*Open Forum Infectious Diseases*

MAJOR ARTICLE

# High Mortality and Associated Risk Factors in Kidney Transplant Recipients With Cryptococcosis—A Nationwide Cohort Study Over a Decade Using USRDS Data

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***Background.*** Cryptococcosis is an invasive fungal disease that significantly contributes to morbidity and mortality among kidney transplant recipients (KTRs). Although various prognostic factors predictive of mortality have been identified, most research has been limited to single-center and small-scale studies.

***Methods.*** We conducted a retrospective cohort study using data from the United States Renal Data System to investigate hospitalizations and outcomes for cryptococcosis among KTRs in the United States from 2006 to 2016. Collected data included demographics, comorbid conditions, hospitalization- and transplant-related complications, and mortality.

***Results.*** A total of 1265 KTRs were hospitalized for cryptococcosis. The mean age was 59.1 ± 11.2 years; 857 (67.7%) were male, 852 (67.4%) were White, 603 (47.7%) resided in the South, and 648 (51.2%) had a diagnosis of cryptococcal meningitis (CM). The overall 6-month mortality rate was 22%. Multivariable logistic regression analyses identified several factors associated with increased 6-month mortality: cirrhosis (adjusted odds ratio [aOR], 3.1; 95% CI, 1.2–7.7), intensive care unit admission (aOR, 2.9; 95% CI, 2.0–4.0), need for pretransplant dialysis (aOR, 2.7; 95% CI, 1.5–4.9), lack of tacrolimus use at follow-up (aOR, 2.2; 95% CI, 1.4–3.3), age ≥60 years (aOR, 2.0; 95% CI, 1.4–2.8), acute kidney injury (aOR, 1.7; 95% CI, 1.2–2.4), post-transplant period exceeding 2 years (aOR, 1.7; 95% CI, 1.1–2.4), and previous hospitalization for complications related to the transplanted kidney (aOR, 1.5; 95% CI, 1.1–2.2).

***Conclusions.*** Early mortality remains high among KTRs hospitalized for cryptococcosis, with cirrhosis identified as the strongest independent risk factor for mortality.

**Keywords.** cirrhosis; cryptococcosis; kidney transplant recipients; mortality; United States Renal Data System Database.

Cryptococcosis is an invasive fungal disease caused by the *Cryptococcus neoformans/gattii* species complex, often resulting from reactivation in the setting of immunosuppression. With better control of HIV disease, cryptococcosis is becoming proportionately more prevalent in non-HIV patient populations, particularly among organ transplant recipients (OTRs) on immunosuppressive drugs [1, 2]. Large United States population-based studies report an overall incidence between 0.2% and 4.1% among solid OTRs [3–5]. Due to its tropism for the central nervous system (CNS), cryptococcosis is the most common cause of CNS disease among these patients, causing cryptococcal meningitis (CM).

Although liver, lung, and heart transplant recipients experience earlier onset of cryptococcosis post-transplant and have higher mortality rates [4, 6], kidney transplant recipients (KTRs) represent an important at-risk group due to the high volume of kidney transplants performed, the less predictive nature of disease occurrence, and the absence of routine antifungal prophylaxis in this population [3, 7]. KTRs typically develop cryptococcosis between 35 and 43 months post-transplant [6, 8]. A retrospective study in France involving 199 cases of meningoencephalitis in KTRs from 2007 to 2018 reported that 20% of cases were due to *Cryptococcus neoformans*, whereas only 2% were due to *Streptococcus pneumoniae* [9]. Similarly, the Swiss Transplant Cohort Study (2008–2018) reported that 26% of 42 CNS infections were due to fungal

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disease (8 aspergillosis, 3 cryptococcosis), surpassing bacterial causes [10].

