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BRIEF COMMUNICATION

Changing trends in mortality among solid organ transplant recipients hospitalized for COVID-19 during the course of the pandemic

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Abbreviations: BMI, body mass index; CNI, calcineurin inhibitor; COVID-19, coronavirus disease 2019; ICU, intensive care unit; mTOR, mammalian target of rapamycin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SOTR, solid organ transplant recipients.

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During the early portion of 2020, short-term mortality among solid organ transplant recipients (SOTR) hospitalized for COVID-19 was high, with estimates ranging from approximately 18%–30%.1–3 Multiple recent studies of hospitalized adults (general population) with COVID-19 have reported that mortality has declined substantially since the start of the pandemic in the United States and Europe, from 20% to 25% during March and April 2020 to less than 10% during July through November 2020.4–7 The overall decline in mortality has been attributed to various factors including earlier diagnosis due to greater access of testing, improvements in the supportive management, and the potential impact of therapies such as corticosteroids and remdesivir.8 Whether similar decreases in mortality have occurred in SOTR has not been reported.

We previously described the 28-day outcomes of SOTR hospitalized for COVID-19 who were enrolled in a multicenter registry between March 1 and April 15, 2020.1 This registry accrued additional cases diagnosed between April 15 and December 31, 2020. Here, we compare outcomes by 28 days among SOTR hospitalized for COVID-19 during the first half of 2020 (March 1, 2020–June 19, 2020) and late 2020 (June 20, 2020–December 31, 2020). Multivariable logistic regression was used to assess comorbidity-adjusted mortality. Time period of diagnosis was available for 1435/1616 (88.8%) SOTR and 971/1435 (67.7%) were hospitalized: 571/753 (75.8%) in early 2020 and 402/682 (58.9%) in late 2020 (p < .001). Crude 28-day mortality decreased between the early and late periods (112/571 [19.6%] vs. 55/402 [13.7%]) and remained lower in the late period even after adjusting for baseline comorbidities (aOR 0.67, 95% CI 0.46–0.98, p = .016). Between the early and late periods, the use of corticosteroids (≥6 mg dexamethasone/day) and remdesivir increased (62/571 [10.9%] vs. 243/402 [61.5%], p < .001 and 50/571 [8.8%] vs. 213/402 [52.2%], p < .001, respectively), and the use of hydroxychloroquine and IL-6/IL-6 receptor inhibitor decreased (329/571 [60.0%] vs. 4/492 [1.0%], p < .001 and 73/571 [12.8%] vs. 5/402 [1.2%], p < .001, respectively). Mortality among SOTR hospitalized for COVID-19 declined between early and late 2020, consistent with trends reported in the general population. The mechanism(s) underlying improved survival require further study.

**KEYWORDS**
clinical research/practice, infection and infectious agents - viral, infectious disease, organ transplantation in general, quality of care/care delivery

1 | INTRODUCTION

Mortality among patients hospitalized for COVID-19 has declined over the course of the pandemic. Mortality trends specifically in solid organ transplant recipients (SOTR) are unknown. Using data from a multicenter registry of SOTR hospitalized for COVID-19, we compared 28-day mortality between early 2020 (March 1, 2020–June 19, 2020) and late 2020 (June 20, 2020–December 31, 2020). Multivariable logistic regression was used to assess comorbidity-adjusted mortality. Time period of diagnosis was available for 1435/1616 (88.8%) SOTR and 971/1435 (67.7%) were hospitalized: 571/753 (75.8%) in early 2020 and 402/682 (58.9%) in late 2020 (p < .001). Crude 28-day mortality decreased between the early and late periods (112/571 [19.6%] vs. 55/402 [13.7%]) and remained lower in the late period even after adjusting for baseline comorbidities (aOR 0.67, 95% CI 0.46–0.98, p = .016). Between the early and late periods, the use of corticosteroids (≥6 mg dexamethasone/day) and remdesivir increased (62/571 [10.9%] vs. 243/402 [61.5%], p < .001 and 50/571 [8.8%] vs. 213/402 [52.2%], p < .001, respectively), and the use of hydroxychloroquine and IL-6/IL-6 receptor inhibitor decreased (329/571 [60.0%] vs. 4/492 [1.0%], p < .001 and 73/571 [12.8%] vs. 5/402 [1.2%], p < .001, respectively). Mortality among SOTR hospitalized for COVID-19 declined between early and late 2020, consistent with trends reported in the general population. The mechanism(s) underlying improved survival require further study.

