter study, and this constitutes important limitations. However, we obtained complete information from our databases, which were updated prospectively during the patient's hospitalizations. The main event (early transplantectomy) is rare and, even if we worked in a large cohort with few exclusion criteria, this would likely lead to a lack of power in the statistical analysis. In addition, some data are missing, as, they were not collected in the initial phase (donor BMI, immunologic data, and anticoagulant treatment before and after surgery, etc).

CONCLUSIONS

Early transplantectomies occur in 4% of adult KT, mostly due to graft thrombosis, and represent half of the cases of graft loss in the first year after transplantation. Obesity and retransplantation are 2 major and independent risk factors. However, because the expected benefits of KT in these populations have been proven, medical and surgical teams must give them access to the waiting list. Donor and recipient vascular characteristics are also important factors, increasing vulnerability to the occurrence of a vascular complication. The knowledge of these data is important and could be applied in our practices, especially during the pretransplantation assessment with the prevention of obesity and prevention of atherosclerosis, but also with meticulous surgery during the kidney procurement and during the KT to prevent vascular complications. In the current context of shortage, early transplantectomies would deserve future clinical trials to know more accurately how to prevent them.

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