Despite the availability of effective antifungal drugs and the use of generally lower-intensity immunosuppressive agents in the current era [11], mortality remains high among KTRs with cryptococcosis. In a US population-based study, 90-day mortality was 13.7%, and 1-year mortality was 24.6% in OTRs [4]. In another nationwide French KTR cohort of 88 cryptococcosis cases, mortality was reported to be as high as 32.8% at 1 year and 42.6% at the last follow-up, possibly reflecting late complications of graft failure and ongoing immunosuppression [8].

Research on cryptococcosis among OTRs is often limited to single-center or small multicenter studies that frequently group multiple types of transplants together [3, 12–17], and kidney transplant–specific studies are primarily single-center [18]. The United States Renal Data System (USRDS), which integrates data from the United Network for Organ Sharing (UNOS) [19] and Medicare claims, covers >100 000 KTRs and provides a comprehensive resource for studying cryptococcosis diagnosis, management, and outcomes across US transplant centers [19]. Previous studies using this database have grouped cryptococcosis with other fungal infections [20, 21] or with infections in general [22] and have not examined unique elements of cryptococcal disease management, such as the use of lumbar punctures or immunosuppressive drug management. Accordingly, we investigated mortality and potential risk factors among patients with cryptococcosis after kidney transplantation using USRDS data.

## METHODS

### Study Design

This was a retrospective cohort study of KTRs hospitalized with a diagnosis of cryptococcosis between January 1, 2006, and December 31, 2016.

### Data Source

Data were obtained from the USRDS, which integrates data from the UNOS and Medicare claims (Supplementary Figure 1). Because the USRDS directly links to UNOS transplant records, we did not need to rely on International Classification of Diseases (ICD) codes to ascertain transplant status.

### Study Population

We identified KTRs aged 18 to 90 years with Medicare as their primary insurance coverage who experienced their first incident hospitalization when a diagnosis code of cryptococcosis was used after transplantation during the study period. We excluded KTRs with a cryptococcosis claim (physician or hospitalization) that preceded the date of their first kidney transplantation or the study period. Restricting the analysis to the first cryptococcosis-related hospitalization increased the likelihood that this admission was attributable to symptomatic cryptococcosis.

### Data Collection

Transplant status was obtained from the USRDS Core files. Baseline demographic data, including age, race, ethnicity, and region of hospitalization, were collected from the USRDS patient data files. The diagnosis of cryptococcosis, cryptococcal meningitis, and comorbid conditions (eg, diabetes, cirrhosis, acute kidney injury [AKI]), HIV and cytomegalovirus (CMV) serostatus, graft rejection, and hospitalizations related to kidney transplant complications were identified using ICD, 9th Revision (ICD-9), codes (through 2015) and then 10th Revision (ICD-10) codes (thereafter). Information on outpatient immunosuppressive drugs (eg, antithymocyte globulin [ATG], tacrolimus, cyclosporine, mycophenolate mofetil [MMF], steroids) during UNOS registration and the first post-transplant visit was obtained using relevant billing codes. Data from the first post-transplant visit were available as required by the UNOS. Immunosuppressive agents administered during index hospitalization were not captured. CMV and HIV serostatus, rejection, and transplant failure incidence reflected those used at the time of UNOS registration (transplant) and UNOS follow-up. Current Procedural Terminology (CPT) codes were used to identify lumbar punctures, other spinal procedures, neurosurgical interventions, and ventriculoperitoneal (VP) shunt placements during the index hospitalization (Supplementary Table 1).

### Outcome Measures

The primary outcome was all-cause mortality at 6 months post–index hospitalization with cryptococcosis. Secondary outcomes were the time from transplantation to initial hospitalization for cryptococcosis and the impact of clinical variables (eg, cirrhosis, acute kidney injury, intensive care unit [ICU] admission) and immunosuppressive drugs on mortality. Mortality data from UNOS were verified using transplant center reports and Medicare records [23].

### Statistical Analysis

Demographics and clinical variables were described as mean ± SD for continuous variables and as number (%) for categorical variables. Comparisons between 6-month survivors and nonsurvivors were performed using the Student *t* test for continuous variables and Fisher exact test or $\chi^2$ test for categorical variables, as appropriate.

