COVID-19 in Kidney Transplant Recipient and Waitlist Patients

Implications of Chest Radiographic Severity Score

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Purpose: To evaluate the chest radiographic severity score (CXR-SS) for coronavirus disease 2019 (COVID-19) patients who are kidney transplant recipients compared with patients on the waitlist.

Study Design and Methods: This retrospective cohort includes 78 kidney transplant recipients (50 men, mean age 59.9 ± 11.9 y) and 59 kidney transplant waitlist patients (33 men, mean age 58.8 ± 10.8 y) diagnosed with COVID-19 between March 15 and May 30, 2020 with reverse transcriptase-polymerase chain reaction. Patient chest radiographs were divided into 6 zones and examined for consolidation. Primary outcome was mortality. Secondary outcomes included hospital admission, intensive care unit (ICU) admission, and intubation. Predictors of our primary and secondary outcomes were identified by bivariate analysis and multivariate regression analysis.

Results: No significant difference was found in CXR-SS between 2 groups (P = 0.087). Transplant recipients had significantly higher rates of hospitalization (odds ratio, 6.8; 95% confidence interval: 1.7, 39.3; P < 0.001), ICU admission (odds ratio, 6.5; 95% confidence interval [CI]: 1.8-35.9; P = 0.002), intubation (odds ratio, 11; 95% CI: 2.4-69.9; P = 0.001), and mortality (odds ratio, 17; 95% CI: 3.9-153.1; P < 0.001). A higher CXR-SS was not predictive of mortality, intubation, or ICU admission. CXR-SS was associated with hospital admission overall (odds ratio, 1.613; 95% CI: 1.04-2.49; P = 0.0314).

Conclusion: The CXR-SS was not predictive of mortality, ICU admission or intubation in our population. Kidney transplant patients with COVID-19 had near universal hospital admission, more than one-third mortality and about a quarter were intubated and admitted to the ICU—all significantly worse outcomes than for patients on the transplant waitlist.

Key Words: Coronavirus disease 2019 pneumonia, chest radiograph, renal transplant

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The chest radiographic (CXR) findings of coronavirus disease 2019 (COVID-19) have been extensively described in recent literature. As radiographs are typically obtained on initial presentation, investigations have shifted toward exploring whether the severity of these radiographic findings is predictive of clinical course and outcomes. To date, several studies have developed radiographic scoring tools and found that CXR scores are independent predictors of outcomes such as mortality, hospital admission, and early intubation within the general population.1–3 The chest radiographic severity score (CXR-SS) is a simple semiquantitative scoring system that was proposed for COVID-19 with the intention that it can have prognostic value for clinical decision making.4 A higher CXR-SS was shown to be an independent predictor for hospitalization and intubation in young and middle-aged adults with COVID-19 who presented to the emergency department.2 Despite the growing volume of literature on findings in the general population, little is known regarding the clinical utility of these scoring methods as well as clinical course in specific susceptible populations.

Our study population is focused on kidney transplant recipients of the Bronx, New York. New York City was the epicenter of disease with the highest death toll during the time period of our study. At the time, the Bronx had the highest rate of COVID-19 infection among the 5 boroughs. With 27.3% of the people living below the poverty line, the impoverished populations within the Bronx are particularly vulnerable to COVID-19 as a result of the already existing socioeconomic disparities and health inequalities.5 In particular, the kidney transplant recipients are our population of interest due to limited studies and lack of consensus regarding the clinical course of COVID-19. Early studies that investigated solid organ transplant recipients diagnosed with COVID-19 noted that these patients have more severe outcomes compared to the general population.6 Conversely, other studies suggest that the risk of transplant recipients is comparable to the general population, or even lower, arguing that long-term immunosuppression may prevent a hyper-inflammatory response.7,8

The purpose of the present study is to investigate the relationship of CXR-SS and mortality for kidney transplant recipients as compared with transplant waitlist patients with COVID-19.
MATERIALS AND METHODS

This is an institutional review board-approved retrospective review of 78 kidney transplant recipients and 59 kidney transplant waitlist patients who were diagnosed with reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed COVID-19 between March 15 and May 30, 2020. The requirement for informed patient consent and HIPPA authorization was waived by the ethics committee for this retrospective study.

Study Population

The study cohort included inpatient and outpatient adults with kidney transplants and patients on the kidney transplant waitlist at a single urban academic medical center that serves a diverse population of low socioeconomic status who were diagnosed with COVID-19 as confirmed by RT-PCR between March 15 and May 30, 2020. Additional inclusion criteria included available CXR at the time of presentation. Patients diagnosed outside of the date range, cases with duplicate or invalid medical record numbers, COVID-19 diagnosed via antibody positivity only or absence of CXR imaging at the time of diagnosis were excluded.

