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Retrieved but not transplanted kidneys: how to limit the losses? A retrospective national study

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SUMMARY

Despite the organ shortage, a significant number of deceased donor kidneys are retrieved but not transplanted (RNTK). This study aims to describe and analyze the main causes of potential grafts discard and to propose adequate solutions. We collected data from the Cristal database of the French Biomedicine Agency about RNTK over one year. Expert opinion was taken from urologists with extensive expertise in renal transplantation. They retrospectively analyzed each record to assess the appropriateness of each graft refusal and subsequent kidney discard. Of 252 kidneys were retrieved but not transplanted in France over one year. The main reasons for discard were vascular abnormalities in 43.7% (n = 110), suspicion of malignant tumor in 18.7% (n = 47), and severe histological lesions on preimplantation biopsy in 12.3% (n = 31). The reason for kidney refusal was undetermined in 4.8% (n = 12). Iatrogenic lesions were responsible for 26.2% (n = 66). Overall, 46.0% (n = 16) and 25.0% (n = 63) of the grafts were, respectively, properly and improperly denied, and the analysis was not possible in 29.0% (n = 73). In total, 36.9% of RNTK could have been transplanted. Reduction of iatrogenic lesions, improvement of microsurgical repair skills, and proper histological examination are necessary to reduce the number of RNTK. A prospective study applying the proposed principles is undoubtedly essential to complete this work.

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Introduction

Kidney transplantation is currently the preferred therapy for end-stage renal disease. Transplantation improves the recipient's life expectancy and quality of life while representing the most cost-effective renal replacement therapy [1]. In France, a single national agency, the "Agence de la biomedicine" (ABM), manages the national waiting list and the national refusal registry and is responsible for all organ allocation. It centralizes data from all retrieved kidneys (either transplanted or not) in a national database (Cristal®).

While the number of kidney grafts performed in France has increased over the past decade, the unmet need for kidney grafts has seen a proportionally larger increase. In an attempt to overcome the kidney graft

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shortage, many strategies have been implemented, including extended criteria for brain dead donors, donation after a cardio-circulatory arrest (DCD), live donor kidney exchanges, ABO-incompatible programs, and the use of the expanded criteria donor (ECD) [2]. Performed renal transplantations increased from 3074 in 2013 to 3567 in 2018. At the same time, the number of patients on the waiting list increased by 35.72% from 14460 to 19625. As a result, the total number of candidates for each available graft raised from 4.7 in 2013 to 5.5 in 2018 [3].

Despite the severe graft shortage, the ABM reports an increase in the percentage of retrieved but not transplanted kidneys (RNTK) that are discarded for being unsuitable for transplantation, from 6% to 9% during ten years [4]. The knowledge of the exact reasons behind RNTK is essential to develop tailored solutions that will help reducing kidney graft waste, especially in the current situation of the increasing unmet need for kidney grafts. However, graft reports submitted to the ABM by transplant surgeons rarely contain sufficient details about the precise reasons justifying to discard the graft. The poor quality of the graft was the most frequent reason reported (65% of cases). A surgical technical problem was reported in only 4% of cases. Iatrogenic lesions during organ procurement were probably underestimated [5].

Our study aims to identify the exact reasons for which kidney grafts were considered unsuitable for transplantation and to analyze the appropriateness of the decision.

Material and methods

Search strategy

We conducted a retrospective cohort study using the CRISTAL database of the ABM. We reviewed the medical records of all RNTK from brain dead donors and patients that received the contralateral grafted kidneys (CGK) in France over twelve months.

We collected data about donor demographics, medical parameters, and survival of the CGK at one-year post-transplantation. We studied summary schemas drawn by the surgeons to describe the anatomy of both kidneys (vessel number, ureter morphology, presence of arterial, or venous patch). We reviewed reports of surgery, histopathology, and kidney procurement. The latter describes specific characteristics of the kidneys (e.g., the location and severity of atheroma lesions and calcifications) and the events that occurred and particularly impacted transplantation (e.g., iatrogenic lesions).

Expert opinions were taken from urologists with extensive expertise in renal transplantation. They retrospectively analyzed each record to assess the appropriateness of each graft refusal and subsequent kidney discard.

