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Complications, Length of Stay, and Cost of Cholecystectomy in Kidney Transplant Recipients

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Abstract

Background: Kidney transplant recipients (KTR) are at increased risk of requiring cholecystectomy. Given physiologic impacts of renal replacement and lifelong immunosuppression, cholecystectomy may be riskier in this unique population.

Methods: Using the National Inpatient Sample, we compared 7,318 KTR to 5,341,427 non-transplant recipients following cholecystectomy from 2000–2011, and investigated outcomes of mortality, morbidity, length of stay (LOS) and cost, adjusting for patient and hospital level factors.

Results: For KTR compared to non-KTR, in-hospital mortality (2.7% vs 1.2%, $p < 0.001$) and morbidity (18.8% vs 13.9%, $p < 0.001$; aOR 1.30 95%CI 1.12–1.51) were higher. LOS and costs were also greater (LOS ratio 1.23 95%CI 1.17–1.28; cost ratio 1.13 95%CI 1.08–1.17). When comparing outcomes at transplant and non-transplant centers, we found no differences.

Conclusions: KTR have higher mortality and morbidity, longer LOS, and greater cost following cholecystectomy compared to non-transplant recipients. Physicians should consider these elevated risks when planning for surgery in KTR and counsel patients accordingly

Summary:

We hypothesized that cholecystectomy may be riskier for kidney transplant recipients (KTR) given their lifelong immunosuppression, physiologic impact of renal failure, and increased risk of gallstone and biliary disease. Using NIS, we compared mortality, morbidity, length of stay and cost in KTR vs non-KTR following cholecystectomy in the US from 2000–2011, adjusting for patient and hospital level factors, including transplant center status. Mortality was higher (OR 2.4), morbidity was higher (OR 1.3), LOS was longer (ratio 1.2), and costs were greater (ratio 1.1) for

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KTR compared to non-KTR following cholecystectomy. While it is clear that KTR are a high risk group following cholecystectomy, the cause of this increased risk requires further investigation.

Keywords

general surgery; kidney transplantation; cholecystectomy

INTRODUCTION

Cholecystectomy is one of the most common general surgery procedures performed in the United States, with more than 400,000 cases performed every year.^{1,2} One unique patient population at increased risk for need of cholecystectomy are kidney transplant recipients (KTR). KTR are at higher risk of developing gallstones and biliary disease than the general population due to their history of renal failure and immunosuppressive medications such as calcineurin inhibitors.^{3,4} This risk, combined with improved post-transplant survival, translates to a higher incidence of cholecystectomy in the kidney transplant population.^{1,3} While post-cholecystectomy morbidity and mortality are low and the average hospital length of stay (LOS) is two days in the general population, it is unclear if the risks are elevated for KTR.⁵⁻⁷ An improved understanding of morbidity, LOS, and associated cost in this population is important for peri-operative planning and risk stratification.

Previous single-center studies have reported that post-operative outcomes for solid organ transplant recipients following general surgical procedures are worse than the non-transplant recipients, with a recent review citing up to 32.7% morbidity and 17.5% mortality for emergency abdominal surgery, in comparison to 9% morbidity and less than 0.5% mortality in non-transplant recipients.^{1,8} For post-transplant cholecystectomy specifically, a national study of solid organ transplants, including heart, lung, and heart-lung recipients, found a complication rate of 13.6% following cholecystectomy, compared to 4.9% for non-transplant recipients.^{1,5} Additionally, these heterogeneous solid-organ transplant recipients had a LOS of 4–8 days, compared to a median 1 day reported for non-transplant recipients.^{5,9} Specifically regarding kidney transplant recipients, the largest case-series of cholecystectomies to date reported outcomes of 17 procedures performed in a cohort of 1,608 KTR at a single transplant center, with a mortality rate of 5.9%.³ Given concerns of increased operative risks, many transplant providers feel that morbidity, LOS and cost might be mitigated if transplant recipients receive their surgical care at transplant centers.¹⁰⁻¹²

To explore post-cholecystectomy outcomes in a more generalizable fashion, we used the National Inpatient Sample (NIS) to investigate the differences in mortality, morbidity, LOS and cost between KTR and non-KTR undergoing cholecystectomy in a large population of patients undergoing cholecystectomy in the United States. We also investigated outcomes based on the location of surgical care at transplant centers compared to non-transplant centers.