Time to mortality was estimated using Kaplan-Meier curves. Additionally, each independent variable was first examined in bivariable models and then entered into a multivariable logistic regression model using a backward elimination strategy

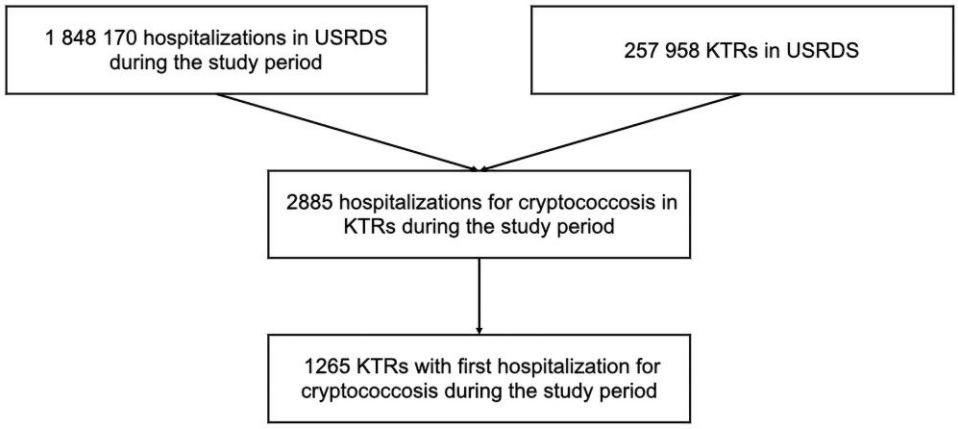


**Figure 1.** Flowchart of selection of relevant KTRs from the USRDS database. Abbreviations: KTRs, kidney transplant recipients; USRDS, United States Renal Data System.

with a significance level cutoff of $P < .05$ to estimate predictors of mortality. Model fit was assessed using the Hosmer-Lemeshow goodness-of-fit statistic. Estimates were reported as adjusted odds ratio (aOR) with corresponding 95% CIs. An alpha level of .05 was considered significant for all statistical tests. As no correction was made for multiple comparisons, all analyses should be considered exploratory.

Statistical analyses were performed using R (version 4.3.1), RStudio (version 2023.06.0 + 421; RStudio, Inc., Boston, MA, USA), and Stata (version 16.1; StataCorp LLC, College Station, TX, USA). We developed an R package (usrdsR) with generic functions to simplify data extraction and analysis from the often complex USRDS database, which we have made publicly available via GitHub [24].

### Ethics

The Institutional Review Board of Albert Einstein College of Medicine approved this study. As this was a retrospective analysis of deidentified data, the requirement for informed consent was waived.

## RESULTS

### Clinical Cohort

The data set includes 1 848 170 hospitalizations among 257 958 KTRs. A total of 1265 KTRs experienced 2885 hospitalizations with a diagnosis of cryptococcosis during the study period (Figure 1). Their first hospitalization was considered the index hospitalization and was included in the analysis.

Table 1 describes the demographic and clinical variables of the cohort. The mean age at hospitalization was 59.1 ± 11.2 years. Most patients were male (857 [67.7%]), and the majority were White (852 [67.4%]), followed by Black (26.2%) and Hispanic (20.6%). Geographically, most resided in the South (603 [47.7%]), followed by the Midwest (274 [21.6%]), West (216 [17%]), and Northeast (164 [12.9%]). The median time from the most recent transplant to the index hospitalization for cryptococcosis (interquartile range) was 30.5 (12.8–74.5) months. A total of 47.9% of the patients had diabetes, 2.8% had a diagnosis of cirrhosis during the index hospitalization, 87.2% required pretransplant dialysis, and 63.7% had prior hospitalization for complications of the transplanted kidney. Among the patients with available data, 740 out of 1047 (70.7%) were CMV seropositive, and 5 out of 833 (0.6%) were HIV seropositive.

