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Knowledge of Chronic Kidney Disease among Liver Transplant Recipients

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Abbreviations:

Body Mass Index	BMI
Blood Pressure	BP
Confidence Interval	CI
Chronic Kidney Disease	CKD
estimated Glomerular Filtration Rate	eGFR
End Stage Renal Disease	ESRD
Hazard Ratio	HR
Hemoglobin A1C	HbA1C
Kidney Disease Knowledge Survey	KiKS
Liver Transplantation	LT

To the editors:

Chronic kidney disease (CKD) after liver transplant (LT) is an important co-morbidity that negatively affects patient and graft survival.[1,2] Additionally, it adds to resource utilization in LT recipients leading to increased healthcare costs.[1-4] Although LT recipients have established framework of care and access to education as a part of transplant process, there may be significant modifiable gaps in their knowledge and understanding of CKD after LT.

Wright et al. developed a reliable and validated instrument called Kidney Disease Knowledge Survey (KiKS) that identified the areas of and risk factors for poor kidney knowledge in the non-transplant CKD population.[5] To assess the CKD knowledge among LT recipients, we modified the KiKS survey by adding four LT specific questions to the KiKS and performed the face validity and content validity before administering the survey to the study cohort. The KiKS-LT survey examined the CKD knowledge in the following domains: 1) general knowledge of kidney disease; 2) LT-specific kidney and immunosuppression knowledge; 3) knowledge of kidney function; and 4) knowledge of symptoms of CKD progression or kidney failure.

Materials and Methods

Study Design and Population:

We conducted a cross-sectional survey study among LT recipients who had a routine post-LT appointment at the University of Michigan liver transplant outpatient clinics between July 1, 2016 and September 30, 2017. The subjects were followed up until May 31, 2018. Our study included the recipients of LT between January 1, 2008 and December 31, 2016, age ≥18 years, ≥3 months post-LT; estimated glomerular filtration rate (eGFR) ≥30 ml/min at the time of survey. We excluded the recipients of kidney transplant at or after LT, eGFR <30 ml/min, on dialysis or listed for kidney transplant. Our Institution Review Board approved the study.

KiKS-LT Survey Instrument:

After a content review of CKD knowledge questionnaire in general population, we chose the validated KiKS survey.[5] To make it LT-specific, we added four LT-specific

questions to KiKS. The KiKS-LT survey comprised of thirty-one questions (Supplemental material) with one best answer. We asked additional questions at the end of KiKS-LT survey from the respondents: Do you use the Patient Portal your electronic health record? 2) How would you like to receive CKD educational and goal setting tool, if interested in learning more about CKD?

To establish the face-validity, content validity and construct validity of KiKS-LT survey, we convened experts in various areas of LT and CKD care [transplant provider with expertise in liver disease, kidney disease and transplant surgery (n=4), nurses (n=2), research personnel (n=2) and transplant pharmacists (n=2)]. We also solicited method input from experts in health literacy, scale validation, and psychometric analysis. We used the Kuder-Richardson-20 coefficient (KR-20) to determine internal consistency.

Statistical Analysis:

Continuous and categorical variables were expressed as median and interquartile range (IQR) and percentage, respectively. eGFR was calculated using the 4-variable Modification of Diet in Renal Disease Study (MDRD) equation. CKD stage was assigned based on KDOQI guidelines. Z-test was used to compare the distribution of CKD knowledge scores of LT recipients with the distribution of CKD knowledge scores in non-transplant recipients (Wright et al.[5]). The main outcome was CKD knowledge score, calculated as the proportion of all correct answers on the KiKS-LT survey by each subject. We used linear regression to examine the associations between CKD knowledge and patient characteristics (age, education level, CKD stage and diabetes). Exploratory analyses were performed for gender, etiology, seen by nephrologist and time from LT to survey. Multi-collinearity of the covariates was tested using tolerance and variance inflation factors.

