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An analysis of unplanned return to the operating room following deceased donor kidney transplantation

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ABSTRACT

Introduction: This study was undertaken to characterize unplanned return to the OR following kidney transplantation(KT).
Methods: All patients undergoing KT at a single center from 1/2015 through 11/2017 were evaluated. The primary endpoint was unplanned return to the OR within 90 days. Perioperative and one year patient and graft outcomes were also determined.
Results: Of 190 patients, 14(7.4%) of patients had unplanned reoperation. The most common individual indications were bleeding from biopsy sites(n = 2), poor vascular flow on postop ultrasound(n = 4), and perforated diverticulitis(n = 2). Forty Three percent of all reoperations were unrelated to the technical conduct of the transplant operation. Reoperated patients had significantly worse survival at one year(78.6% vs. 96.6%), although graft function in survivors was similar to those who did not return to the OR.
Conclusion: Reoperation following KT is frequently unrelated to the technical conduct of the transplant procedure, thus it may not be useful as a quality metric.

Introduction

Although unplanned return to the operating room following surgery is a relatively rare event, it often carries significant negative implications on outcomes. Furthermore, unplanned reoperations is often viewed as reflecting a problem with the index operation itself. Because of this, the rate of unplanned reoperations has been proposed as a useful quality indicator in general surgery.[1,2]

Renal transplantation has long been the therapy of choice for end stage renal disease,[3,4] with one year graft survival following renal transplantation currently standing at over 90%.[5] With better immunosuppression and fewer graft losses due to immunologic causes, greater emphasis must now be placed on reducing surgical complications in order to improve overall outcomes.[6] The surgical technique for kidney transplantation has remained relatively standardized since its introduction, allowing for comparisons to be made across centers and eras in terms of surgical complications.[7] The above factors suggest that unplanned reoperation may be a useful quality indicator in renal transplantation as well. Because the literature on reoperation following kidney transplant is so sparse, the incidence of and reasons for reoperation need to be better elucidated before adopting it as a quality measure.[1,8] This study was thus undertaken to investigate the incidence, timing, and causes for unplanned reoperation following renal transplantation at a single center.

Methods

Study population and statistical methods

Retrospective chart review of all kidney transplants performed at a single center between 1/2015 and 11/2017 was performed. Patient and donor demographics, details of the transplant hospitalization, and follow up information were collected. The primary outcome of interest was unplanned return to the operating room within 90 days following transplantation. Continuous variables were analyzed using Student's t-test and categorical variables were analyzed using chi-squared or Fisher's exact test, where appropriate. Patient survival analysis was performed according to Kaplan-Meier, with groups compared by the log rank test. Patient

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survival was measured from the time of transplant until death or last follow up. Patients alive at the end of analysis were censored. Graft survival was determined using competing risks methodology. Graft survival was measured from time of transplant until return to dialysis or transplant nephrectomy, with death with a functioning graft treated as a competing risk. Differences in the cumulative incidence of graft survival between groups were compared using the methodology of Fine and Gray. Multivariable analysis of patient and graft survival were not performed as there were not enough deaths in the cohort to support a multivariable model without overfitting.[9]

Immunosuppression

Induction immunosuppression consisted of either alemtuzumab (30 mg IV), basiliximab (20 mg IV at the time of operation and on postoperative day 4), or less commonly antithymocyte globulin (4.5 mg/kg IV, typically in three divided doses). Alemtuzumab was the preferred induction agent during the study period. Basiliximab was chosen for patients thought to be frail. Maintenance immunosuppression consisted of either tacrolimus and zortress (initial trough goals of 3–5 ng/ml) or standard dose tacrolimus (trough 8–11 ng/ml) in combination with mycophenolate mofetil (1 gm bid) or mycophenolic acid (720 mg bid). Patients receiving alemtuzumab induction did not receive any steroids following an initial four dose taper of intravenous methylprednisolone. Patients undergoing basiliximab or antithymocyte globulin received oral prednisone as part of their initial maintenance immunosuppression, with weaning determined on a case by case basis. The immunosuppression regimen was not modified for patients with delayed graft function.