During the hospital course, 69.4% of the patients underwent lumbar punctures, and 51.2% had a diagnosis code of CM. A significant proportion required ICU admission (44.1%) and developed AKI (49.1%). Additionally, 14% experienced rejection episodes, and 18.8% had transplant failures at UNOS registration and/or during 1-year follow-up.

### Clinical Factors Associated With Mortality

The overall 6-month mortality rate from the index hospitalization was 22% (280/1265) (Figure 2). Nonsurvivors were significantly older than survivors (62.8 ± 11.3 vs 58.1 ± 10.9 years; $P < .001$) and more likely to be male (72.8% vs 66.3%; $P = .04$). Race was not associated with 6-month mortality (Table 1).

Additional clinical variables associated with mortality at 6 months included diagnosis code of CM (56.7% in nonsurvivors vs 49.6% in survivors; $P = .04$), ICU admission (68.2% vs 37.2%; $P < .001$), AKI (61.7% vs 45.5%; $P < .001$), cirrhosis (6.4% vs 1.8%; $P < .001$), need for pretransplant dialysis (93.5% vs 85.4%; $P = .001$), longer time since the last transplant (median, 43.6 months vs 28.3 months; $P < .001$), and history of hospitalizations for complications related to the transplanted kidney (72.8% vs 61.1%; $P < .001$).

### Immunosuppressive Drug Use

Table 2 details the immunosuppressive drugs patients were taking at the time of transplant and at the first outpatient

**Table 1. Demographic and Clinical Characteristics of Kidney Transplant Recipients During the Index Hospitalization for Cryptococcosis**

| Variables | Total (n = 1265) | Alive at 6 Months (n = 985) | Dead at 6 Months (n = 280)[a] | *P* Value |
|---|---|---|---|---|
| Demographic characteristics | | | | |
| Age at diagnosis, mean ± SD, y | 59.1 ± 11.2 | 58.1 ± 10.9 | 62.8 ± 11.3 | <.001 |
| Sex, No. (%) | | | | |
| Female | 408 (32.3) | 332 (33.7) | 76 (27.1) | .04 |
| Male | 857 (67.7) | 653 (66.2) | 204 (72.8) | |
| Race, No. (%) | | | | |
| White | 852 (67.4) | 655 (66.6) | 197 (70.3) | .1 |
| Black | 332 (26.2) | 270 (27.4) | 62 (22.1) | |
| Other | 79 (6.2) | 58 (5.9) | 21 (7.5) | |
| Ethnicity, No. (%) | | | | |
| Hispanic | 256 (20.6) | 203 (20.9) | 53 (19.4) | .5 |
| BMI at registration, mean ± SD, kg/m$^2$ | 27.3 ± 7.8 | 27.3 ± 8.1 | 27.6 ± 6.6 | .5 |
| US region, No. (%) | | | | |
| West | 216 (17) | 166 (16.8) | 50 (17.8) | .6 |
| Midwest | 274 (21.6) | 217 (22) | 57 (20.3) | |
| South | 603 (47.7) | 472 (47.9) | 131 (46.7) | |
| Northeast | 164 (12.9) | 125 (12.7) | 39 (13.9) | |
| Clinical variables | | | | |
| Cryptococcal meningitis, No. (%) | 648 (51.2) | 489 (49.6) | 159 (56.7) | .04 |
| Procedures performed, No. (%) | | | | |
| Lumbar puncture(s) | 878 (69.4) | 690 (70) | 188 (67.1) | .3 |
| Other spinal procedures | 70 (5.5) | 48 (4.8) | 22 (7.8) | .054 |
| Neurosurgical procedures | 30 (2.3) | 19 (1.9) | 11 (3.9) | .052 |
| Lung procedures | 354 (27.9) | 84 (30) | 270 (27.4) | .3 |
| Comorbid conditions, No. (%) | | | | |
| ICU admission | 558 (44.1) | 367 (37.2) | 191 (68.2) | <.001 |
| AKI | 622 (49.1) | 449 (45.5) | 173 (61.7) | <.001 |
| Diabetes | 606 (47.9) | 485 (49.2) | 121 (43.2) | .07 |
| Cirrhosis | 36 (2.8) | 18 (1.8) | 18 (6.4) | <.001 |
| CMV serostatus, positive | 740/1047[b] (70.6) | 582 (71.2) | 158 (68.7) | .4 |
| Pretransplant dialysis | 1030/1180 (87.2) | 783 (85.4) | 247 (93.5) | .001 |
| Transplant complications | | | | |
| Time post–last transplant, median (IQR), mo | 30.5 (12.8–74.5) | 28.3 (12.4–69.3) | 43.6 (14.8–91.2) | <.001 |
| No. of transplants, median (min–max) | 1 (1–5) | n/a | n/a | |
| Rejection episodes, any, No. (%) | 178 (14) | 144 (14.2) | 34 (12.1) | .2 |
| Transplant failures, any, No. (%) | 238 (18.8) | 187 (18.9) | 51 (18.2) | .7 |
| Prior hospitalization for complications of transplanted kidney, No. (%) | 806 (63.7) | 602 (61.1) | 204 (72.8) | <.001 |