Eligibility criteria and data extraction

Two independent trained researchers, in addition to the expert urologists, evaluated the eligibility of all collected cases. A record was considered eligible when sufficient information was available about: donor demographics (age, medical history, and cause of death), anatomical description of the RNTK, events that could have impacted transplantation, and survival of CGK at one-year from transplantation. Those specific points of interest were extracted from each included record and filled by the first researcher on a Data Sheet, which was cross-examined by the second researcher.

Each record was classified into one of three categories: RNTK probably incorrectly denied—RNTK correctly denied—impossible retrospective assessment.

We divided patients into two groups based on the cause of the discard of the contralateral kidney being related either to the general state of the donor or to a problem of the graft itself, and we compared the rate of graft loss within the first year, and the 1-year graft survival of these recipients to that of the recipients from other donors (ECD, DCD, and all donors).

In the case of one kidney discarded and the other kidney transplanted were the experts aware of the fate of the transplanted kidney.

Statistical analysis

The statistical methods included the descriptive analysis of all study variables and comparisons between donors with one or two RNTK and successful donors using independent tests. Categorical variables were expressed as numbers (percentage) then compared using chi-square or Fisher's exact tests as appropriate. Normally distributed quantitative variables were expressed as mean ± standard deviation and compared using Student's t-test for independent values. A P-value < 0.05 was considered significant.

Results

We found that 252 kidneys were retrieved and not transplanted. Among 1,479 brain-dead donors with at least one kidney retrieved, 186 (13%) had at least one

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RNTK, between them 115 had the contralateral kidney transplanted (Fig. 1). Older donor age was significantly associated with kidney refusal and discard. The mean age of donors of RNTK was significantly higher than the age of successful donors, being, respectively, 65 years +/− 15, with 50% above 65 years and 54 years +/− 19 with 32% above 65 years ($P < 0.001$). Extended criteria donors had significantly higher rates of kidney refusal and discard. The proportion of ECD was 85% in the RNTK group compared to 58% in the successful donor group ($P < 0.001$).

Among the 252 RNTK, the 3 main causes of kidney discard were vascular abnormalities ($n = 110$, 43.7%), suspicion of malignant tumor ($n = 47$, 18.7%), and severe histological lesions on preimplantation biopsy ($n = 31$, 12.3%). The other causes of kidney discard were incomplete flush ($n = 9$, 3.6%), renal hypotrophy ($n = 8$, 3.2%), capsule laceration ($n = 6$, 2.4%), ureteral section ($n = 5$, 2.0%), pelvic kidney ($n = 4$, 1.6%), extensive cold ischemia time ($n = 4$, 1.6%), donor infection ($n = 3$, 1.2%), ureteral dilatation ($n = 3$, 1.2%), large hematoma ($n = 3$, 1.2%), large cyst ($n = 3$, 1.2%), high resistance on machine perfusion ($n = 2$, 0.8%), pyelonephritis sequelae ($n = 1$, 0.4%), and pelvic stone ($n = 1$, 0.4%). The reason for kidney refusal was undetermined in 12 cases (4.8%).

Among the 110 grafts discarded for vascular abnormalities, an arterial problem was identified in 86.4% ($n = 95$) of cases, from which 64.2% ($n = 61$) were atheromatous lesions, 29.5% ($n = 28$) were iatrogenic lesions (concerning 19 polar arteries and 9 main arteries), and 6.3% ($n = 6$) were arterial malformations. The remaining 13.6% of vascular abnormalities were iatrogenic venous lesions ($n = 15$).

Among the 47 grafts discarded for tumoral causes, the tumor was most frequently located in the kidney and discovered during retrievement (35% of cases). Final histology was benign in one-third of cases.

Severe histological lesions on pre-implantation biopsies were the reported reason for 31 kidney refusals (12.3%). However, our retrospective analysis identified that only 24 (77.4%) biopsies were adequate according to the Banff classification. Histoprognostic scores of Remuzzi [6] and Andrés [7] were not calculated at the time of biopsy. Retrospective calculation of these two scores provided an estimate that seven grafts could have been proposed as dual kidney grafts.

Iatrogenic lesions were responsible for 26.2% ($n = 66$) of the RNTK. The causes of discard due to iatrogenic lesions were vascular injuries ($n = 43$, 65.2%), cannulation incidents ($n = 9$, 13.6%), capsule lacerations ($n = 6$, 9.1%), ureteral sections ($n = 5$, 7.6%), and hematomas ($n = 3$, 4.5%). Among the 43 vascular injuries, there were 28 arterial and 15 venous injuries.

