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Surgical Approach, Cost, and Complications of Appendectomy in Kidney Transplant Recipients

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Abstract

Kidney transplant recipients (KTR) have greater morbidity and length of stay (LOS) following certain surgical procedures than non-KTR. Given that appendectomy is one of the most common surgical procedures, we investigated differences in outcomes between 1336 KTR and 2,640,247 non-KTR post-appendectomy at transplant and non-transplant centers in the US from 2000–2011, using NIS data and adjusting for patient and hospital level factors. Postoperative complications were identified using ICD9 codes. Among KTR, there were no post-appendectomy in-hospital deaths, compared to a 0.2% in non-KTR ($p=0.5$). Overall complications were similar among KTR and non-KTR (17.0% vs 11.6%; aOR:0.77_{1.12}_{1.61}). LOS and costs were greater for KTR compared to non-KTR (LOS ratio 1.19_{1.31}_{1.45}; cost ratio 1.11_{1.17}_{1.26}). Only 44.8% of KTR had laparoscopic approach compared to 54.5% of non-KTR, but had similar complication rates (10.6 vs 8.7%, $p=0.5$). When treated at transplant centers, KTR had similar complications (aOR 0.44_{0.79}_{1.43}), but longer LOS (ratio 1.21_{1.37}_{1.55}) and greater hospital-associated costs (ratio 1.19_{1.29}_{1.41}) than non-KTR. Conversely, at non-transplant centers, KTR and non-KTR had similar complications (aOR

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0.751.23_{2.0}), LOS (ratio 0.840.96_{1.09}), and cost (ratio 0.931.01_{1.10}). Contrary to other procedures, KTR did not constitute a high-risk group for patients undergoing appendectomy.

Keywords

general surgery; kidney transplantation; appendectomy

INTRODUCTION

Appendicitis is one of the most common surgical diseases in the United States, with a lifetime risk of 6.7% in females and 8.6% in males.¹ Like the general population, kidney transplant recipients (KTR) are at risk of requiring appendectomy, although the incidence of appendicitis in KTR has not been well documented outside of small case series.^{2–9} Further, while post-appendectomy morbidity is low in the general population (4.1–6.4%) and average post-operative length of stay (LOS) is short (0–2.4 days), it is unknown if risk, LOS, and thus hospital associated cost is amplified for KTR.^{10,11} As post-transplant survival improves, the number of KTR undergoing appendectomy will likely increase proportionally.^{3,12,13} Therefore, improved understanding of morbidity, length of stay, and associated cost in this population is important for peri-operative planning and risk stratification.

Previous studies have reported that post-operative outcomes for solid organ transplant recipients following general surgical procedures are worse than the general population, with a recent review citing up to 32.7% mortality and 17.5% morbidity for emergency abdominal surgery, in comparison to 9% morbidity in non-transplant recipients.^{2,11} For appendectomy specifically, in the largest case-series to date that included transplant recipients, there were only 17 appendectomies reported, and only 3 of those performed on KTR. In this small population, the documented complication rate was surprisingly high at 24%. Additionally, these patients had a mean length of stay of 7 days, compared to a median 1 day reported recently for non-transplant patients.^{3,11} However, many transplant providers feel that morbidity, LOS and cost might be mitigated if transplant recipients receive their surgical care at transplant centers.^{14,15}

Additionally, the surgical approach for appendectomy has changed over time. Currently, laparoscopic appendectomy is the standard approach, with 76% of appendectomies performed laparoscopically as of 2010.¹¹ However, controversy still exists regarding the safety and appropriateness of the laparoscopic approach for transplant recipients. While a recent review discussing the role of laparoscopy in transplant recipients advocated for the broader application of laparoscopy in the KTR population, it only cited a 2-patient case series of KTR safely undergoing appendectomy.^{16,17} The lack of literature supporting the safety of laparoscopic appendectomy among KTR may be inhibiting more widespread utilization of this approach.