Abbreviations: AKI, acute kidney injury; BMI, body mass index; CMV, cytomegalovirus; ICU, intensive care unit; IQR, interquartile range; n/a, not available.

[a]Mortality indicates all-cause deaths occurring within 6 months following the index hospitalization for cryptococcosis.

[b]Denominator indicates the total number available for each variable when data were missing.

follow-up. At initial UNOS registration, a high proportion of individuals had received antithymocyte globulin (44.7%), steroids (97.2%), MMF (90.2%), and tacrolimus (82.1%). During the UNOS follow-up appointment, the majority remained on steroids (90.1%), MMF (93.5%), and tacrolimus (84.7%).

Not being on tacrolimus at UNOS registration was significantly associated with 6-month mortality (74.9% of nonsurvivors vs 84.2% of survivors were on tacrolimus; $P < .001$). This relationship persisted at the time of follow-up (76.2% of nonsurvivors vs 87.1% of survivors were on tacrolimus; $P < .001$). Conversely, use of cyclosporine after transplant was significantly more prevalent among nonsurvivors (24%) than among survivors (16.9%; $P = .008$), although this difference was not observed at the subsequent follow-up visit.

#### Multivariable Logistic Regression Analysis

Variables independently associated with 6-month mortality, in the order of highest odds of death at 6 months, were cirrhosis during the index hospitalization (aOR, 3.1; 95% CI, 1.2–7.7), ICU admission (aOR, 2.9; 95% CI, 2.0–4.0), need for pretransplant dialysis (aOR, 2.7; 95% CI, 1.5–4.9), lack of tacrolimus use at follow-up (aOR, 2.2; 95% CI, 1.4–3.3), age ≥60 years (aOR, 2.0; 95% CI, 1.4–2.8), AKI during the index hospitalization (aOR, 1.7; 95% CI, 1.2–2.4), post-transplant period exceeding

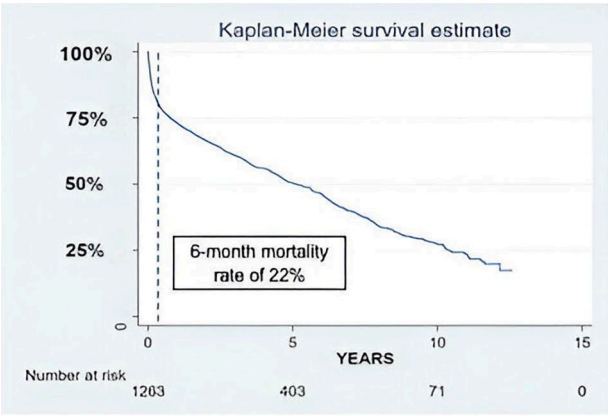


**Figure 2.** Kaplan-Meier survival curve for the 1265 kidney transplant recipients hospitalized with cryptococcosis. The vertical dashed line indicates the 6-month time point.