2 | MATERIALS AND METHODS

2.1 | Study design and patients

We performed a multicenter observational cohort study of SOTR with laboratory-confirmed SARS-CoV-2 infection, as described previously.1 This study was approved by the institutional review board (IRB) at the University of Washington with a waiver of informed consent.
Data were collected using an online data collection tool, REDCap (Research Electronic Data Capture), as described previously.1,3 A summary of all collected variables is shown in Table S1. Only patients who were hospitalized within 28 days of diagnosis, and for whom 28-day follow-up forms were completed, were included in this analysis. Patients were excluded if they were hospitalized for another indication prior to or concurrent with their first positive SARS-CoV-2 test (Figure S1). For example, a patient admitted to the hospital for a hip fracture with a positive SARS-CoV-2 screening test on admission would have been excluded. Patient race and ethnicity were collected as distinct variables and reported by the contributor based on observations or documentation in the electronic medical record. Race and ethnicity were collected as part of the registry to characterize the study population.

Contributors were instructed to submit cases of COVID-19 in SOTR that were diagnosed between March 1 and December 31, 2020. Because dates are considered potentially identifiable protected health information, the month and day of COVID-19 diagnosis could not be reported. Instead, season of diagnosis (the Northern Hemisphere’s winter, spring, summer, or fall) was captured. Cases were considered to have occurred during the early period of 2020 if they were diagnosed in the winter or spring (corresponding to March 1–June 19, 2020) and were considered to have occurred during the late period of 2020 if they occurred during the summer or fall (corresponding to June 20–December 31, 2020). The time cutoff in June 2020 was used in accordance with a mortality inflection point observed in the general population4,5 and because it closely coincided with two major advances for COVID-19: evidence supporting the use of corticosteroids for patients requiring supplemental oxygen and the emergency use authorization of remdesivir in the United States.9

Statistical analysis

Demographic and baseline characteristics were assessed as counts and percentages for categorical values and as a mean (standard deviation) or median (interquartile range) for continuous variables. χ² and Fisher’s exact tests were used to assess proportions of categorical variables. Continuous variables were assessed using Student’s t-test or the Wilcoxon rank-sum test. Death by 28 days was the primary outcome, and admission to the intensive care unit (ICU), use of mechanical ventilation, initiation of renal replacement therapy, pathogen-proven bacterial and fungal pneumonia, bloodstream infection, acute cellular rejection, and duration of hospitalization were secondary outcomes. Age, sex, organ transplanted, geographic location, comorbidities, and features related to immunosuppression were evaluated as potential risk factors for mortality using univariable logistic regression (Table S2). These covariates were selected a priori based on hypotheses and/or prior studies showing a relationship with COVID-19 mortality.10,11 A multivariable logistic regression model was constructed using covariates with at least a prevalence of 5% and a p < .01 in the univariable analysis. The final multivariable model included age, receipt of lung transplant hypertension, diabetes mellitus, heart failure, obesity, chronic kidney disease, coronary artery disease, and chronic lung disease. Age was assessed as a dichotomous variable (age ≤ 65 years vs. >65 years) based on clinical relevance and in accordance with prior studies.5,12 Stata version 16.1 (StataCorp) and R version 4.0.2 were used to perform statistical analyses.

RESULTS

Study population

Of 1616 SOTR with COVID-19 in 2020, the time period of diagnosis was available for 1435 patients (88.8%). Of these 1435 patients, 973 (67.8%) were hospitalized for COVID-19 within the 28 days following diagnosis: 571/753 (75.8%) during the early period and 402/682 (58.9%) during the late period (p < .001, Figure S1). Overall, the baseline characteristics of hospitalized patients excluded due to an unknown period of diagnosis were similar to those of the included population with an available time period of diagnosis (Table S3).