To investigate the differences in surgical approach, mortality, morbidity, length of stay and cost between KTR and non-KTR undergoing appendectomy, we studied a large population of patients undergoing this procedure using the National Inpatient Sample. We also

investigated the effect of receiving surgical care at a transplant center on approach and post-operative outcomes.

METHODS

Study population

We studied 1336 adult KTR and 2,640,247 non-KTR undergoing appendectomy for appendicitis from January 1, 2000 – December 31, 2011. We included all patients who had International Classification of Disease, Ninth Revision (ICD-9) procedure codes for laparoscopic or open appendectomy and an ICD-9 diagnosis code for appendicitis. KTR were distinguished from non-KTR by the presence of ICD-9 diagnosis codes consistent with prior KT. We excluded patients with ICD-9 codes indicating a history of other solid or non-solid organ transplants (Appendix A).

Data Source

Patients were drawn from the Nationwide Inpatient Sample (NIS). Available through the Health Care Cost and Utilization Project, the NIS contains data from approximately 7 million hospital stays yearly, and is made up of a stratified sample of 20% of the non-federal hospitals in the United States. The stratified sample is self-weighted to allow for population based estimates.¹⁸ Information provided in the NIS includes patient level hospital discharge data such as patient demographics, as well as diagnostic and procedural ICD9 codes for the index hospital admission. All study methods were approved by the Johns Hopkins Hospital Institutional Review Board.

Patient and Hospital Level Characteristics

In addition to examining basic demographic information of the study population and surgical approach (laparoscopic vs open), the Charlson Comorbidity Index score was calculated for each patient.^{19,20} Hospital characteristics examined included standard NIS categories of location (rural or urban), size (small, medium, large), teaching status, and region (north east, mid-west, south, or west). In addition, we categorized hospitals as transplant centers or non-transplant centers, where a transplant center was defined as a hospital where at least one kidney transplant was performed during the study period.

Surgical Outcomes

Between-group characteristics were compared using chi-squared tests for categorical variables and t-tests for continuous variables. We defined peri-operative mortality as a death during the index hospital admission. Peri-operative morbidity, defined as the occurrence of intraoperative or postoperative complications during the index hospital admission, was identified by ICD9 code and categorized into system-based groups as established in previous studies (Appendix B).²¹ Multi-level (hierarchical) regression models with random intercepts for each hospital were adjusted for patient-level (sex, age, African American race, Charlson Comorbidity Index, primary insurance status, and surgical approach) and hospital-level factors (location, size, region, teaching status, and transplant center status). Complication rates were compared using hierarchical logistic regression. Length of stay was examined using hierarchical negative binomial regression. A mixed linear regression model was used

to examine log transformed costs, which were determined using the NIS cost-to-charge ratio files.

Transplant Center

We also investigated effect modification the above outcomes based on whether the appendectomy was performed at a transplant center or a non-transplant center. To evaluate the effect of transplant center status on the relationship of KTR and the outcomes above, we created an interaction term for KTR status with transplant center status in an approach similar to the regression models described above.

Statistical Analysis

Confidence intervals are reported as per the method of Louis and Zeger.²² Statistical analysis was performed using Stata 14.0 (StataCorp, College Station, Texas). For all analyses, a two-tailed p-value of < 0.05 was considered statistically significant.

RESULTS

Study Population

Out of 2,641,583 appendectomies performed for appendicitis during the study period, 1336 (0.05%) were done in KTR. KTR were older (46.5 vs 40.6 years, $p < 0.001$), more likely to be African American (13.6 vs 7.0%, $p < 0.001$), carried a greater comorbidity burden as reflected by a higher Charlson Comorbidity Index score (28.6% vs 4% with score 2, $p < 0.001$), less likely to be female (41.6 vs 47.1%, $p = 0.07$), and less likely to have private insurance (40.6 vs 60.6%, $p < 0.001$). Nearly half (49.6%) of all appendectomies performed on KTR were performed at one of the 222 hospitals identified as transplant centers, whereas only 13% of non-KTR had appendectomies at transplant centers (Table 1).