Two independent lists were initially provided by our institutional kidney transplant team. The kidney transplant waitlist registry started with 1414 patients. After exclusion, 59 patients were identified in the waitlist group. The kidney transplant list started with 190 patients who had already been diagnosed with COVID-19. After exclusion, 78 patients remained in the transplant recipient group. The kidney transplant patients received their transplant a median of 56.4 (interquartile range [IQR], 20.6 to 123.1) months before the study period. See Figure 1 for the flowchart detailing the inclusion and exclusion criteria of our study. For the purposes of this study, the kidney transplant waitlist was selected as the control to minimize the confounding effect of underlying comorbidities. Consequently, matching was not performed.

Clinical Data Collection

Clinical records were manually reviewed by 2 researchers independently using EPIC electronic medical record systems. Demographic variables collected included age, sex, self-reported race, and ethnicity. Additional clinical variables obtained included body mass index (BMI).

Outcomes

The primary outcome for our study was patient mortality. Secondary outcomes included hospital admission, intensive care unit (ICU) admission and intubation.

Laboratory Data Collection

Index laboratory values within 2 days of imaging date were collected. The laboratory values collected included white blood cell, hemoglobin, platelet, neutrophil, lymphocyte, neutrophil-lymphocyte ratio (NLR), monocyte, sodium, creatinine, creatine phosphokinase, lactate dehydrogenase, C-reactive protein, D-Dimer, ferritin, procalcitonin, aspartate transaminase/alanine transaminase, and fibrinogen.

Imaging Data Collection

Index CXR at earliest COVID manifestation was jointly reviewed by 2 radiologists who practiced during the local COVID pandemic surge (L.B.H., a fellowship trained chest radiologist with 30 years of experience, and S.S., a second-year radiology resident), in consensus for each patient. To minimize bias, the radiologists were blinded to patient histories other than COVID-19 positivity. The vast majority were portable radiographs, as per institutional protocol, to limit further spread of the disease by limiting patient movement.

CXR-SS, a semiquantitative scoring system proposed for assessing COVID-19 severity, was used to score the CXR images. Each frontal CXR was divided into 3 zones per lung for a total of 6 zones: upper zones (apices to superior portion of the hilum), middle zone (between superior and inferior hilar margins), and lower zones (between inferior hilar margins to costophrenic sulci). Each zone was given a score of 0 if opacity was absent and a score of 1 if opacity was present. The scores were summed to yield a score between 0 and 6. See Figures 2 and 3 for representative examples of the CXR-SS scoring system.
FIGURE 2. Example chest radiographs of kidney transplant recipients with their corresponding chest severity score. A, Chest radiograph of a 39-year-old man with autosomal dominant polycystic kidney disease status posttransplant who presented to the emergency with shortness of breath and was found to be positive for COVID-19 via nasopharyngeal swab. He required supplemental oxygen via nasal cannula and was subsequently discharged with isolation precautions. Portable chest radiograph demonstrates bilateral patchy opacities with a peripheral predominance, left greater than right. Total score of 5. B, Chest radiograph of a 64-year-old man with multiple comorbidities who was admitted for COVID-19 requiring intubation. He tested positive via nasopharyngeal swab and ultimately passed away following hypoxic respiratory failure and cardiac arrest. Portable chest radiograph demonstrates hazy opacities at the right lateral costal margin and left lateral midlung. Total score of 4. C, Chest radiograph of a 75-year-old man with multiple comorbidities who was admitted for COVID-19. He tested positive via nasopharyngeal swab and passed away due to hypoxic respiratory failure. Portable chest radiograph demonstrates bilateral peripheral and basilar predominant hazy opacities; total score of 6.

Statistical Analysis

Comparison of age, BMI, laboratory results and CXR-SS between the kidney transplant patients and patients on the waiting list were performed using the Mann-Whitney U tests, while comparisons on sex, race, ethnicity were performed using the Fisher exact tests.

Clinical outcomes (mortality, hospital admission, ICU admission, intubation) between transplant and waitlist groups were compared using the Fisher exact test. The association of CXR-SS and those outcomes were assessed using logistic regressions with age, BMI, sex, log (creatinine), group included as the co-variates.