We found significant differences in the morphological characteristics between RNTK and their CGK (Table 1). RNTK had more capsule lacerations, arterial, venous, and ureteral sections. We found more hypotrophy and multiple arteries in the RNTK group. However, the proportion of calcified atherosclerotic lesions was similar.

Among the 252 RNTK, the retrospective analysis of causes for refusal showed that 116 grafts (46.0%) and 63 grafts (25.0%) were, respectively, adequately and improperly denied. Reasons for refusal and proposed repairs are listed in Table 2. The causes of proper denial are described in Table 3. For the remaining 73 kidneys (29.0%), the analysis of the reasons for refusal (Table 4) was not possible.

We analyzed the survival of 115 renal transplantation of the contralateral kidney of RNTK cases. Among them, 10 (8.7%) recipients died in the first-year post-transplant. The causes of death were infection ($n = 5$), cardiovascular ($n = 3$), acute rejection ($n = 1$), and not reported in one case. Seventeen recipients (14.8%) lost their graft with a mean follow-up of 4 +/− 4 months.

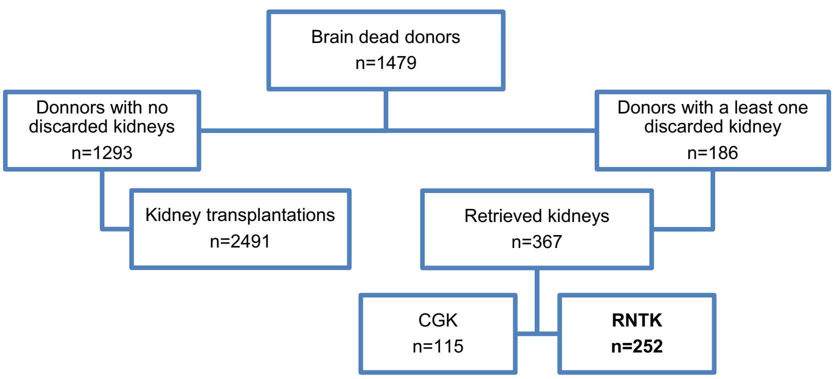

Figure 1 Flow chart of kidneys retrieved from brain dead donors over 12 months in France. CGK, contralateral grafted kidneys; RNTK, retrieved but not transplanted.

Table 1. Comparison of morphological characteristics between retrieved but not transplanted and contralateral grafted kidneys.

Characteristics of grafts	RNTK (252)	CGK (115)	*P*-value
Ostium calcifications	51 (20%)	19 (17%)	0.57
Trunk calcifications	66 (26%)	25 (22%)	0.53
≥ 3 arteries	16 (6%)	0	0.007
Arterial dissections	12 (4.7%)	0	0.02
Arterial sections	35 (13.8%)	1 (0.8%)	<0.001
Venous lesions	17 (6.7%)	0	0.006
Ureters sections	12 (5%)	0	0.02
Capsule lacerations	23 (9%)	3 (2.6%)	0.04
Hypotrophy	28 (11%)	1 (0.9%)	<0.001

CGK, contralateral grafted kidneys; RNTK, retrieved but not transplanted.

The 1-year graft and patient survivals were, respectively, 77% and 91%. This is extraordinarily low compared to the literature and could lead to an overestimation of the benefit of using some of the discarded kidneys.

The median cold ischemia time (CIT) was 13h20 min (IQR 9-20h); grafts from overweight donors were associated with an increased CIT by 4% ($P = 0.03$) compared to normal BMI donors, right kidneys were associated with a 4% increased CIT ($P < 0.002$), and donor biopsy had a 19% increased CIT ($P < 0.003$). Obese recipients were associated with an increased CIT by 11% ($P = 0.02$). Transport that involved mechanical perfusion at some point was associated with a 36% increased CIT ($P < 0.001$).