Results

There were 190 patients included in the study, 141 of who received deceased donor transplants and 49 who underwent living donor transplants. The majority (61.6%) of patients were Caucasian (58.7%) males with a mean age of 53.8(14.7) years. The mean length of stay following transplantation was 4.5(4.1) days. The remaining patient demographics are presented in Table 1. The ninety day readmission rate was 36.8%, while ninety day mortality was 1.6%. A total of 14 (7.4%) patients required an unplanned return to the operating room within 90 days of kidney transplantation.

Table 1
Overall cohort characteristics. Continuous variables are expressed as mean (standard deviation) and categorical variables are expressed as count (percent).

Age	53.8 (14.7)
Male	88 (62.4%)
Race	
African American	64 (33.7%)
Caucasian	117 (61.6%)
Hispanic	3 (1.6%)
Asian	5 (2.6%)
Native American	1 (0.5%)
Recipient Diabetes	72 (38.0%)
Pretransplant Dialysis	166 (87.4%)
Previous Kidney Transplant	22 (11.6%)
Calculated PRA	25.7 (36.0)
KDPI (for deceased donors)	35.3(23.2)
Ischemic Time (minutes)	675 (477)
Delayed Graft Function	42 (22.1%)
LOS Post Transplant (days)	4.5 (4.1)
90 Day Readmission	70 (36.8%)
90 Day Mortality	3 (1.6%)
Creatinine at 30 Days	1.67 (1.01)
Creatinine at 3 Months	1.38 (0.52)
Creatinine at 6 Months	1.33 (0.47)
Unplanned Reoperation	14 (7.4%)

The median day of reoperation post kidney transplant was 12.5(range 0–83). Half of unplanned reoperations occurred during the index hospitalization for the transplant procedure, while the remaining occurred during a readmission. Reoperative patient demographics and circumstances of reoperation are summarized in Table 2. Four reoperations were performed for ultrasound findings concerning for vascular compromise. In two of these cases (one live donor and one deceased donor) the kidney was found to be well perfused without any vascular complication. In one case (a pediatric en-bloc kidney) there was malperfusion of the graft due to torsion which was salvaged by repositioning. In the final case (a living donor), arterial inflow was compromised due to a technical error which required reimplantation of the graft. Two reoperations were for bleeding (one was from a percutaneous biopsy site, the other was from an intraoperative biopsy site that bled late due to supratherapeutic enoxaparin started for an internal jugular vein thrombus). The remainder of reasons for reoperation included adhesive small bowel obstruction, acute cholecystitis with choledocholithiasis, perforated diverticulitis (2 cases), hip fracture, thrombosis of a dialysis fistula, perinephric hematoma, and tracheostomy performed for post-transplant respiratory failure. Overall, 28.6% of reoperations were for acute general surgery indications. Six (42.9%) of the reoperations were unrelated to the technical conduct of the transplant operation (the bowel obstruction was deemed transplant related as the point of obstruction was an adhesion to the transplanted kidney). When stratified by donor type, 8.2% (4 patients) of living donor recipients underwent unplanned reoperation compared to 7.1% (10 patients) of deceased donor recipients ($p = 0.759$). Three of the reoperations (75%) in the living donor group were transplant related, while only 50% (5 reoperations) were transplant related in the deceased donor group ($p = 0.580$).

Recipients who underwent reoperation were significantly older than those who did not (61.6 vs. 53.2 years; $p = 0.04$). Neither race nor gender were significantly different in the patient undergoing unplanned reoperation versus those who did not (Table 3). History of previous kidney transplant, pre-transplant dialysis, and diabetes were also not significantly associated with unplanned reoperation. Delayed graft function (requirement for dialysis within 7 days following transplantation) was more common in patients undergoing reoperation (71.4% vs. 18.2%; $p < 0.001$). There was a significant trend towards longer length of stay in the patient undergoing reoperation (12.1 days vs. 3.9 days; $p = 0.023$), while readmission was significantly more frequent in the reoperation group (78.6% vs. 33.5%; $p = 0.001$). Death within 90 days of transplant was significantly more common in those undergoing reoperation (14.3% vs. 0.6%; $p = 0.015$). Graft function (defined by serum creatinine) was worse at 30 days in the reoperation group but became similar by 3 and 6 months post-transplant(Table 3).