The association between values of laboratory tests with CXR-SS were assessed using linear regression models. The association between laboratory tests with mortality were assessed using logistic regression with mortality as the binary response. Significance for statistical analysis was set at $\alpha<0.05$ and a Bonferroni correction for multiple hypothesis was applied. After adjustment, the threshold for significance was set at $\alpha<0.00278$.

A $P$-value of $<0.05$ was considered statistically significant. Statistical analyses were performed using R version 3.6 (R foundation for statistical computing, Vienna, Austria), and GraphPad Prism Version 7.04.

RESULTS

The cohort comprised 78 COVID-19-positive kidney transplant recipients [50 men, mean age 59.9 ± 11.9 y] and 59 COVID-19-positive kidney transplant waitlist patients [33 men, mean age 58.8 ± 10.8 y] of comparable age, sex, race and ethnicity (Table 1).

The median CXR-SS for kidney transplant patients with COVID-19 was 3 (IQR = 1 to 5) in comparison with a CXR-SS of 2 (IQR = 0 to 4, $P=0.087$) for patients on the kidney transplant waitlist (Fig. 4).

Kidney transplant patients had significantly worse outcomes compared with the transplant waitlist patients with COVID-19. Mortality was 37% (29/78) as compared with 3% (2/59) (odds ratio: 17, 95% confidence interval [CI]: 3.9-153.1, $P<0.001$) for the transplant versus waitlist groups, respectively. Kidney transplant patients had higher rates of ICU admission (odds ratio: 6.5, 95% CI: 1.8-35.9, $P=0.001$), intubation (odds ratio: 11, 95% CI: 2.4-96.9, $P<0.001$), hospital admission (odds ratio: 6.8, 95% CI: 1.7-39.3, $P=0.002$) (Table 2).

Transplant patients had statistically significant higher levels of hemoglobin and an elevated NLR with decreased levels of lymphocytes, creatinine, creatine phosphokinase, ferritin and procalcitonin, (Table 3). A positive correlation is seen between CXR-SS and lactate dehydrogenase ($P<0.001$), C-reactive protein ($P<0.001$), fibrinogen ($P<0.001$), and NLR ($P<0.001$) (e-Table 1, Supplemental Digital Content 1, http://links.lww.com/JTI/A211). Lower index levels of creatinine were associated with increased mortality ($P=0.00278$) (e-Table 2, Supplemental Digital Content 1, http://links.lww.com/JTI/A211).

We observed no association between the CXR-SS and mortality after controlled for group, with age, sex, BMI, creatinine as other covariates (Table 4). When analyzed independently, CXR-SS was not associated with mortality or hospital admission. Furthermore, in the transplant recipient group, CXR-SS was also not associated to ICU admission or intubation (Table 4). CXR-SS was associated with hospital admission overall. There was no other association between the CXR-SS and primary or secondary outcomes.

DISCUSSION

Limited literature has investigated the prognostic value of CXR with respect to COVID-19 outcomes and less is known regarding the prognostic value of these scoring tools in susceptible populations. The present study explored the predictive value of the CXR-SS for COVID-19 outcomes in our underserved and ethnically diverse kidney transplant and transplant waitlist population. The CXR-SS was not predictive of mortality, intubation, or ICU admission, although a higher CXR-SS was an independent predictor of hospital admission. This finding is in accordance with Toussie et al.\(^2\) who found that the CXR-SS was an
We found an overwhelming disparity in outcomes between the transplant recipient and transplant waitlist populations. Kidney transplant recipients with COVID-19 faced significantly worse outcomes compared with those on the waitlist: near universal hospital admission, more than one-third died and about a quarter were intubated and admitted to the ICU. Despite this, we found no significant differences between the CXR-SS for the 2 groups, although there was a trend toward a higher score in the transplant recipients.

The CXR-SS was positively associated with CRP, LDH, fibrinogen, and NLR—inflammatory markers that have been shown to be associated with poor outcomes in the general population.10-15 Despite this association, these laboratory markers were not independent predictors of mortality. Remarkably, a lower creatinine was the only clinical variable found to be associated with mortality, likely secondary to the normalizing effect of renal transplantation on creatinine levels.

A few quantitative radiographic scoring tools for COVID-19 have been proposed in recent literature. In early October 2020, Balbi and colleagues found that the quantitative CXR scoring system known as the Brixia score was able to predict mortality in patients who presented to the ED with COVID-19. However, normal radiographs were only seen in 2% of their population and most patients presented with advanced disease.16 In contrast to the Brixia score, the value of the CXR-SS is underscored by its simplicity. CXR-SS is less nuanced in that it does not require one to distinguish alveolar predominance from interstitial predominance or unilateral from bilateral disease. As such, it is a quick and robust method of quantifying the severity of CXR, which is highly desirable given the high prevalence of COVID-19 in the emergency setting and the current lack of a validated scoring tool.