The mean age was similar in the early (57 ± 13 years) and late (58 ± 14 years) periods (p = .28). The proportions of cases from the Northeastern and Midwestern United States were higher in the early period compared to the late period (284/571 [49.7%] vs. 74/402 [18.4%], p < .001 and 97/571 [17.0%] vs. 7/402 [1.7%, p < .001), and the proportions of cases from the Southern and Western United States were lower in the early period compared to the late cohort (100/571 [17.5%] vs. 194/402 [48.3%], p < .001 and 74/571 [13.0%] vs. 119/402 [29.6%, p < .001). Black patients accounted for a higher proportion of cases in the early period than the later period (221/523 [42.3%] vs. 113/375 [30.1%, p < .001). Hispanic or Latinx patients accounted for a lower proportion of cases in the early period than in the late period (151/545 [27.7%] vs. 142/293 [36.2%, p = .006). There was a higher proportion of kidney recipients and a lower proportion of lung recipients in the early cohort compared to the late cohort (383/571 [67.1%] vs. 225/402 [56.0%, p = .001, and 41/571 [7.2%] vs. 63/402 [15.7%, p < .001, respectively). The proportion of patients with absolute lymphopenia on presentation increased from the early to the late periods (150/535 [28.0%] vs. 131/365 [35.9%, p = .01). The proportion with abnormal chest imaging at presentation was similar between time periods (450/541 [83.2%] vs. 294/362 [81.2%, p = .45). Additional baseline characteristics of hospitalized patients in each time period are shown in Table 1.
| Covariate, n (%) | Early period (n = 571) | Late period (n = 402) | p-value |
|------------------|------------------------|-----------------------|---------|
| Male             | 366 (64.1)             | 244 (60.9)            | .3      |
| Race             |                        |                       |         |
| Asian            | 28 (5.4)               | 18 (4.8)              | <.001   |
| Black            | 221 (42.3)             | 113 (30.1)            |         |
| Indigenous People| 4 (0.8)                | 10 (2.7)              |         |
| Pacific Islander | 1 (0.2)                | 3 (0.8)               |         |
| White            | 269 (51.4)             | 231 (61.6)            |         |
| Hispanic or Latinx ethnicity | 151 (27.7) | 142 (36.2) | .006 |
| Age > 65 year    | 167 (29.3)             | 135 (33.6)            | .15     |
| Mean age (SD), years | 57.0 (13.5) | 57.6 (14.1) | .47      |
| Geographic location |                    |                       |         |
| Northeastern U.S. | 284 (49.7) | 74 (18.4) | <.001 |
| Midwestern U.S.  | 97 (17.0)              | 7 (1.7)               | <.001   |
| Southern U.S.    | 100 (17.5)             | 194 (48.3)            | <.001   |
| Western U.S.     | 74 (13.0)              | 119 (29.6)            | <.001   |
| International    | 16 (2.8)               | 8 (2.0)               | .42     |
| Organ            |                        |                       |         |
| Kidney           | 383 (67.1)             | 225 (56.0)            | <.001   |
| Liver            | 76 (13.3)              | 62 (15.4)             | .35     |
| Heart            | 68 (11.9)              | 52 (12.9)             | .63     |
| Lung             | 41 (7.2)               | 63 (15.7)             | <.001   |
| Other            | 3 (0.5)                | 0 (0.0)               |         |
| Underlying comorbidities |            |                       |         |
| Hypertension     | 458 (80.2)             | 296 (73.6)            | .02     |
| Diabetes mellitus| 301 (54.3)             | 191 (47.5)            | .04     |
| Heart failure    | 47 (8.2)               | 18 (4.5)              | .02     |
| Obesity (BMI ≥ 30 kg/m²) | 201 (35.8) | 135 (35.1) | .81     |
| Chronic kidney disease | 202 (35.4) | 125 (31.1) | .16     |
| Coronary artery disease | 124 (21.7) | 58 (14.4) | .004    |
| Chronic lung disease | 52 (9.1)  | 15 (3.7)  | .001    |

(Continues)
TABLE 1 (Continued)

| Covariate, n (%) | Early period (n = 571) | Late period (n = 402) | p-value |
|------------------|------------------------|-----------------------|---------|
| **Baseline immunosuppression** | | | |
| Induction in the past 3 months<sup>a</sup> | 28 (7.0) | 30 (5.3) | .27 |
| CNI, antimitabolite, corticosteroids | 305 (53.4) | 204 (50.8) | .41 |
| Any CNI<sup>f</sup> | 528 (92.5) | 368 (91.5) | .6 |
| Any antimitabolite<sup>f</sup> | 406 (71.1) | 313 (77.8) | .02 |
| Any corticosteroid<sup>f</sup> | 438 (76.7) | 277 (68.9) | .01 |
| Any mTOR inhibitor | 32 (5.6) | 23 (5.7) | .94 |
| **Presenting features** | | | |
| Lymphopenia (ALC < 0.5 × 10⁹/L)<sup>h</sup> | 150 (28.0) | 131 (35.9) | .01 |
| Abnormal chest imaging<sup>i</sup> | 450 (83.2) | 294 (81.2) | .49 |

Abbreviations: ALC, absolute lymphocyte count; BMI, body mass index; CNI, calcineurin inhibitor, mTOR, mammalian target of rapamycin; SD, standard deviation, U.S., United States.