Cox regression was used to examine the effect of CKD knowledge on CKD progression to stage 4-5 CKD during the follow up period. The time to event was calculated from date of survey to the date of event or end of follow up period. The model was adjusted for age at survey, decile of knowledge score, diabetes, answering 'yes' to learn more about post-LT CKD, hypertension and eGFR at the time of survey.

We performed all statistical analyses using SPSS, version 24 (IBM Corp., Armonk, NY).

Results

After obtaining the informed consent, the KiKS-LT survey was administered to 175 subjects. One withdrew consent, and 11 did not return the survey. The final study cohort consisted of 163 LT recipients (Table 1). More than half of the respondents (55%) were actively using patient portal messaging through electronic health records. Sixty-five percent of those who responded 'yes' interested in learning more about CKD in LT recipients through an educational tool. Three fourths of those interested in learning more about CKD wanted to be contacted either via patient portal of electronic health record or via telephone.

The median eGFR at the time of survey was 57.7 ml/min. More than half had stage 3 CKD. Only 14% had seen a nephrologist. The prevalent risk factors for CKD like diabetes, hypertension and obesity were present in 26%, 42% and 40% of the respondents, respectively. The median time from LT to survey was 2.7 years (IQR: 1.1-6.1 years). Median time from survey to last follow up was 16 months (IQR: 14-17 months).

Primary and Secondary Outcomes:

The 31-question KiKS-LT survey was analyzed for internal consistency (Kuder-Richardson 20= 0.769). Table 2 shows the degree of difficulty and item correlation. The mean knowledge score defined as proportion correct answer of KiKS-LT survey was 0.60 [95% CI:0.57-0.63]. The CKD knowledge score among LT recipients with stage 1-3 CKD was significantly lower compared to the non-LT CKD population surveyed by Wright et al. using KiKS (0.66 [95% CI, 0.65-0.67])[5].

Independent Predictors of CKD Knowledge among LT Recipients:

Figure 1 showed the spread of eGFR within each decile of CKD knowledge score. In an adjusted analysis, younger age (β=-0.003 per year decrease in age; p=0.02), higher CKD stage (β=0.041 per stage increase in CKD; p=0.04) at the time of

survey were associated with high CKD knowledge. Education above high school and diabetes were independently associated with 8.3% (p=0.002) and 7.7% (p=0.01) increase, respectively, in the CKD knowledge.

Progression to Advanced CKD and Predictors:

Nine patients progressed to stage 4-5 CKD after the median follow up of 16 months (IQR: 14-17 months) from the date of survey. As expected, eGFR at the time of survey (HR=0.92 [95% CI 0.86-0.99]; p=0.02) was the independent predictor of stage 4-5 CKD. Those who answered “yes” to more CKD education trended towards lower risk of advanced CKD (p=0.14) compared to those who responded “no”.

Discussion

This is the first study to examine the CKD knowledge among LT recipients with stage 1-3 CKD using modified KiKS-LT survey. The distribution of CKD knowledge scores among LT recipients was lower than the distribution of those with CKD in non-LT population. Only 14% had established nephrology care in our cohort. This may be because majority had early stage CKD (eGFR>45 ml/min).

We also showed that presence of diabetes and high CKD stage were associated with higher CKD knowledge among LT recipients.

The majority of participants were aware that calcineurin inhibitors are a risk factor of CKD. Interestingly, time from LT to survey was not associated with the patient’s level of CKD knowledge. This finding suggests that educational programs are needed for LT recipients regardless of transplant duration.

Our study indicates that CKD knowledge among LT recipients is low and may be a barrier for self-care. Encouragingly, more than two thirds of the LT recipients were interested in learning more about CKD progression and prevention. The majority indicated that they would like to get the education remotely instead of at their clinic visit.

Many studies have addressed the burden of post-LT CKD progression.[1-3]

In conclusion, the results of this study will facilitate evidence-based development of a personalized CKD education and goal-setting tool for LT recipients with early stages of CKD.

