Risk of COVID-19 associated pulmonary aspergillosis in intensive care patients based on duration of corticosteroid administration

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Background

- Coronavirus disease 2019 (COVID-19) associated pulmonary aspergillosis (CAPA) has emerged as a complication in critically ill COVID-19 patients
- Steroids are standard of care for COVID-19 patients and a known risk factor for opportunistic infections, such as CAPA, due to their immunosuppressive properties
- Previous literature has shown that steroids carry an increased risk of secondary infections and are a known risk factor for pulmonary aspergillosis, but the duration of use associated with this risk remains unknown

Purpose

To evaluate if the duration of steroids therapy ≤10 days vs >10 days affects the risk of developing CAPA

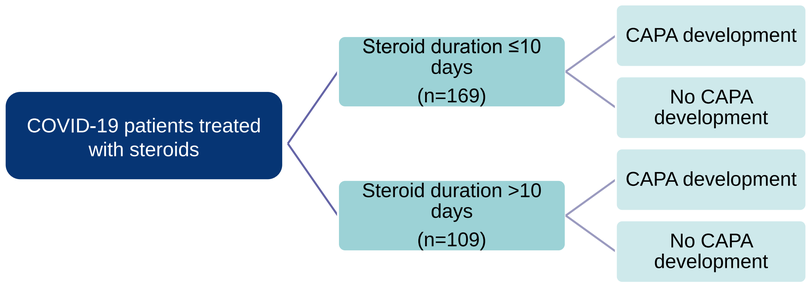
Study Design

- Single-center, retrospective, cohort study from March 2020 to December 2021

Inclusion:
- Adult patients
- Severe COVID pneumonia requiring mechanical ventilation
- Received at least 3 days of steroid therapy

Exclusion:
- Pregnant patients
- Incarcerated patients

Figure 1: Study Design



Outcomes

Primary
- Incidence of CAPA post steroid therapy for COVID-19 based on duration of steroid exposure

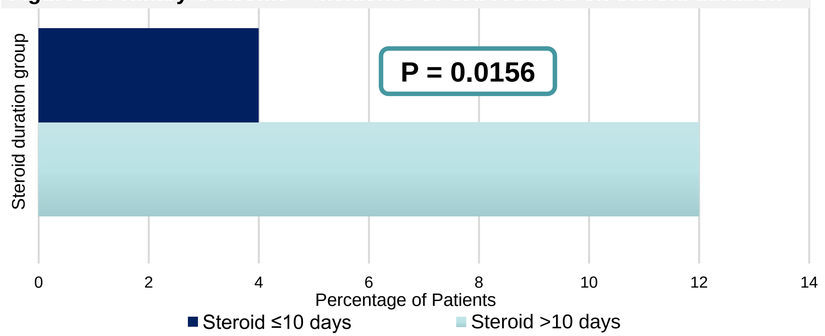
Secondary
- Ventilator-free days at 28 days
- Ventilator-free days at 60 days
- Inpatient mortality

Results

Table 1: Baseline Characteristics	Steroid Duration ≤10 days (n=169)	Steroid Duration >10 days (n=109)	P-value
Age, median in years (IQR)	57 (47-66)	59 (50-69)	0.1907
Female, n (%)	92 (54.4)	52 (47.7)	0.2728
BMI, median (IQR)	32 (27-38)	32 (26-40)	0.5218
Tobacco use, n (%)			0.4280
Current	9 (5.3)	9 (8.3)	
Former	38 (22.5)	22 (20.2)	
Never	114 (67.5)	76 (69.7)	
Unknown	8 (4.7)	2 (1.8)	
Comorbidities, n (%)			
Diabetes	88 (52.1)	52 (47.7)	0.4773
COPD	5 (3.0)	8 (7.3)	0.1429
Asthma	8 (4.7)	8 (7.3)	0.3678
Acute kidney injury	41 (24.3)	9 (8.3)	0.0007
Cancer	20 (11.8)	8 (7.3)	0.2154
Solid organ transplant	3 (1.8)	8 (7.3)	0.0271
Prior steroid use†, n/total n (%)	10/88 (11.4)	22/89 (24.7)	0.0210
Laboratory values, median (IQR)			
WBC	9.2 (6.9-13.2)	13.3 (8.7-17.8)	<0.0001
SOFA score	6 (4-9)	8 (5-11)	0.0055
PaO2/FiO2 ratio	98 (66-163)	78 (58-168)	0.2399
Inpatient therapy, median (IQR)			
Total steroid duration	6 (5-8)	18 (14-23)	<0.0001
Prednisone equivalence†	280 (200-400)	750 (549-1253)	<0.0001
Tocilizumab	6 (3.6)	17 (15.6)	0.0004

†Data not available for all patients; analyzed in smaller subset of patients

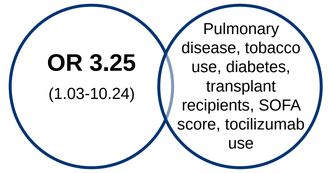
Figure 2: Primary Outcome – Incidence of CAPA based on steroid duration



Results

Figure 3: Multivariate Analysis

Steroid duration as an independent risk factor for CAPA



Steroid duration as an independent risk factor for mortality

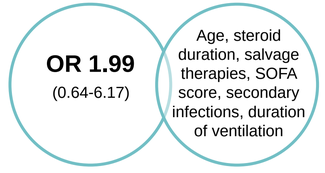


Table 2. Secondary Outcomes	Steroid ≤10 days	Steroid >10 days	P-value
Ventilatory-free days at 28 days, median (IQR)	1.5 (0-28)	0 (0-0)	<0.0001
Ventilator-free days at 60 days, median (IQR)	38.5 (0-60)	0 (0-0)	<0.0001
Inpatient mortality, n (%)	73 (43.2)	84 (77.1)	<0.0001
Secondary Infections†, n/total n (%)	44/88 (28.4)	72/89 (44.9)	0.0220

†Data not available for all patients; analyzed in smaller subset of patients

Limitations

- Single-center, retrospective study
- Small sample size
- Higher severity of illness in >10 day steroid duration group

Conclusions

- Duration of steroid treatment >10 days in critically ill patients was associated with an increased risk of CAPA
- Inpatient mortality, mechanical ventilation-free days at 28 days and secondary infections were all significantly worse for >10 days steroid cohort
- Critically ill patients may require steroids for reasons beyond COVID-19 and clinicians should be cognizant of the risk of CAPA with prolonged courses

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