<sup>a</sup>Race was available for 523 patients in the early period and 375 patients in the late period.

<sup>b</sup>Ethnicity was available for 545 patients in the early period and 293 patients in the late period.

<sup>c</sup>Kidney includes 16 kidney/pancreas recipients. Liver includes 28 liver/kidney and 1 liver/pancreas/small bowel recipients. Heart includes 13 heart kidney and 1 heart/kidney/small bowel recipients. Lung includes 2 heart/lung, 1 liver/lung, and 1 lung/kidney/islet cell recipients. Other organ recipients include 2 small bowel recipients and 1 vascular composite allograft recipient.

<sup>d</sup>BMI was available for 561 patients in the early period and 385 patients in the late period.

<sup>e</sup>Induction immunosuppression refers to polyclonal antilymphocyte globulin (early period, n = 16; late period, n = 17), alemtuzumab (early period, n = 2; late period, n = 0), basiliximab (early period, n = 9; late period, n = 6), pulse steroids at ≥500 mg methylprednisolone/day for ≥3 days (early period, n = 6; late period, n = 14), rituximab (early period, n = 1; late period, n = 2), and plasmapheresis (early period, n = 0; late period, n = 1). Some patients received more than one induction agent.

<sup>i</sup>Includes tacrolimus and cyclosporine.

<sup>f</sup>Includes mycophenolate mofetil, mycophenolic acid, azathioprine, and leflunomide.

<sup>h</sup>Dose of baseline corticosteroids consistent of ≤5 mg/day of prednisone or equivalent (early period, n = 414; late period, n = 267) or >5 mg/day of prednisone (early period, n = 24; late period, n = 10).

<sup>g</sup>Absolute lymphocyte count was measured in 535 patients in the early period and 365 patients in the late period.

<sup>i</sup>Chest imaging was performed in 541 patients in the early period and 362 patients in the late period. Refers to changes from baseline for patients with abnormal chest imaging prior to COVID-19.
3.2 | Outcomes by 28 days during study periods

Among SOTR hospitalized for COVID-19, crude mortality by 28 days declined between the early and late periods (112/571 [19.6%] vs. 55/402 [13.7%], respectively, p = .016). Unadjusted survival curves are shown in Figure 1. After adjusting for differences in baseline comorbidities between time periods, the odds of death remained lower in the late period (aOR 0.67, 95% CI 0.46–0.98, p = .04). The proportion of patients admitted to the ICU was similar in early and late periods (213/551 [38.6%] vs. 152/388 [39.2%], p = .87, respectively). The proportion of patients who required any form of supplemental oxygen increased between the early and late periods (395/571 [71.0%] vs. 303/394 [76.9%], p = .04, respectively), but the use of mechanical ventilation declined between the early and late periods (171/554 [30.9%] vs. 93/394 [23.6%], p = .014, respectively). Initiation of renal replacement therapy among patients who did not require dialysis prior to admission declined between the early and late periods (89/528 [17.8%] vs. 48/402 [12.9%], p = .051). The median length of hospitalization was similar in the early and late periods (10 days [IQR: 5–19] and 8 days [IQR: 5–18], p = .08, respectively). The proportion of patients who developed bacterial pneumonia, bloodstream infections, and acute cellular rejection were similar between the two time periods (Table 2).

3.3 | Therapeutic interventions used during study periods

The use of hydroxychloroquine and monoclonal antibodies targeting interleukin 6 (IL-6) or the IL-6-receptor (IL-6R) declined between the early and late periods (Table 3). The use of corticosteroids (at a dose equivalent to ≥6 mg dexamethasone/day) and remdesivir increased between the early and late periods (62/571 [10.9%] vs. 243/402 [61.4%], p < .001, and 50/571 [8.8%] vs. 213/402 [53.0%], p < .001, respectively). Twenty patients in the early period and four patients in the late period received a monoclonal antibody targeting the SARS-CoV-2 spike protein during their clinical course; no patients in the early period were treated with anti-SARS-CoV-2 monoclonal antibodies. Three hospitalized patients in the late period received a monoclonal antibody targeting the SARS-CoV-2 spike protein during their clinical course; no patients in the early period were treated with anti-SARS-CoV-2 monoclonal antibodies. In both the early and late periods, immunosuppression was reduced in over 70% of patients (Table 3). In patients taking antimetabolites at the time of COVID-19 diagnosis, cessation of the antimetabolite was common in both the early and late periods (270/406 [66.5%] vs. 206/313 [66.5%], respectively, p = .87). In patients taking calcineurin inhibitors at the time of COVID-19 diagnosis, reduction of target calcineurin troughs was more common in the early period compared to the late period (160/571 [30.3%] vs. 49/402 [13.3%], respectively, p < .001).