References:

1. Ojo AO, Held PJ, Port FK, et al. Chronic renal failure after transplantation of a nonrenal organ. *The New England journal of medicine.* 2003;349(10):931-940.
2. Sharma P, Goodrich NP, Schaubel DE, Guidinger MK, Merion RM. Patient-specific prediction of ESRD after liver transplantation. *Journal of the American Society of Nephrology : JASN.* 2013;24(12):2045-2052.
3. Sharma P, Schaubel DE, Guidinger MK, Goodrich NP, Ojo AO, Merion RM. Impact of MELD-based allocation on end-stage renal disease after liver transplantation. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons.* 2011;11(11):2372-2378.
4. Goodrich NP, Schaubel DE, Smith AR, Merion RM, Sharma P. National Assessment of Hospitalization Rates for Incident End-Stage Renal Disease After Liver Transplantation. *Transplantation.* 2016;100(10):2115-2121.
5. Wright JA, Wallston KA, Elasy TA, Ikizler TA, Cavanaugh KL. Development and results of a kidney disease knowledge survey given to patients with CKD. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2011;57(3):387-395.

Figure legend:

Figure 1: Distribution of eGFR at the time of survey within each decile of CKD knowledge score

Footnote: The ends of the box are the upper and lower quartiles, so the box spans the interquartile range.

Table 1: Characteristics of LT recipients at the time of survey (n=163)

Characteristics at Survey	Median (IQR) or N (%)
Age at survey (years)	60 (51-64)
Male gender	117 (71.3%)
Race	
Caucasians	140 (85.9%)
African Americans	14 (8.6%)
Hispanics	1 (0.6%)
Asians	5 (3.1%)
Others	3 (1.8%)
Etiology of liver disease	
Hepatitis C	54 (33.1%)
Alcoholic liver disease	27 (16.6%)
Cryptogenic cirrhosis/NAFLD	22 (13.5%)
Autoimmune/PBC/PSC	35 (21.5%)
Others	25 (15.4%)
HCC	43 (26.4%)
Time from LT to survey	2.7 years (1.1-6.1)
Serum Creatinine	1.2 mg/dl (1.0-1.4)
eGFR	57.7 ml/min (47-76)
Stage 1 CKD	22 (13.5%)
Stage 2 CKD	55 (33.7%)
Stage 3 CKD	86 (52.8%)
Established Nephrology Care	23 (14.1%)
BMI at survey	28.2% (24.9-32.9%)
<25	41 (25%)
25-29	57 (35%)
30-34	38 (23%)
≥35	27 (17%)
Systolic BP	137 mmHg (125-150)
Diastolic BP	75 mmHg (67-75)

Hypertension	69 (42.3%)
Diabetes	42 (25.8%)
Education	
High school or less	65 (39.9%)
Some college or completed college	60 (36.8%)
Grad school or higher	13 (7.9%)
Missing	25 (15.3%)
Use patient portal of electronic health record	92 (56.4%)
Interested in education	106 (65%)
via phone	47 (44%)
patient portal	33 (31%)
at clinic visit	26 (25%)