Unadjusted overall patient survival was significantly less in the patients who required early reoperation (Fig. 1). Three, six, and twelve month survival were 99.4%, 98.9%, and 96.6% for patients who did not require reoperation versus 85.7%, 78.6%, and 78.6% for patients who required reoperation ($p < 0.001$). The cumulative incidence of graft failure (excluding death with a functioning graft) at 3, 6, and 12 months was not significantly different in patients who underwent reoperation versus those who did not (0.6%, 1.2%, 2.6% vs. 0.0% at all points, respectively; $p = 0.728$).

Discussion

This study demonstrated an unplanned reoperation rate of 7.4%

Table 2
Details of patients undergoing unplanned return to the operating room.

Age	Gender	Donor Type	Diabetic	Pretransplant Dialysis	Indication for Reoperation	Post Transplant Day of Reoperation	Transplant Related
60	M	Deceased	Yes	Yes	Bleeding from intraoperative biopsy site while supratherapeutic on anticoagulation	8	Yes
66	F	Deceased	Yes	Yes	Bleeding from percutaneous biopsy site	13	Yes
77	M	Deceased	Yes	Yes	Perforated Diverticulitis	83	No
78	F	Deceased	No	Yes	Perforated Diverticulitis	5	No
64	F	Deceased	No	Yes	Small Bowel Obstruction from adhesion to transplanted kidney	12	Yes
74	F	Deceased	No	Yes	Cholecystitis	14	No
54	F	Deceased	No	Yes	Tracheostomy for Respiratory Failure	17	Yes
63	M	Deceased	Yes	Yes	Hip Fracture after fall	64	No
73	F	Living	Yes	Yes	Clotted Dialysis Fistula	31	No
63	M	Living	Yes	No	Open Biopsy for Graft Dysfuction, Washout of hematoma	34	Yes
44	M	Deceased	No	Yes	No flow on ultrasound, on complication found on exploration	0	Yes
71	M	Living	Yes	Yes	Possible Renal Vein Thrombosis on Ultrasound, Vein patent on exploration	3	Yes
36	F	Deceased	No	Yes	Poor Flow on Ultrasound, kidneys (en-bloc) torsed at reoperation, repositioned	0	Yes
40	F	Living	No	No	Poor Flow on Ultrasound, arterial complication on exploration, kidney reimplanted	1	Yes

within 90 days of renal transplantation. Half of these cases occurred during the index administration (3.7% of all patients). The most common indication for reoperation was postoperative ultrasound findings concerning for a vascular complication. Half of these reoperations proved nontherapeutic, with a well perfused kidney and no evidence of vascular compromise found on re-exploration. In the remaining two cases, a pediatric en-bloc transplant and a live donor transplant with two renal arteries, early exploration allowed for graft salvaging intervention. Whether Doppler ultrasound is performed on a routine basis or selectively following kidney transplant varies by center, and there is little data in the literature to guide one practice or the other. Matar performed a study of 80 routine ultrasound examinations in pediatric kidney transplant recipients and found that only one study abnormality led to an intervention.[10] In our study, ultrasound findings led to a graft saving intervention in half of cases while the other half led to unnecessary reoperation. In special cases such as pediatric-enbloc grafts or living donor transplants with unexpected poor early function, it may be the case that routine postoperative doppler ultrasound is beneficial (although we really can't draw solid conclusions based on so few cases); however, further study in larger numbers of cases will be necessary to determine whether a selective or routine postoperative ultrasound is the better strategy.

Bleeding was another of the most common individual indications for reoperation. Both episodes of bleeding in this study were from biopsy sites, with one occurring on postoperative day 8 in a patient supratherapeutic on anticoagulation, and the other occurring on postoperative day 13 from a percutaneous biopsy site obtained for evaluation of delayed graft function. These cases highlight the importance of careful attention to anticoagulation therapy when it is required as well as the need to be judicious in the use of percutaneous biopsy in the perioperative period.

The findings in our compare favorably to the 26.3% reoperation rate reported by Birkmeyer's study examining reoperation within 30 days of renal transplant.[1] Urologic complications are highlighted as an important reason for reoperation in Birkmeyer's study.[1] Perhaps more in line with expectations, Moghadamyeghaneh reported a 2.2% rate of reoperation during the index

Table 3
Comparison between patients who underwent reoperation and those who did not. Continuous variables are expressed as mean (standard deviation) and categorical variables are expressed as count (percent).