4 | DISCUSSION

In this large multicenter observational cohort study, mortality among SOTR hospitalized for COVID-19 declined during the pandemic, even when controlled for baseline comorbidities, similar to trends reported in the general population.

We explored potential explanations for the observed reduction in mortality during the most recent study period. We noted key differences in patient characteristics between the study periods: the prevalence of heart and lung disease, high-risk comorbidities that are strongly associated with mortality in SOTR with COVID-19, was significantly lower in the late, more recent period. However, mortality remained lower in the late period after adjusting for these confounding conditions, consistent with findings from the general population demonstrating decreased mortality among persons of all ages and in those with multiple medical comorbidities. Thus, differences in underlying comorbidities between study periods are unlikely to fully explain the observed decrease in mortality and suggest that other factors were likely contributory.

We also assessed COVID-19 illness severity between time periods as a possible explanation for the observed decline in mortality. SARS-CoV-2 testing availability increased significantly throughout 2020, potentially facilitating earlier detection of milder cases of COVID-19 during the late study period. Indeed, we observed a significantly lower rate of hospitalization after diagnosis in the late (more recent) period. To minimize the impact of potential variations in baseline severity of illness between time periods, we limited our analysis to hospitalized patients with the rationale that indications for hospitalization likely remained similar between periods. Importantly, surrogate markers of disease severity among hospitalized patients included in the analysis did not vary substantially between time periods. There was no difference in the prevalence of abnormal chest imaging or ICU admission between time periods, and absolute lymphopenia at illness presentation was more common in the later...
TABLE 2 Outcomes by 28 days in solid organ transplant recipients hospitalized for COVID-19 during early and late 2020

| Outcomes, n (%) | Early period (n = 571) | Late period (n = 402) | Unadjusted OR (95% CI) | p-value | Adjusted OR (95% CI), p-value |
|-----------------|-----------------------|----------------------|------------------------|---------|----------------------------|
| Death           | 112 (19.6)            | 55 (13.7)            | 0.7 (0.5–0.9)          | .016*   | 0.67 (0.46–0.98), p = .037  |
| ICU admission   | 213 (38.7)            | 152 (39.2)           | 1.0 (0.8–1.3)         | .87     |                            |
| Any supplemental oxygen | 395 (71.0)        | 303 (76.9)           | 1.4 (1.0–1.8)         | .04*    |                            |
| Nasal cannula or simple facemask | 167 (30.0)       | 152 (38.5)           | 1.5 (1.1–1.9)         | .01*    |                            |
| High flow nasal cannula | 43 (7.7)          | 49 (12.4)            | 1.7 (1.1–2.6)         | .02*    |                            |
| Noninvasive positive pressure ventilation | 14 (2.5)           | 9 (2.3)              | 0.9 (0.4–2.1)         | .82     |                            |
| Mechanical ventilation | 171 (30.9)        | 93 (23.6)            | 0.7 (0.5–0.9)         | .014    |                            |
| New RRTd        | 89 (17.8)             | 48 (12.9)            | 0.7 (0.5–1.0)         | .051    |                            |
| Infectionc      |                       |                      |                       |         |                            |
| Bacterial pneumonia | 43 (7.5)          | 34 (8.5)             | 1.2 (0.7–1.8)         | .60     |                            |
| Fungal pneumonia | 2 (0.4)              | 5 (1.3)              | 3.6 (0.7–18.5)        | .13     |                            |
| Bloodstream infection | 37 (6.5)          | 28 (7.0)             | 1.1 (0.6–1.8)         | .77     |                            |
| Acute cellular rejection | 4 (0.7)           | 6 (1.5)              | 2.1 (0.6–7.7)         | .29     |                            |
| Median length of hospitalization, days (IQR)b | 10 (5–19)         | 8 (5–18)             | .08                  |         |                            |

Abbreviations: CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; OR, odds ratio; RRT, renal replacement therapy.