The comparison of patients based on the cause of the discard of the contralateral kidney is detailed in Table 5. The first group included 57 recipients in whom grafts were denied due to factors concerning the donor. The second group contained 58 recipients in whom graft refusal was related to a problem of the graft itself. The rate of graft loss within the first year was higher in the first group (23% vs. 7% in group 2, $P = 0.03$). The causes of discard of both kidneys in one donor were detailed in Table 6. The comparison of the 1-year graft survival of the CKG (which contralateral kidney has been discarded) recipients to that of recipients from other donors (ECD, DCD, and all donors) (Fig. 2) revealed that, when the reason for discard was attributable to the donor conditions, the global 1-year graft survival of contralateral kidney recipients was equivalent to the graft survival of donors older than 70 years and ECD donors. Data concerning all the other donors were obtained from the CRISTAL database of the ABM.

Discussion

Registries analysis suggests that there are considerable regional and center variations in the discard rate and that many discarded organs would have provided a sufficient survival benefit to the patients, to justify the transplantation rather than remaining on the waiting list [8]. To minimize the discard of potential grafts, organ offering systems should be designed to identify kidneys at increased risk of discard and ensure that they are offered to centers where they are most likely to be implanted [9].

In the UK, the “Declined Kidney Scheme” was introduced in 2006, in an attempt to maximize the use of transplantable kidneys, by transferring hard-to-place organs to specific centers that are willing to implant them. This system enabled a single individual (surgeon or donor co-coordinator) to refuse the use of a kidney.

Table 2. Causes of improperly discarded kidneys.

Causes of discard	*n*	Possible repairs
Patch calcifications	14	Arterial suture without patch
Proximal sections of the main artery	2	Arterial suture without patch
Distal sections of the main artery	2	End-to-end anastomosis
Distal sections of polar artery	5	Microsurgical end-to-end anastomosis
Proximal sections of polar artery	7	Polar reimplantation
Venous sections	11	End-to-end anastomosis or venous plasty with iliac vein graft
Ureteral sections	5	Pyelo-ureteral anastomosis
Ureteral dilatations	3	Pyelo-ureteral anastomosis
Large capsule lacerations	6	Hemostatic mesh
Large cysts	3	Wall resection
Pyelic centimetric stone	1	Treatment in the recipient
Long duration of cold ischemia	4	Simultaneous offering to participating centers

Table 3. Causes of justified discarded kidneys.

Causes of discard	*n*	Justifications
Arterial dissections	12	
Calcifications of the arterial trunk	10	Confirmation by pathological examination
Arterial stenosis	4	Confirmation by pathological examination
Fusiform aneurysm extended	2	
Arterial thrombosis	2	
Venous traction lesions	3	
Malignant tumor	33	Histological confirmation of malignancy (10 on the graft and 23 on other sites)
Severe histological lesions on preimplantation biopsy	24	
Unwashed kidneys	9	Secondary to cannulation incident
Hypotrophy	8	Confirmation by pathological or radiological examination
Pyelonephritis sequelae	1	Confirmation by pathological or radiological examination
Pelvic kidneys	4	
Donor infections	3	
Large hilar hematoma	1	Confirmation by pathological examination

Table 4. Causes of uninterpretable discarded kidneys.

Causes of uninterpretable discard	Number	Justifications
Arterial calcifications	35	The description on the slip without confirmation by pathological examination
Tumor suspicions	14	Final benign histology but not available in emergency : precautionary principle
Severe histological lesions on preimplantation biopsy	7	Retrospective calculation of Andès or Remuzzi score: could be proposed as dual kidney graft
Large hematomas	2	The description on the slip without confirmation by pathological examination
Retro-aortic multiple veins	1	The description on the slip without confirmation by pathological examination
High resistance on infusion machine	2	Numbers and kinetics not available
Undetermined causes	12	Slips reporting no significant abnormality

Table 5. Comparison of survival depending on the cause of the discard of the contralateral kidney.

Cause of discard	Factors concerning the donor*	The graft itself†	*P*-value
n	57	58	
Death	5 (9%)	5 (9%)	1
Recovered cardiac arrest	13 (23%)	4 (7%)	0.03
Functional graft	39 (68%)	49 (84%)	0.45

*Atheroma, hypotrophy, and severe histological lesions.

†Iatrogenic lesions, tumors on the graft, organizational incidents, pelvic kidneys, pelvic stone, ureteral dilatation, cyst, tuberculosis, and undetermined causes.