MATERIAL AND METHODS

Data Source

Patients were drawn from the NIS. Available through the Healthcare 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.¹³ The NIS captures inpatient data for individual hospital visits. It does not capture follow-up data or outpatient information, allowing for inferences to be drawn related to the index admission only. Information provided in the NIS includes patient level hospital discharge data such as patient demographics, as well as diagnostic and procedural ICD-9 codes for the index hospital admission. All study methods were approved by the Johns Hopkins Hospital Institutional Review Board.

Study population

We studied 7,318 adult KTR and 5,341,427 non-KTR undergoing cholecystectomy 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 cholecystectomy. 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).

Patient and Hospital Level Characteristics

In addition to examining basic demographic characteristics and surgical approach (laparoscopic vs. open), the Charlson Comorbidity Index score was calculated for each patient.^{14,15} Hospital characteristics examined were standard NIS categories of location (rural or urban), size (small, medium, large), teaching status, and region (Northeast, Midwest, South, or West). We categorized hospitals as transplant centers (a hospital where at least one kidney transplant was performed during the study period) or non-transplant centers.

Clinical Outcomes

We defined mortality as death during the primary surgical hospital admission. Morbidities, defined as intraoperative or postoperative complications during the index hospital admission, were identified by ICD-9 code and categorized into system-based groups as established in previous studies (Appendix B).¹⁶ The NIS does not capture follow-up or long term outcomes. Incidences of mortality and morbidity were modeled using hierarchical multivariable logistic regression. Length of stay was examined using hierarchical multivariable negative binomial regression. Multivariable mixed linear regression was used to examine log-transformed costs. The NIS contains data on total charges for hospital admission, representing the amount that hospitals bill for the admission. The Healthcare Cost and Utilization Project Cost-to-Charge Ratio Files, designed to be used with certain databases including NIS, enable the conversion from charges to cost, on a hospital-specific basis, for all hospitals represented in the database.

Multivariable models for each outcome included random intercepts for each hospital and were adjusted for surgical approach (laparoscopic or open), patient characteristics (sex, age, African American race, Charlson Comorbidity Index, primary insurance status), and hospital factors (location, size, region, teaching status, and transplant center status).

Effect Modification by Transplant Center

We investigated whether the association of KTR status with mortality, morbidity, LOS and cost varied by treatment at transplant centers compared to non-transplant centers. To evaluate this, we created an interaction term for KTR status with transplant center status in the regression models described above.

Statistical Analysis

We used χ^2 tests to evaluate categorical variables and Student's t test for continuous variables to compare KTR with non-KTR. We used multivariable regression models described above to evaluate control for a variety of patient and hospital characteristics, in addition to surgical approach. For all analyses, a two-tailed p-value of < 0.05 was considered statistically significant. Confidence intervals are reported as per the method of Louis and Zeger.¹⁷ Statistical analysis was performed using Stata 14.0 (StataCorp, College Station, Texas).

RESULTS

Study Population

A total of 7,318 KTR and 5,341,427 non-KTR underwent cholecystectomy during the study period. KTR were a similar age (median 54 [IQR 44–63] years vs. median 56 years [IQR 40–72]; $p=0.051$), more likely to be male (55.3 vs 34.3%, $p<0.001$), African American (13.8 vs 9.3%, $p<0.001$), have public insurance (66.8% vs 46.3%, $p<0.001$) and have a higher Charlson Comorbidity Index scores (36.4% vs 16.9% with score ≥ 2) compared to non-KTR. KTR were less likely to have a laparoscopic cholecystectomy than non-KTR (68.2% vs 77.7%, $p<0.001$) (Table 1), and KTR were less likely to have a laparoscopic cholecystectomy when treated at transplant centers compared to non-transplant centers (60.7% vs 71.9%).