	No Reoperation (n = 131)	Reoperation (n = 10)	p-value
Age	53.2 (14.7)	61.6 (13.6)	**0.039**
Male	105 (60.0%)	6 (42.9%)	0.21
Race			0.888
African American	60 (34.1%)	4 (28.6%)	
Caucasian	107 (60.8%)	10 (71.4%)	
Hispanic	3 (1.7%)	0 (0%)	
Asian	5 (2.8%)	0 (0%)	
Native American	1 (0.6%)	0 (0%)	
Recipient Diabetes	65 (36.9%)	7 (50.0%)	0.332
Pretransplant Dialysis	154 (87.5%)	12 (85.7%)	0.692
Previous Kidney Transplant	20 (11.4%)	2 (14.3%)	0.668
Calculated PRA	25.5 (35.7)	27.9 (41.0)	0.813
KDPI (deceased donors only)	34.3 (23.1)	48.6 (21.0)	0.06
Ischemic Time (minutes)	665.1 (474.2)	805.2 (514.2)	0.292
Delayed Graft Function	32 (18.2%)	10 (71.4%)	< **0.001**
LOS Post Transplant (days)	3.9 (1.6)	12.1 (11.9)	< **0.001**
90 Day Readmission	59 (33.5%)	11 (78.6%)	**0.001**
90 Day Mortality	1 (0.6%)	2 (14.3%)	**0.015**
Creatinine at 30 Days	1.62 (0.98)	2.37 (1.31)	**0.01**
Creatinine at 3 Months	1.36 (0.48)	1.56 (0.93)	0.448
Creatinine at 6 Months	1.33 (0.47)	1.47 (0.57)	0.343

Bold indicates statistical significance at the $p < 0.05$ level.

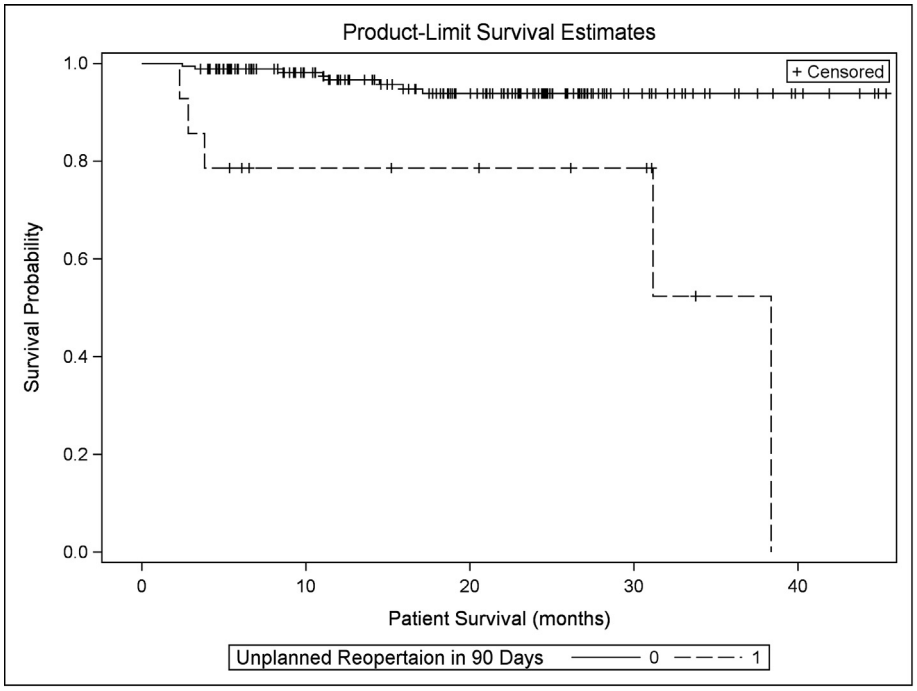

Fig. 1. Kaplan-Meier estimates of patient survival (in months) for those who underwent reoperations versus those who did not.

hospitalization in a study utilizing the National Inpatient Sample (NIS).[8] Early reoperations in the NIS study were most commonly due to bleeding (64% of reoperations), followed by urologic complications. The most common day for reoperation in that study was postoperative day 1[8].