2 years (aOR, 1.7; 95% CI, 1.1–2.4), and previous hospitalization for complications related to the transplanted kidney (aOR, 1.5; 95% CI, 1.1–2.2) (Figure 3).

**Table 2. Immunosuppressive Drug Use Among Kidney Transplant Recipients at the Time of Transplantation (UNOS Registration) and at the UNOS Follow-up Appointment**

| Immunosuppressive Drugs | Total (n = 1265) | Alive at 6 Months (n = 985) | Dead at 6 Months (n = 280) | *P* Value |
|---|---|---|---|---|
| **Time of transplantation (UNOS registration)** | | | | |
| Steroids | 1199 (97.2) | 928 (96.8) | 271 (98.5) | .1 |
| ATG | 552 (44.7) | 428 (44.6) | 124 (45) | .9 |
| Alemtuzumab | 112 (9) | 93 (9.7) | 19 (6.9) | .1 |
| Anti-IL-2 receptor antibody | 366 (29.6) | 280 (29.2) | 86 (31.2) | .5 |
| Tacrolimus | 1013 (82.1) | 807 (84.2) | 206 (74.9) | <.001 |
| Cyclosporine | 228 (18.4) | 162 (16.9) | 66 (24) | .008 |
| MMF | 1121 (90.2) | 873 (91.1) | 248 (90.1) | .6 |
| mTOR inhibitor | 75 (6) | 57 (5.9) | 18 (6.5) | .7 |
| Azathioprine | 85 (6.8) | 67 (6.9) | 18 (6.5) | .7 |
| **UNOS follow-up appointment** | | | | |
| Steroids | 963 (90.1) | 748 (89.9) | 215 (91.1) | .5 |
| Tacrolimus | 905 (84.7) | 725 (87.1) | 180 (76.2) | <.001 |
| Cyclosporine | 245 (22.9) | 180 (21.6) | 65 (27.5) | .057 |
| Mycophenolate mofetil | 999 (93.5) | 777 (93.3) | 222 (94) | .7 |
| mTOR inhibitor | 156 (14.6) | 115 (13.8) | 41 (17.3) | .1 |
| Azathioprine | 106 (9.9) | 86 (10.3) | 20 (8.4) | .3 |

Abbreviations: ATG, antithymocyte globulin; IL-2, interleukin-2; mTOR, mechanistic target of rapamycin; MMF, mycophenolate mofetil; UNOS, United Network for Organ Sharing.

## DISCUSSION

In this large-scale, retrospective, national study of 1265 Medicare-insured KTRs diagnosed with cryptococcosis using the USRDS database over a decade, we observed a 6-month mortality rate of 22% following the index hospitalization, associated with a number of clinical factors. This aligns with prior studies reporting mortality rates ranging from 20% to 49% among OTRs [6, 8, 17, 25], and it approaches the 32.8% mortality at 12 months observed in a recent French KTR study [8].

Among the clinical risk factors identified, cirrhosis was the strongest, conferring a 3-fold increase in the odds of death within 6 months compared with those without cirrhosis. This is consistent with findings in other OTRs [4] and in liver transplant recipients [26]. The likely mechanism involves impaired cell-mediated immunity and complement deficiencies that compromise opsonization and antibody-mediated protection [27–29]. Additionally, increased toxicity from antifungals and subsequent acute renal failure may contribute to the high mortality in patients with cirrhosis [29].