Callaghan and al. found in 2014 that 65% of kidneys were unnecessarily discarded. The two most common reasons were poor perfusion (25%) and poor donor past medical history in 25%. A new Kidney Fast Track Scheme (KFTS) was later developed. It replaced the first one, omitted the single-member decision whether to discard or accept a kidney, and minimized the cold ischemic time by the simultaneous offering to all participating centers, in an attempt to increase the use of discarded kidneys [9]. Mittal et al., in 2017, showed that the use of the KFTS reduced the rate of discarded kidneys that could be useful to 32% [8]. Discard rates in UK are similar to those reported by Eurotransplant (11%) [10] but lower than those in the United States (US) (16%) [9].

The proportion of RNTK has been growing steadily in the United States, and the contributing factors remain unclear. Among the kidneys retrieved between 2000 and 2015, 17.28% (36700/212305) were discarded. Biopsy findings were the most common reason

Table 6. Causes of discard of both kidneys in one donor.

Kidney 1	Kidney 2	Number of donors
Hypotrophy	Hypotrophy	6
Ostium calcifications	Ostium calcifications	16
Trunk calcifications	Trunk calcifications	16
Tumor	Hypotrophy	1
Arterial section	Ostium calcification	7
Capsule laceration	Capsule laceration	2
Capsule laceration	Venous lesion	3
Donor infection	Donor infection	1
Trunk calcifications	Undetermined	4
Trunk calcification	Ostium calcification	9
Ostium calcifications	Arterial lesion	2
Undetermined	Undetermined	4

consisting of 38.2%. Even the median Kidney Donor Risk Index of discarded kidneys was significantly higher than transplanted organs (1.78 vs. 1.12). Significant geographic variations in the odds of discard were found across the United States. Organs procured on weekends were significantly more likely to be discarded than transplanted even after adjusting for organ quality, due to the influence of resource limitations during weekends [11]. Kidneys with atherosclerotic lesions or fibrosis (involving more than 20%) [12] and those retrieved from donors with multiple unfavorable characteristics (older age, female, black, obese, diabetic, hypertensive, and hepatitis C-positive) were more likely to be discarded. However, the reason for the discard of potentially transplantable kidneys was not fully understood [13]. Our findings are consistent with previous literature data, as donors for RNTK were significantly older. We also found that atheromatous and histological lesions were among the main causes of discard.

Several studies have compared the results of kidneys that were accepted for transplantation primarily and secondarily (after being rejected by one or more teams in the beginning) [14–17]. Overall, patient and graft survivals at five years were similar between recipients with kidneys rejected by at least two centers and recipients with kidneys directly accepted [18]. A “cascade effect of discard” was described. It is defined by the communicative effect of the refusal between different teams, once a graft is refused in one or more centers. And this increases the odds of cold ischemia and the risk of transformation of a marginal kidney to eventually an ungrafted one [14–17]. In our study, this « cascade effect » probably played a role in the decision. Modifications of the kidney distribution system to direct more efficiently organs with high Probability of Discard/Delay ratio to the centers that will use them were suggested by Massie et al. to reduce discard of potential grafts [19].

The study of the Eurotransplant registry allowed Maurits et al. in 2009 to conclude that the use of liberal donor criteria and a rescue allocation (RA) policy can reduce kidneys’ discard. The RA consisted of offering a renal graft after five non-acceptances, to all centers in the region of the procurement. And when all centers decline the acceptance of the graft, a second line competitive center allocation is considered in the greater area of procurement to any recipient from their waiting list [20].

The data about the iatrogenic lesions behind RNTK were underestimated by the French State Agency, which reported a “surgical technique problem” only in 4% of cases [5]. Our results showed that iatrogenic lesions were involved in the refusal of 17.1% (n = 43) of all the RNTK. Moreover, iatrogenic lesions accounted for 43.1% of the vascular abnormalities behind RNTK, divided between arterial (29.5%) and venous (13.6%). As a solution, Mersa et al. suggested that, when the diameter of a transected polar artery is > 3 mm, it can be repaired using microsurgical techniques [21]. In our study, 64.2% of the vascular abnormalities behind RNTK were atheromatous lesions. Khan et al. in 2018 suggested that eversion endarterectomy (EE) appears to be a safe procedure that can prevent discard of marginal donor kidneys exhibiting severe atherosclerosis involving the renal artery. After a subintimal dissection of the Carrel aortic patch surrounding the renal artery, a complete eversion