Mortality and Morbidity

Among KTR, there were no in-hospital deaths following appendectomy, compared to a 0.2% incidence in non-KTR ($p = 0.5$). The crude rate of overall morbidity was 17% for KTR vs 11.6% for non-KTR ($p = 0.003$). Specifically, KTR had higher rates of wound complications (2.5% vs 0.5%, $p < 0.001$), infectious complications (4.9% vs 1.7%, $p < 0.001$), and pulmonary complications (4.3% vs 1.7%, $p < 0.001$) (Table 2). However, after adjusting for patient and hospital level factors, the odds of overall morbidity were the same comparing KTR vs non-KTR (aOR 0.77 1.12_{1.61}), although the odds of infectious (aOR 1.24 2.24_{4.08}), pulmonary (aOR 1.01 1.97_{3.81}), and mechanical wound complications (aOR 1.54 3.54_{8.09}) were still significantly higher for KTR (Table 3).

Length of Stay and Cost

Median length of stay was 3 days in KTR vs 2 days in non-KTR ($p < 0.001$) (Table 2). After adjusting for patient and hospital level characteristics including operative approach, LOS was 1.31-fold longer for KTR (ratio 1.19 1.31_{1.45}) (Table 3). The average cost for appendectomy was \$9,175 for KTR and \$6,806 for non-KTR ($p < 0.001$). After adjusting for

patient and hospital level characteristics including operative approach, cost was 1.17-fold higher for KTR (ratio 1.11 1.17 1.26).

Surgical Approach

Appendectomy was performed laparoscopically in 44.8% of KTRs compared to 54.4% of non-KTRs ($p = 0.002$). KTR had significantly more complications following open appendectomy than non-KTR (22.4% vs 14.8%, $p 0.009$), but a similar complication rate following laparoscopic approach (10.6% vs 8.7%, $p 0.5$) (Table 4). Comparing laparoscopic and open approach in KTR only, there were significantly fewer wound (0% vs 4.6%, $p 0.016$) and gastrointestinal (3.2% vs 9.9%, $p 0.03$) complications following laparoscopic approach (Table 5). Compared to non-KTR, KTR had longer LOS following both laparoscopic (3 vs 2 days, $p < 0.001$) and open approaches (4 vs 3 days, $p < 0.001$). Additionally, cost was higher for KTR following both laparoscopic and open procedures when compared to non-KTR (lap \$8676 vs \$7063, $p < 0.001$; open \$9901 vs \$6308, $p < 0.001$) (Table 4).

Transplant Center Status

When treated at transplant centers, KTR had similar morbidity to non-KTR (aOR 0.44 0.79 1.43). However, after adjustment, LOS was 1.37-fold longer for KTR compared to non-KTR at transplant centers (ratio 1.21 1.37 1.55). Additionally, after adjustment, hospital associated cost was 1.29-fold higher for KTR than non-KTR at transplant centers (ratio 1.19 1.29 1.41). When treated at non-transplant centers, KTR and non-KTR had similar morbidity, LOS, and cost (Table 6). After controlling for patient and hospital level factors, KTR were significantly less likely to have a laparoscopic procedure at transplant centers than non-KTR (aOR 0.36 0.55 0.85).

DISCUSSION

As the largest national study of kidney transplant recipients undergoing appendectomy, we report that KTR have similar mortality (0% vs 0.2%) and overall morbidity (17.0% vs 11.6% in-hospital complication rate) as non-KTR. However, KTR are more susceptible to wound (aOR 1.54 3.54 8.09), infectious (aOR 1.24 2.24 4.08), and pulmonary complications (aOR 1.01 1.97 3.81) than non-KTR. While KTR had significantly longer LOS (ratio 1.37) and higher cost (ratio 1.29) than non-KTR at transplant centers, there was no difference in cost or length of stay between KTR and non-KTR at non-transplant centers.