A CT severity scoring system has been proposed and assessed by another study and its application on our patient population had been considered.17 However, in keeping with

### TABLE 1. Patient Demographics and Characteristics

| Variable            | Transplant Waitlist (n = 59) | Transplant Recipients (n = 78) | P   |
|---------------------|------------------------------|--------------------------------|-----|
| Age (y*)            | 58.8 ± 10.7                  | 59.8 ± 11.9                    | 0.58|
| Gender              |                              |                                | 0.73|
| Men                 | 33 (56)                      | 50 (64)                        |     |
| Women               | 26 (44)                      | 28 (36)                        |     |
| BMI†                | 28.15 (23.48-33.13)          | 28.65 (23.7-32.0)              | 0.63|
| Ethnicity           |                              |                                | 0.42|
| Spanish/Hispanic/   |                               |                                |     |
| Latino              | 28 (47.5)                    | 33 (42)                        |     |
| Not Spanish/        |                               |                                |     |
| Hispanic/Latino     | 28 (47.5)                    | 36 (46)                        |     |
| Unknown             | 3 (5)                        | 9 (12)                         | 0.46|
| Race                |                              |                                |     |
| Asian/Pacific       | 3 (5.1)                      | 1 (1.3)                        |     |
| Islander            |                              |                                |     |
| Black/African       | 21 (35.6)                    | 23 (29.5)                      |     |
| American            |                              |                                |     |
| White               | 3 (5.1)                      | 9 (11.5)                       |     |
| Other               | 27 (45.8)                    | 39 (50)                        |     |
| Declined/Unavailable| 5 (8.4)                      | 6 (7.7)                        |     |

Unless otherwise specified, data are numbers, with percentages in parentheses.
*Data is mean with SDs.
†Data is median, with interquartile range in parentheses.
Artificial intelligence (AI) and machine learning will likely play a future role to assist the radiologist in imaging diagnosis as demonstrated by recent studies, including one that demonstrated that a trained AI model can successfully diagnose COVID-19 pneumonia using CXR with a precision of 98.9% and a recall of 94.8% and another that used AI as a prognostication tool in patients with COVID-19 pneumonia based on CXR in combination with clinical variables. While the potential of AI is recognized, until it becomes universally accessible, the simplicity and accessibility of the CXR-SS scoring tool allows it to stand independently for its potential predictive value.

To date, there remains a limited understanding of the impact of COVID-19 within the kidney transplant population. A recent study in the United Kingdom that focused on the risks of receiving a kidney transplantation during the COVID-19 era found that the overall mortality rates were equivalent in waitlist and kidney transplant populations \( (P = 0.69) \). The breakdown of this study showed that COVID-19 was more commonly diagnosed in the waitlist population, which the authors attributed to routine dialysis. However, after confirmation of COVID-19 diagnosis by PCR, transplant patients were found to have a higher mortality. Evidence of higher mortality in transplant recipients has similarly been documented in the general transplant population. An England national cohort study found that, post-COVID-19 diagnosis, solid-organ transplant recipients had a significantly higher mortality relative to those on the waitlist \( (25.8\% \text{ [154 of 597]} \text{ compared with } 10.2\% \text{ [20 of 197]}) \). In accordance with these reports, we found a higher mortality in transplant recipients with confirmed COVID-19 infection.

Limitations to the present study include its retrospective nature. We were unable to reliably collect data on some important variables including patient oxygenation status. Our patient population was obtained from a single center, limiting the statistical power and generalizability of our study. The limited availability of testing kits and health care resources early on during the peak of the COVID-19 pandemic in New York City may have contributed to our smaller study population. The generalizability of our study is further limited by how our study groups were generated. While the transplant waitlist group was generated from a registry of all current patients on the waitlist, the transplant recipient group was prospectively generated from patients who presented with COVID-19. The differential methods in patient selection may have introduced selection bias and limited the scope of our study. In addition, the CXR-SS was generated in consensus by a senior chest radiologist and a radiology resident, not permitting evaluation for agreement or accounting for differences in clinical experience.