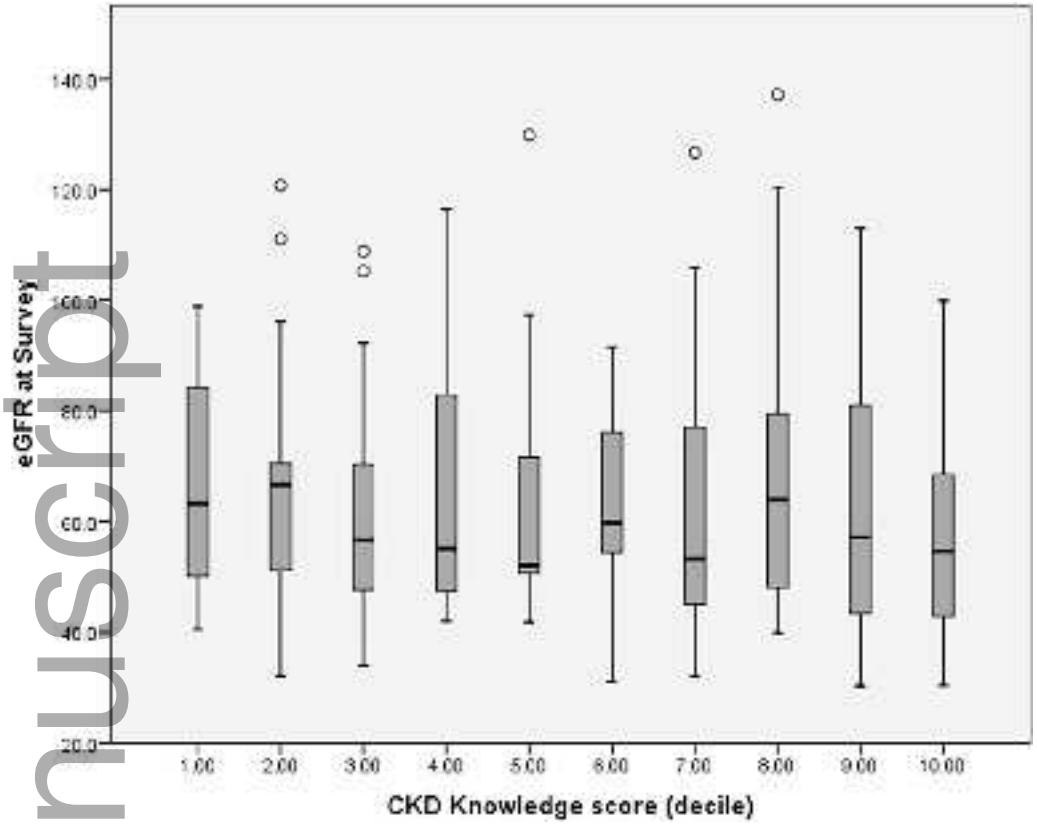
Footnote: BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; HCC, hepatocellular carcinoma; IQR, interquartile range; LT, liver transplantation; NAFLD, non-alcoholic fatty liver disease; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis

Table 2: Degree of difficulty and item correlation grouped by the domains

Table 2: Item difficulty and Item Correlation

Topic	Item difficulty (% correct)	Item-Rest Correlation
General Knowledge		
• Understanding the risk factors of CKD	83%	0.32
• Understanding increased risk of heart disease	75%	0.27
• Understanding increased risk of mortality	96%	0.26
• Definition of GFR	56%	0.35
• Knowing there are stages of CKD	85%	0.37
• Medications a person with CKD should avoid	60%	0.27
• Medications important to kidney health	86%	0.36
• Treatment options for kidney failure	88%	0.34
• Understanding BP goals	85%	0.19
• Definition of HbA1C	60%	0.20
• Understanding blood sugar goals	47%	0.26
LT-specific kidney and immunosuppression knowledge		
• Understanding that risk of CKD is increased	67%	0.29
• Understanding side effects of calcineurin inhibitors	82%	0.328
• Immunosuppression and graft health	85%	0.11
• Understanding common cause(s) of death after LT	9.2%	-0.07
Knowledge of Kidney function		
• Role in glucose control	65%	0.37
• Role in bone health	26%	0.41
• Role in anemia	59%	0.42
• Role in hair loss	81%	0.36
• Role in BP control	55%	0.49
• Urine production	74%	0.30
• Role in waste clearance	67%	0.35
Knowledge of symptoms CKD progression or failure		
• No symptoms	12%	0.004
• Unusual itching	45%	0.47
• Confusion	64%	0.44

• Metallic/bad taste	47%	0.38
• Shortness of breath	41%	0.42
• Increased fatigue	80%	0.58
• Hair loss	76%	0.46
• Difficulty sleeping	61%	0.44
• Weight loss	45%	0.37



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