We found that 0.05% of appendectomies for appendicitis were performed in KTR. Estimates of the incidence of appendectomy in solid organ transplant recipients is similar with reports ranging from 0.18% to 0.29%.^{2,3} Our finding of no mortalities in KTR in the NIS was consistent with low mortality published in case reports and small series on appendectomy in KTR^{2-6,9}, though a single-center series of 416 KTR undergoing abdominal surgery reported a 30% mortality rate, but only two of these 416 cases were appendectomies.¹² Further, we found that there was not a higher complication rate overall for KTR compared to non-KTR undergoing appendectomy. The largest single-center series of 17 cases of appendicitis in solid organ recipients reported a post-appendectomy complication rate of 24%³, similar to

the 17% complication rate in KTR in our study. These findings support our hypothesis that although KTR have been shown to have higher morbidity and mortality following abdominal surgery¹², appendectomy may not follow this pattern.^{2,3}

Although we did not find a difference in overall complication rate between KTR and non-KTR, we did find that KTR suffered more wound, infectious, and pulmonary complications. This is likely influenced by immunosuppression. The impact of immunosuppression on wound healing and increased risk of infection is well documented in the literature, particularly in the immediate post-transplant setting.^{23–26} Even with modern immunosuppressant regimens including agents such as mycophenolate mofetil and tacrolimus, higher rates of wound healing and infectious complications have been documented in KTR.^{27–29}

We found that KTR have a 1.3-fold longer LOS than non-KTR, with a longer median LOS for both laparoscopic appendectomy (KTR 3 days, non-KTR 2 days) and open appendectomy (KTR 4 days, non-KTR 3 days) as compared to the median 1 day LOS that Ingraham et al. reported in their study of National Surgical Quality Improvement Project (NSQIP) data.¹¹ This might be influenced by the use of laparoscopy. We found that the rate of use of laparoscopy was much lower in both KTR (44.8%) and non-KTR (54.6%) compared to 76% laparoscopic appendectomy from the NSQIP database.¹¹ Importantly, we found that complication rates for laparoscopic appendectomy were not higher than for open appendectomy in KTR, confirming the findings of small case series.^{16,17} This suggests that laparoscopic appendectomy is safe for appropriately selected KTR, and although this has been alluded to, this has not been demonstrated previously in a qualitative manner. Additionally, we report costs ranging from \$6,000–9,000. A prior study of total hospital charges for appendectomy, which are higher than costs, reported a range of total charges from \$20,000 to nearly \$39,000.¹⁰ While we found that KTR had significantly higher cost than non-KTR, we were limited by the nature of our study data in more granular examination of costs.

Despite the sentiment expressed in multiple opinion pieces including book chapters and editorials, there is no evidence demonstrating improved outcomes for transplant recipients at transplant centers.^{14,30} Indeed, we found no difference in morbidity and mortality between KTRs treated at transplant centers and non-transplant centers, however, we did find an increase in length of stay and cost at transplant centers.

This study has a few limitations which warrant further discussion. An important limitation is the lack of clinical granularity of NIS data. For example, the NIS does not include information on transplant laterality or history of previous KTR, therefore we were not able to adjust for these potential confounders. Additionally, without more detailed information on the specific costs and events occurring during a hospital stay, we are unable to determine the underlying reasons for cost and length of stay differences between KTR and non-KTR, and between transplant centers and non-transplant centers. We were unable to determine whether, for example, those KTR presenting to non-transplant centers who were sicker were transferred to transplant centers for care. An additional limitation inherent in the design of the NIS is the lack of linkage of patients across multiple hospitalizations. The magnitude of

the NIS, however, offers an understanding of the national outcomes of surgically treated appendicitis in KTR and avoids the bias and limited power associated with single-center studies. Finally, there has been a recent surge in non-operative management of appendicitis, however we cannot reliably assess this using the NIS, so we limited our study to operative management.