Reference is early period.

P-values reflect χ² and Fisher’s exact tests for heterogeneity for dichotomous outcomes and Wilcoxon rank-sum test for the continuous outcome (length of hospitalization). *Indicates statistical significance at α = .05.

Adjusted odds ratio is based on multivariable logistic regression for the primary outcome (death). The multivariable model adjusted for age (> 65 years vs. ≤65 years), receipt of lung transplant hypertension, diabetes mellitus, heart failure, obesity, chronic kidney disease, coronary artery disease, and chronic lung disease.

ICU admission status available for 551 patients in the early period and 388 patients in the late period.

ICU admission status available for 551 patients in the early period and 388 patients in the late period.

Infections include bacterial pneumonia, fungal pneumonia, and bloodstream infections. Only pathogen-proven infections were included. Some patients experienced more than one infection.

Length of hospital stay was available for 547 patients in the early period and 391 patients in the late period. The number of days refer to the number of days hospitalized during the first 28 days following Covid-19 diagnosis.

The adoption of therapeutic corticosteroids, prone positioning to improve oxygenation without mechanical ventilation, and overall adaptation of health care systems to the pandemic have been cited as potential reasons for lower contemporary mortality in the general population.4,5,7,18 The decrease in use of renal replacement therapy observed in this cohort is consistent with findings from the general population and may reflect changes in the approach to volume management over the course of the pandemic.19 We observed a decline in the use of mechanical ventilation, despite an increase in the proportion of patients requiring any form of supplemental oxygen. The observed decrease in mechanical ventilation likely reflects global changes in the approach to the management of COVID-19 over time, as early intubation at the onset of hypoxemia was a frequent practice early but became less common over time.20 The current observational study design does not allow for definitive testing of these hypotheses and associations between specific interventions and outcomes should be interpreted with caution. Substantial confounding by indication, whereby sicker patients were more likely to receive therapeutic interventions, precludes meaningful assessment of the association between various treatments and outcomes on
TABLE 3 Treatments for Covid-19 in solid organ transplant recipients hospitalized for Covid-19 during early and late 2020

| Treatment, n (%) | Early period (n = 571) | Late period (n = 402) | p-valuea |
|------------------|------------------------|-----------------------|----------|
| Corticosteroids6 | 62 (10.9)              | 243 (61.4)            | <.001*   |
| Remdesivir       | 50 (8.8)               | 213 (53.0)            | <.001*   |
| Anti-IL-6/IL-6R agents | 73 (12.8)       | 5 (1.2)               | <.001*   |
| Hydroxychloroquine | 329 (60.0)         | 4 (1.0)               | <.001*   |
| Convalescent plasma | 48 (8.4)          | 119 (29.6)            | <.001*   |
| Monoclonal antibodies targeting SARS-CoV-2 | 0 (0.0) | 3 (0.8) | .07 |
| Any decrease in maintenance of immunosuppressionb | 322 (79.1) | 265 (65.9) | .05* |
| Hold antimetabolitec | 270 (66.5)       | 206 (50.8)            | .87      |
| Decrease antimetabolitec | 51 (12.6)        | 31 (9.9)              | .27      |
| Decrease CNI trough goald | 160 (30.3)       | 49 (13.3)             | <.001*   |

Abbreviations: CNI, calcineurin inhibitor; CI, confidence interval; IL-6R, interleukin-6 (IL-6), interleukin-6 receptor; OR, odds ratio.

*p-values reflect χ2 and Fisher’s exact tests for heterogeneity.

Indicates statistical significance at α = .05.

Dosed at ≥6 mg dexamethasone equivalents per day.

Complete cessation or reduction in the dose of or goal trough of at least one maintenance immunosuppressive agent. Some patients had more than one change. In the early period, corticosteroids were stopped in 2/438 (0.5%) patients taking steroids at baseline. In the late periods, steroids were stopped in 1/277 (0.3%) and decreased in 1/277 (0.3%) patients taking steroids at baseline.

Refers to percentage of patients taking a calcineurin inhibitor at baseline (528 patients in the early period and 368 patients in the late period).

Refers to percentage of patients taking a corticosteroid at baseline (438 patients in the early period and 277 patients in the late period). Corticosteroid dose was decreased in one patient in the late period; all other steroid decrease involved complete cessation.

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