Mortality and Morbidity

Mortality was higher following cholecystectomy during the index admission for KTR compared to non-KTR (2.7% vs 1.2%, $p < 0.001$, Table 2). After adjusting for patient and hospital characteristics, the odds of in-hospital mortality following cholecystectomy in KTR was 2.39-fold higher than non-KTR (aOR 1.66 2.39_{3.44}). KTR were more likely than non-KTR to have postoperative complications during their index surgical hospitalization (18.8% vs 13.9%, $p<0.001$). KTR had more in-hospital wound complications (2.0% vs 0.8%, $p < 0.001$), infectious complications (4.4% vs 2.1%, $p<0.001$), genitourinary complications (1.4% vs 0.8%, $p=0.01$) and intraoperative complications (3.7% vs 2.4%, $p=0.001$) than non-KTR. After adjustment, the odds of any in-hospital morbidity were 1.3-fold higher in KTR than non-KTR (aOR_{1.12}1.30_{1.51}). Specifically, KTR had higher wound (aOR_{1.27}1.90_{2.84}),

infectious (aOR $1.44^{1.89}_{2.48}$), and intraoperative (aOR $1.03^{1.39}_{1.86}$) complications when compared to non-KTR (Table 2).

Length of Stay and Cost

Median LOS was longer in KTR compared to non-KTR (5 days vs 3 days, $p < 0.001$, Table 2). After adjusting for patient and hospital level characteristics including operative approach, LOS was 1.23-fold longer for KTR (ratio $1.17^{1.23}_{1.28}$) compared to non-KTR. The median cost for cholecystectomy was \$12,077 for KTR and \$9,002 for non-KTR ($p < 0.001$). After adjustment, cost was 1.13-fold higher for KTR than non-KTR (ratio $1.08^{1.13}_{1.17}$, Table 2).

Transplant Center

KTR were more likely to be treated at kidney transplant centers than non-KTR (54.6% vs 16.8%, $p > 0.001$, Table 1). The association of KTR status and mortality did not differ by center type (aOR: $1.48^{2.45}_{4.04}$ vs $1.36^{2.3}_{3.93}$; interaction $p = 0.9$, Table 3). When comparing those treated at transplant centers and non-transplant centers, the association of KTR status and complications (aOR: $1.00^{1.24}_{1.52}$ vs $1.11^{1.37}_{1.69}$, interaction $p = 0.5$), LOS (ratio: $1.18^{1.25}_{1.32}$ vs $1.14^{1.21}_{1.28}$, interaction $p = 0.4$), and cost (ratio: $1.07^{1.13}_{1.18}$ vs $1.09^{1.15}_{1.21}$, interaction $p = 0.7$), did not differ (Table 3).

DISCUSSION

In this national study of 7,318 kidney transplant recipients undergoing cholecystectomy, we found that KTR had 2.4-fold higher in-hospital mortality and 30% higher overall in-hospital morbidity when compared to non-KTR. KTR were more susceptible to in-hospital wound (aOR 1.90), infectious (aOR 1.89), and intraoperative complications (aOR 1.39) than non-KTR. KTR had 23% longer LOS and 13% higher cost than non-KTR ($p < 0.001$). These associations did not vary between transplant centers and non-transplant centers.