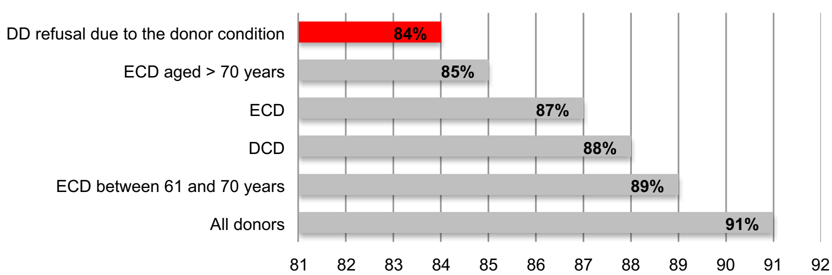

Figure 2 Comparison of the one-year graft survival between recipients of the contralateral kidney and other types of donors. DD, deceased donor (contralateral kidney); DCD, donation after a cardio-circulatory arrest; ECD, expanded criteria donor.

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was performed with a subsequent removal cast. They used heparinized saline to wash debris from the arterial lumen. The artery was carefully flushed in an antegrade manner to check for patency, integrity, leaks, or disruption. The procedure had acceptable short-term outcomes and can be promising [22].

Our review showed that one-third of RNTK for suspected malignant tumor could have been grafted because final histology was benign. Some groups have even transplanted kidneys with small malignancy tumor, after tumorectomy and verification of negative margins by pathological examination. Buell et al. reported a series of 14 transplanted carcinoma-bearing kidneys [23]. No recurrence occurred during a median follow-up of 69 months. On 43 grafts, Nicol at al. showed similar results, except one case of tumor recurrence diagnosed nine years after transplantation [24]. Effectively, the survival of this group of patients was significantly better than patients on the waitlist treated by dialysis [25]. These results suggest that for small tumors, with a low Fuhrman grade, transplantation could be a feasible option after tumorectomy [26].

Our analysis suggested that 25% of the RNTK were probably improperly denied and that 46% of the RNTK were duly turned down. The addition of the inadequately denied grafts (n = 63), to those refused for a tumor suspicion with benign final histology (n = 14) and those turned down for an iatrogenic and avoidable lesion (12 arterial dissections, 3 venous traction lesions, and 1 retro-aortic multiple veins), results in 93 RNTK that could have been grafted, corresponding almost to one-third of the RNTK (36.9%). To reduce the number of RNTK, report of the procurement, photographs, and reason of refusal have to accompany every graft. A microsurgical vascular repair can be considered when the diameter of a transected polar artery is > 3 mm. Eversion endarterectomy is a potential solution for some calcified vessels. Histological examination of the graft should be made systematically and has to be exhaustive. Discards should be made by an expert surgeon trained in microsurgery or at least 2 surgeons.

Analysis of data from the United States Renal Data System and the Eurotransplant registry suggests that one-year graft survival rate is more than 90% in deceased and living donor kidney transplantation [27]. In our study, this rate was much lower in recipients of grafts which contralateral kidney was discarded. This finding can be explained by the fact that the retrieved kidney discard was not exclusively related to the graft itself, but could be caused by other concomitant factors in the donor like atheroma, hypotrophy, or severe histological lesions.

Although this survival rate is low, we still believe that our suggestions to save the discarded kidneys and limit the losses are still applicable, whether kidneys that we could have been used came from the group in which both kidneys were discarded or not.

Finally, we have to highlight the importance of specific and supervised surgical training by delivering not only technical training but also insights on ischemia-reperfusion issues, extended criteria donors, donor disease transmission, ethics, and legal matters. In France, this training is delivered by the "Ecole Francophone de Prélèvement Multi Organe" (EFPMO; French School for Multiorgan Procurement) [28], in order to harmonize procurement practices and improve surgeons' skills and patients' outcomes [29].

Conclusion

In our study, among 252 RNTK, 93 (36.9%) could have been grafted. In a period of graft's shortage, appropriate evaluation of kidneys is essential. Strategies to limit the number of RNTK include the reduction of iatrogenic lesions and the improvement of microsurgical repair skills and histological examination. A prospective study applying the proposed principles is undoubtedly essential to complete our work.

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