In conclusion, we report that kidney transplant recipients have similar rates of overall complications when compared to non-transplant recipients. Despite similar complication rates, appendectomy at transplant centers is associated with longer LOS and higher cost for KTR, but it is unclear what is driving this major discrepancy. Our findings suggest that, in certain KTR, appendectomy at non-transplant centers using a laparoscopic approach is safe and cost effective.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix A. ICD9 codes for diagnosis, procedure, inclusion and exclusion criteria

Diagnosis

Appendicitis 540.0, 540.1, 540.9, 541, 542, 789.03

Procedure

Appendectomy, laparoscopic 47.07

Appendectomy, open 47.0

Inclusion

Kidney transplant recipient: V42.0

Exclusion

Other (non-kidney) transplant recipients: V42.1, V42.2, V42.6, V42.7, V42.8, V42.81, V42.82, V42.83, V42.84, V42.89, V42.9

Complications from history of other (non-kidney) transplant: 996.80, 996.82, 996.83, 996.84, 996.85, 996.86, 996.87, 996.88, 996.89

Appendix B. International Classification of Diseases, 9th Revision, clinical modification codes for postoperative in-hospital complications. Adapted from Guller et al.²¹

Mechanical Wound

Delayed wound healing, 998.83

Postoperative hematoma, 998.12

Postoperative seroma (non-infected), 998.13

Disruption of operative wound, 998.3

Persistent postoperative fistula, 998.6

Infectious

Postoperative infection, 998.5

Postoperative skin abscess, 998.59

Postoperative septic wound complications, 998.59

Postoperative skin infection, 998.59

Postoperative intraabdominal abscess, 998.59

Postoperative subdiaphragmatic abscess, 998.59

Postoperative infected seroma, 998.51

Urinary

Postoperative urinary retention, 997.5

Postoperative urinary tract infection, 997.5
Pulmonary
Postoperative atelectasis, 997.3
Postoperative pneumonia, 997.3
Postoperative acute respiratory insufficiency, 518.5
Postoperative acute pneumothorax, 512.1
Adult respiratory distress syndrome, 518.5
Postoperative pulmonary edema, 518.4
Gastrointestinal tract
Postoperative small-bowel obstruction, 997.4
Postoperative ileus, 997.4
Postoperative ileus requiring nasogastric tube, 997.4
Postoperative nausea, 997.4
Postoperative vomiting, 997.4
Postoperative pancreatitis, 997.4
Complication of anastomosis of gastrointestinal tract, 997.4
Cardiovascular
Postoperative deep venous thrombosis, 997.79
Postoperative pulmonary embolism, 415.11
Postoperative stroke, 997.02
Phlebitis or thrombophlebitis from procedure, 997.2
Cardiac arrest/insufficiency during or resulting from a procedure, 997.1
Intraoperative
Accidental puncture or laceration, complicating surgery, 998.2
Foreign body accidentally left during procedure, 998.4
Hemorrhage/bleeding complicating procedure, 998.11

Table 1

Characteristics of the study population and procedure details.

	KTR (n=1,336)	Non-KTR (n=2,640,247)	p-value
Age, mean (SD)	46.5 (13.0)	40.6 (16.6)	<0.001
Female, %	41.6	46.9	0.07
African American, %	13.6	6.9	<0.001
Charlson Comorbidity Index, %			<0.001
0	43.8	85.0	
1	27.6	10.9	
2	28.6	4.1	
Insurance Status, %			<0.001
Public	57.2	21.2	
Private	40.6	60.7	
Other	2.3	18.3	
Laparoscopic, %	44.8	54.4	0.002
Performed at transplant center, %	49.6	13.0	<0.001

Table 2

Unadjusted outcomes following appendectomy in kidney transplant recipients vs non-transplant patients.