We found a 2.4-fold higher odds of in-hospital mortality in KTR after adjusting for multiple patient and hospital characteristics, markedly higher than previous single-institution studies of 0–5.9% mortality in KTR.^{3,18} However, our findings are from a larger, more generalizable cohort, supporting that cholecystectomy is inherently higher risk for KTR than non-KTR, independent of other patient, hospital, and procedure specific variables. The mortality difference between KTR and non-KTR is 1.5%, we feel that while this difference is numerically small, it is clinically important, given the perception of cholecystectomy as a relatively benign surgical procedure. Further, we found the rate of overall in-hospital complications to be significantly higher in KTR. These findings are consistent with in-hospital morbidity of 12.5% reported in a case series of KTRs following cholecystectomy.¹⁹ Specifically, we found that KTR suffered more in-hospital wound, infectious, and intraoperative complications than non-KTR. Although the underlying cause for this increase in complications is multifactorial, we suspect it is influenced at least in part by immunosuppression of KT recipients. The impact of immunosuppression on wound healing and infection is well documented, particularly in the immediate post-transplant setting.^{20–23} Even with improved immunosuppressant regimens, higher rates of wound healing issues and infectious complications have been documented in KTR.²⁴ Additionally, increased

complications could be related to the hypothesized global tissue damage caused by years of renal failure and/or dialysis for KTR.^{25,26}

We found the median LOS for KTR to be significantly longer than non-KTR (5 vs 3 days). We report a shorter median LOS than previous studies of solid organ transplant recipients undergoing cholecystectomy (9 days)¹, but slightly longer LOS than other reports for the general population (1–3 days).⁵ Additionally, we report significantly higher cost for KTR compared to non-KTR. A recent study reported median cost of cholecystectomy in the general population ranging from \$8,552 to \$13,526 for average length hospital stays, which is similar to our finding of \$9,002 for non-transplant recipients.²⁷ However, median cost for KTR was 13% higher following adjustment. Although this difference is significant, the nature of our study precluded our ability to draw causal inferences and the data available in the NIS does not support a more granular examination of the reasons for higher costs and longer LOS in KTR.

Despite the sentiments expressed in multiple opinion pieces including book chapters and editorials, we did not find better outcomes for transplant recipients at transplant centers.^{10,12,28} While there was a significantly higher percentage of cholecystectomies performed at transplant centers in the KTR population (54.6%) compared to the non-KTR group (16.8%), the mortality, morbidity, LOS and cost were similar for KTR regardless of center type. In our examination of these outcomes, we adjusted for surgical approach, controlling the impact that laparoscopic vs. open case differences had on the association of KTR status and our outcomes of interest.

This study has some limitations that warrant further discussion. An important limitation was the lack of clinical granularity of NIS data. While the admitting diagnosis was routinely recorded and helpful in determining the indication for surgery, it was often vague, hindering our ability to adjust for cholecystectomy indication. Without detailed information on the specific costs and events occurring during a hospital stay, we were also unable to determine the underlying reasons for cost and length of stay differences between KTR and non-KTR. For example, we were unable to determine whether those KTR presenting to non-transplant centers that were sicker were transferred to transplant centers for care. An additional limitation inherent in the design of the NIS was the lack of linkage of patients across multiple hospitalizations or visits, thereby limiting our ability to comment on later graft or patient outcomes. Our study is limited by its cross-sectional nature, and does not allow us to draw causal inferences as to why the KTR population are a high-risk group following cholecystectomy. While we can hypothesize several biologic and physiologic mechanisms, our study does not examine underlying causation.

As a cross-sectional sample, the NIS collects information on a single hospital stay, and does not provide information on follow-up or longer term outcomes. As such, we were limited to the analysis of mortality and morbidity events on the primary admission for cholecystectomy. We appreciate that there is a potential for mortality and morbidity related to the surgery after discharge, but were unable to capture these. Patients with shorter hospital stays have inherently less time to develop in-hospital complications, which may introduce bias into the interpretation of complication rate for patients with a shorter LOS, particularly

non-KTR. However, we believe that discussing inpatient complications has its own inherent value and can inform clinicians of the high-risk nature of treating KTR. The magnitude of the NIS offers insight into national outcomes of cholecystectomy in KTR and avoids the bias and limited power associated with single-center studies. It also allows us to perform multivariable analyses, investigate interactions, and study outcomes at transplant vs non-transplant centers.