Consistent with other studies [4], we found that older age was significantly associated with mortality. Correlated factors, such as the need for pretransplant dialysis, prolonged use of immunosuppressive therapy, an increased burden of transplant-related comorbidities due to longer post-transplant duration, and complications such as renal failure [6], were also identified as mortality predictors and likely compound the risk. Moreover, not using tacrolimus as the main immunosuppressant at UNOS registration and 1-year follow-up was linked to higher mortality within 6 months. Patients unable to use tacrolimus may represent a sicker subgroup, possibly those with severe renal failure or drug–drug interactions, requiring alternative, potentially less effective agents such as cyclosporine.

Overall, mortality in this cohort appears to be driven by multiple clinical and host factors that are likely to modulate the immune response and/or serve as surrogates for poor outcomes. Notably, while CNS involvement is generally considered the most concerning manifestation of cryptococcosis (coded in 51% of our cohort), it was less predictive of mortality in this study than cirrhosis, age, and AKI. This finding aligns with previous observations in KTRs, where no significant difference in mortality was found between those with vs without CM [8], and in other OTRs, in whom renal failure was the greatest predictor of mortality [6].

Cases in our cohort occurred at a median of 30.5 months post-transplant, and up to 44 months in those who did not survive, a period when patients typically receive triple immunosuppressive maintenance therapy (corticosteroids, calcineurin inhibitors, mycophenolate) and may have heterogeneous levels of cellular immunity. Although profound CD4+ deficiency is known to drive CNS disease and cryptococcemia, leading to poor outcomes in uncontrolled HIV or early post-transplant periods when potent antilymphocytic induction is used in liver or heart recipients, profound immunosuppression may not be the most important driver of outcomes in the later-stage KTR

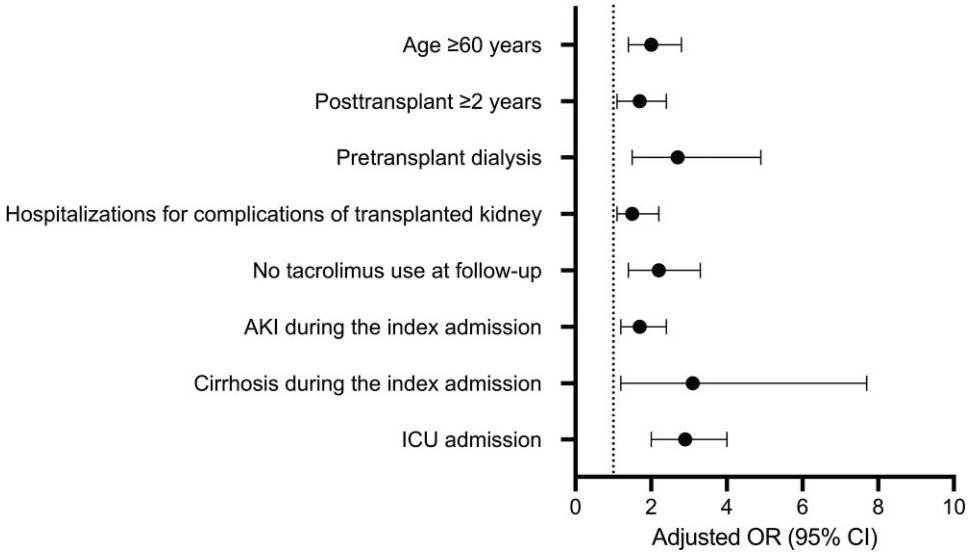


**Figure 3.** Multivariable logistic regression analysis of predictors of 6-month mortality. Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; OR, odds ratio.

population, when immunosuppression levels are more variable [4, 6, 30, 31]. Although other clinical and immunological variables may have contributed to disease pathogenesis in this cohort, data on fungal burden, immunologic parameters, and other clinical variables were not part of the data set. Therefore, we were not able to assess their contribution to disease pathogenesis and mortality.