Outcome	KTR (n = 1336)	Non-KTR (n = 2,640,247)	P value
Mortality (%)	0	0.2	0.5
Any Complication (%)	17.0	11.6	0.003
System specific complications [^] (%)			
Wound	2.5	0.5	<0.001
Infection	4.9	1.7	<0.001
Pulmonary	4.3	1.7	<0.001
Cardiovascular	0	0.5	0.3
Genitourinary	1.1	0.6	0.3
Gastrointestinal	6.9	7.1	0.9
Intraoperative	1.4	0.8	0.2
LOS, median days (IQR)	3 (2–6)	2 (1–4)	<0.001
Cost, median \$ (IQR)	9,175 (6,715–13,915)	6,802 (5,076–9,358)	<0.001

[^] see Appendix B for breakdown of complications by system

Table 3

Adjusted outcomes following appendectomy in kidney transplant recipients vs non-transplant patients ^{*}.

Outcome	KTR vs Non-KTR	95% CI
Any complications, OR	1.12	0.77–1.61
System specific complications [^] , OR		
Wound	3.54	1.54–8.09
Infection	2.24	1.24–4.08
Pulmonary	1.97	1.01–3.81
Genitourinary	1.18	0.29–4.82
Gastrointestinal	0.75	0.44–1.28
Intraoperative	1.23	0.39–3.86
LOS, ratio	1.31	1.19–1.45
Cost, ratio	1.17	1.11–1.26

^{*} adjusted age, race, gender, Charlson comorbidity score, insurance status, operative approach, hospital bed size, hospital region, teaching status, transplant center status

[^] see Appendix B for breakdown of complications by system

Table 4

Unadjusted outcomes following laparoscopic vs open appendectomy in kidney transplant recipients and non-transplant patients.

Outcome	KTR (n = 1336)	Non-KTR (n = 2,640,247)	P value
Any Complication (%)	17.0	11.6	0.003
Laparoscopic	10.6	8.7	0.5
Open	22.4	14.8	0.009
LOS, median days (IQR)	3 (2–6)	2 (1–4)	<0.001
Laparoscopic	3 (1–4)	2 (1–3)	<0.001
Open	4 (2–7)	3 (2–5)	<0.001
Cost, median \$ (IQR)	9,175 (6,715–13,915)	6,802 (5,076–9,358)	<0.001
Laparoscopic	8,676 (6,575–11,524)	7,063 (5,520–9,230)	<0.001
Open	9,901 (6,787–15,832)	6,308 (4,496–9,627)	<0.001

[^] see Appendix B for breakdown of complications by system

Table 5

Outcomes following laparoscopic vs open appendectomy in kidney transplant recipients ONLY.

Outcome	Laparoscopic (n = 599)	Open (n = 737)	P value
Performed at transplant center (%)	40.7	59.3	0.003
Any complications (%)	10.6	22.4	0.009
System specific complications [^] (%)			
Wound	0	4.6	0.016
Infection	4.1	5.9	0.5
Pulmonary	2.6	5.7	0.2
Cardiovascular	0	0	1.0
Genitourinary	0.8	1.3	0.7
Gastrointestinal	3.2	9.9	0.03
Intraoperative	0.8	2.0	0.4
LOS, median days (IQR)	3 (1–4)	4 (2–7)	<0.001
Cost, median \$ (IQR)	8,676 (6575 – 11524)	9,901 (6787–15,832)	0.07

[^] see Appendix B for breakdown of complications by system

Table 6

Adjusted outcomes of kidney transplant recipients vs. non-transplant patients by center type.

Outcome	Transplant center	Non-transplant center	p-value for interaction
Any complications, OR	0.95 (0.54–1.67)	1.23 (0.75–2.0)	0.5
LOS, ratio	1.36 (1.22–1.55)	0.96 (0.84–1.08)	<0.001
Cost, ratio	1.29 (1.19–1.41)	1.01 (0.93–1.10)	0.004
Laparoscopic approach	0.55 (0.36–0.85)	0.79 (0.51–1.21)	0.2