Conclusion

In this large, national study, we report that KTR had higher in-hospital mortality, greater in-hospital morbidity, longer LOS and higher cost when compared to non-transplant recipients undergoing cholecystectomy, regardless of center type. Surgeons should consider these elevated risks when planning for surgery in the KTR population, counsel patients accordingly, and monitor vigilantly for immediate post-operative complications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Kidney transplant recipients have higher post-cholecystectomy mortality and morbidity
- Length of stay after cholecystectomy is longer for kidney transplant recipients
- Cost of cholecystectomy is greater for kidney transplant recipients
- Post-cholecystectomy outcomes for KTR are similar regardless of location of care

Table 1.

Characteristics of the study population, hospital and procedure details for kidney transplant recipients (KTR) and non-KTR undergoing cholecystectomy between 2000–2011.

	KTR (n= 7,318)	Non-KTR (n= 5,341,427)	p-value
Age, median (IQR)	54 (44–63)	56 (40–72)	<0.001
Male, %	55.3	34.3	<0.001
African American, %	13.8	9.3	<0.001
Charlson Comorbidity Index, %			<0.001
0	35.5	61.7	
1	28.1	21.4	
2	36.4	16.9	
Insurance Status, %			<0.001
Public	66.8	46.3	
Private	30.0	42.5	
Other	2.2	11.2	
Laparoscopic, %	68.2	77.7	<0.001
Performed at transplant center, %	54.6	16.8	<0.001

Table 2.

Unadjusted and adjusted* outcomes following cholecystectomy in kidney transplant recipients (KTR) vs non-KTR.

	unadjusted			Adjusted*	
Outcome	KTR (n = 7318)	Non-KTR (n = 5,341,427)	p value	KTR vs Non-KTR	95% CI
Mortality, %	2.7	1.2	<0.001	aOR 2.39	1.66–3.44
Any Complication, %	18.8	13.9	<0.001	aOR 1.30	1.12–1.51
System specific complications, ^ %					
Wound	2.0	0.8	<0.001	aOR 1.90	1.27 –2.84
Infection	4.4	2.1	<0.001	aOR 1.89	1.44–2.48
Pulmonary	3.3	3.3	0.9	aOR 0.99	0.72–1.35
Cardiovascular	1.2	1.2	0.9	aOR 0.89	0.51–1.54
Genitourinary	1.4	0.8	0.01	aOR 1.48	0.91–2.41
Gastrointestinal	5.9	5.8	0.8	aOR 0.88	0.69–1.12
Intraoperative	3.7	2.4	0.001	aOR 1.39	1.03–1.86
LOS, median days (IQR)	5 (3–9)	3(2–6)	<0.001	ratio 1.23	1.17–1.28
Cost, median \$ (IQR)	12,077 (7,71719,766)	9,002 (6,18213,886)	<0.001	ratio 1.13	1.08–1.17

^ see Appendix B for breakdown of complications by system

* adjusted for age, race, gender, Charlson comorbidity score, insurance status, hospital bed size, hospital region, teaching status, surgical approach

Table 3.

Adjusted outcomes of kidney transplant recipients (KTR) vs. non-KTR by center type following cholecystectomy. *

Outcome	KTR vs non-KTR at transplant center	KTR vs non-KTR at non-transplant center	p-value for interaction
Mortality, OR	2.45 (1.48 – 4.04)	2.31 (1.36 – 3.93)	0.9
Any complications, OR	1.24 (1.00 – 1.52)	1.37 (1.11 – 1.69)	0.5
LOS, ratio	1.25 (1.18–1.32)	1.21 (1.14 – 1.28)	0.4
Cost, ratio	1.13 (1.07–1.18)	1.15 (1.09–1.21)	0.7

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