#### Strengths and Limitations

To our knowledge, this study represents the largest cohort of KTRs with cryptococcosis studied over a 10-year period. The USRDS is the largest and most comprehensive national end-stage renal disease and chronic kidney disease surveillance system linked to Medicare claims, providing highly representative data on this patient population [32]. Moreover, no other large-scale, US-based, KTR-focused study on cryptococcosis outcomes has been conducted in the past decade that reflects current management practices [3, 6].

Despite these strengths, our study has several limitations. First, we identified cryptococcal cases by 2 ICD-9 codes denoting CM and non-CM cryptococcosis, without microbiological corroboration. Thus, details on the site or extent of disease in non-CM cases were not available. Moreover, the CM vs non-CM categorization itself may be prone to misclassification due to potential coding errors in clinically derived (rather than research-based) databases, particularly among HIV-negative patients who may present with atypical symptoms and thus be inaccurately coded. Additionally, the relatively low observed rate of lumbar puncture may reflect coding inaccuracies rather than actual clinical practice. Similar concerns about potential misclassification when using ICD codes have previously been noted in other large claims-based epidemiological studies of cryptococcosis [33, 34]. Nevertheless, although our study is subject to possible misclassification bias, we do not believe that subclassifying non-CM cases by disease site would have substantially affected our results. Our findings indicate that clinical and host factors, rather than CM vs non-CM status, were more strongly associated with outcomes.

Second, because we relied on billing codes, we lacked detailed clinical information, such as symptom duration, measures of fungal burden (eg, blood or cerebrospinal fluid cryptococcal antigen titers or culture results), antifungal treatment regimens, antifungal-related toxicities, inpatient immunosuppressive therapy, adjustments to immunosuppression during hospitalization, and data on specific types of kidney graft complications. Data on immunosuppressive medications were derived from outpatient physician billing codes, which do not capture inpatient use. We were unable to discern if the AKI coded during hospitalization was due to drug toxicity, the disease process itself, or both.

Finally, our study did not include a control group of KTRs without cryptococcosis, limiting our ability to assess cryptococcal-attributable mortality. We were also unable to evaluate outcomes beyond mortality, such as immune reconstitution inflammatory syndrome or graft rejection, which could result from alterations in immunosuppression. Such events may significantly affect morbidity and quality of life yet are not well captured by existing data sources.

## CONCLUSIONS

In summary, this retrospective study demonstrates that cryptococcosis, which occurred late in the post–kidney transplant

period, was associated with high 6-month mortality among KTRs between 2006 and 2016. These findings underscore the need for early recognition and diagnosis, given the substantial mortality observed in our cohort. There were several risk factors for mortality that may have therapeutic implications. For example, transplant recipients with cirrhosis may benefit from earlier testing and risk stratification for earlier detection and intervention before advanced disease develops. Undertesting for cryptococcal antigen in the outpatient setting has been previously reported [35], often due to the underappreciation and neglect of cryptococcosis as a low-incidence disease. Finally, our findings call for ongoing analyses of cryptococcosis mortality in KTRs, with additional clinical and immunological data to provide a more mechanistic understanding of cryptococcal pathogenesis in this high-risk population.

## Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

***Author contributions.*** Conception or design of the work (H.Y., V.S.H., L.P.), data analysis (V.S.H., M.C.H.), data interpretation (all authors), drafting the article (all authors), critical revision of the article (H.Y., V.S.H., L.P.), and final approval of the version to be published (all authors).

***Data source.*** The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the US government.

***Data sharing and reproducibility.*** Data were obtained from the USRDS via a data use agreement and can be obtained from the USRDS upon submission and approval of a project. The statistical code used to analyze the data is available in the Supplementary Data. The R package used in the analysis is available at https://github.com/VagishHemmige/usRds.

***Prior presentations.*** 2021 American Transplant Congress (ATC) poster presentation. Abstract number: 724.

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***Potential conflicts of interest.*** All authors: no reported conflicts.

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