One limitation to the radiographic diagnosis of COVID-19 pneumonia in this population was the high prevalence of pulmonary edema, which may limit the

![Figure 4](https://example.com/figure4.png)

**FIGURE 4.** Distribution of CXR-SS among patients in the entire cohort (A). Images (B) and (C) show the score distributions for the waitlist and transplant patients, respectively.

| Outcome                      | Transplant Recipients (n = 78) | Transplant Waitlist (n = 59) | Odds Ratio (Transplant:Waitlist) | 95% CI       | \( P \)  |
|------------------------------|--------------------------------|-----------------------------|---------------------------------|--------------|---------|
| Mortality                    | 29 (37)                        | 2 (3)                       | 17                              | 3.9-153.1    | < 0.001 |
| Hospital admission           | 75 (96)                        | 47 (78)                     | 6.8                             | 1.7-39.3     | 0.002   |
| ICU admission                | 20 (26)                        | 3 (5)                       | 6.5                             | 1.8-35.9     | 0.001   |
| Intubation                   | 21 (27)                        | 2 (3)                       | 11                              | 2.4-96.9     | < 0.001 |

Unless otherwise specified, data are numbers, with percentages in parentheses.

ICU indicates Intensive care unit.
identification of consolidation on CXR. In addition, we relied on the assumption that using transplant waitlist patients as controls would minimize the effect of confounding variables. We recognize that the kidney transplant recipients and waitlist patients are overall heterogeneous populations such that some element of confounding may remain. Variables such as receiving a living or deceased donor transplant, history of transplant complications, time since transplantation and immunosuppression regimen create differential risk profiles even within the transplant population. Consequently, those that were diagnosed and presented with COVID-19 may not be representative of the general transplant population.

The CXR-SS was not predictive of mortality, ICU admission or intubation in our underserved and high-risk kidney transplant and waitlist COVID-19 population, although it predicted hospital admission; in parallel, we underscored the poor prognosis of COVID-19 in our kidney transplant recipients. As a robust and simple means of evaluating CXR on initial COVID-19 presentation, further investigation of the CXR-SS is warranted in varied populations.

| Variable | Waitlist n | Transplant n | P |
|----------|------------|--------------|---|
| WBC (4.8-10.8 k/μL) | 55 | 78 | 0.838 |
| Hemoglobin (14.0-17.4 g/dL) | 55 | 78 | <0.001 |
| Platelets (150-400 k/μL) | 185 (131, 276) | 179 (122.8, 244.8) | 0.278 |
| Neutrophils (1.8-7.7 k/μL) | 3.8 (2.9, 7.6) | 4.9 (3.675, 6.9) | 0.309 |
| Lymphocytes (1.0-4.8 k/μL) | 0.8 (0.6, 1.2) | 0.6 (0.4, 0.9) | <0.001 |
| Monocytes (0.3-0.5 k/μL) | 0.3 (0.3, 0.6) | 0.5 (0.3, 0.6) | 0.503 |
| Sodium (135-145 mEq/L) | 136 (133, 139) | 135 (131, 139) | 0.174 |
| Creatinine (<1.50 mg/dL) | 9 (5.2, 12.3) | 2.2 (1.4, 2.948) | <0.001 |
| CPK (<200 U/L) | 152 (80.5, 424) | 104.5 (54.5, 219.8) | 0.03 |
| LDH (<240 U/L) | 354.5 (265, 544.3) | 350 (281, 406) | 0.534 |
| CRP (<0.8 mg/dL) | 12.2 (5.55, 23.55) | 9.85 (4.9, 15.85) | 0.1 |
| D-dimer (0-0.5 mg/mL) | 1.685 (0.925, 3.143) | 1.69 (0.79, 2.66) | 0.343 |
| Ferritin (25-270 ng/mL) | 2369 (1028, 3470) | 1072 (616, 2324) | 0.022 |
| Procalcitonin (<0.1 ng/mL) | 2 (0.7, 4.975) | 0.3 (0.1, 1.1) | <0.001 |
| AST (<50 U/L) | 29.5 (22.75, 57.25) | 24.5 (21, 35.25) | 0.025 |
| ALT (<40 U/L) | 18 (14.00, 49.25) | 16 (11, 23) | 0.031 |
| Fibrinogen (187-502 mg/dL) | 580.5 (474.0, 709.3) | 610 (508.5, 745.8) | 0.426 |
| NLR | 5.5 (2.75, 9.222) | 7.938 (5.333, 12) | <0.001 |

Data is represented in medians with interquartile range in parentheses. P-values were obtained by Mann-Whitney test. A P-value <0.05 was considered statistically significant.

ALT indicates alanine transaminase; AST, aspartate transaminase
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