Surprisingly, nearly 43% of all reoperations in this study were not at the original operative site or related to the technical conduct of the transplant operation itself. This stands in contrast to Birkmeyer's finding in a wider cohort of general surgery patients that 85% of reoperations resulted from problems at the original surgical site.[1] This finding suggests that unplanned return to the operating room is not as useful of a quality indicator for renal transplantation as it is in other general surgery specialties, particularly for deceased donor transplantation. One of the most common complications resulting in reoperation was perforated diverticulitis, which occurred in two patients on postoperative days 5 and 83, respectively, resulting in one morality. Perforated diverticulitis is a relatively well described complications following kidney transplantation, and is reported to occur in approximately 1–2% of patients.[11,12] Although this incidence may be lessened by elective sigmoidectomy prior to transplant in patients with a history of symptomatic diverticulitis, such an approach would be impractical and likely harmful for all patients with diverticulosis. Perforated diverticulitis in an immunosuppressed patient does have a more subtle presentation and is associated with high morbidity and mortality, so a high index of suspicion and aggressive workup are required for renal transplant patients presenting with lower abdominal pain.

The remainder of complications leading to reoperation in this study cohort included bowel obstruction, cholecystitis, hip fracture, and prolonged respiratory failure requiring tracheostomy. With the exception of the bowel obstruction, these complications were unrelated to the site of the kidney operation and thus not truly useful as a quality indicator for renal transplant. One could make the argument that they are related to the transplant event; however, as it is likely that immunosuppression played a significant role in each complication. This highlights the importance of vigilance in avoiding over-immunosuppression and in maintaining a high index of suspicion for acute abdominal conditions such as cholecystitis and diverticulitis in immunosuppressed patients.

It is worth noting the dichotomy in reasons for reoperation with living versus deceased donor transplantation. Three of four reoperations in the living donor cohort were at the original operative site and thus deemed to be related to the index operation. This stands in contrast to deceased donor transplant, in which only 50% of reoperations were related to the transplant procedure. The shorter vessels involved in live donor transplantation and the inability to have a Carrell patch with multiple arteries may play a role in this difference. Another contributing factor may be the expectation of immediate graft function in living donor transplant, with an increased index of suspicion for technical complications in the case of slow or delayed graft function. This high index of suspicion could lead to additional ultrasounds, with potentially misleading findings, as well as a lower threshold to re-explore the graft to definitively rule out a potentially reversible technical complications.

Unplanned reoperation following kidney transplantation represents a major setback to an already medically fragile group of patients. One year survival for patients who require reoperation is 18% lower than for those who don't require reoperation. For those who do survive; however, renal graft survival and function does not appear to be significantly affected. One potential confounding factor in our analysis of graft survival is the fact that delayed graft function was more common in the reoperation group. Since delayed graft function is a well-studied risk factor for decreased graft survival, the higher DGF prevalence in the reoperation group may likely introduces significant confounding into the association between return to the operating room and graft survival. Unfortunately, there were not enough graft losses in the study to permit the sort of robust multivariable analysis that would be needed better clarify any potential causal relationship between reoperation subsequent graft loss. The relationship between delayed graft

function and unplanned reoperation is also worth dissecting. An early complication requiring reoperation such as bleeding can certainly result in renal injury in the form of acute tubular necrosis and subsequently delayed graft function. There is also the possibility that delayed graft function may play a causative role in the path of events that lead to reoperation. For example, a kidney with unexpected poor early function may cause the surgeon to order more ultrasounds, which has the potential to lead to nontherapeutic reoperations as discussed above.

In summary, unplanned reoperation is a relatively uncommon event following kidney transplantation, and is frequently unrelated to the technical conduct of the transplant operation itself. The remainder of reoperations are due to general surgery type complications and are likely influenced by immunosuppression. The weakness of this study is its single center nature, small sample size, and the infrequency of the event of interest (reoperation), which does not permit for meaningful multivariable analysis of factors contributing to reoperation. The strength of the study is that it follows patients beyond the index hospitalization and early perioperative period, which is a frequent limitation of large scale database studies which may thus miss capturing events.[8]

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