Categorization of COVID-19 severity to determine mortality risk

Marie C. Bradley, PhD, MScPH, Mpharm[1]; Elizabeth M. Garry, PhD, MPH[4] ; Andrew Weckstein, BA[4]; Kenneth Quinto, MD, MPH[3]; Tamar Lasky, PhD[2], FISPE; Sandy Leonard, MPH[5]; Sarah Vititoe, MPH[4]; Nicolle M. Gatto, PhD, MPH[4]

[1]Division of Epidemiology, Office of Surveillance and Epidemiology, Center For Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD
[3]Office of the Commissioner, Food and Drug Administration, Silver Spring, MD
[3]Office of Medical Policy, Food and Drug Administration, Silver Spring, MD
[4]Aetion Inc, New York City, NY
[5]Partnerships and RWD, HealthVerity, Philadelphia, PA, USA.

Introduction

- Respiratory support, indicated by use of supplemental oxygen or non-invasive ventilation, (O2/NIV), and invasive mechanical ventilation, (IMV) in hospitalized patients with COVID-19 appears to be a critical indicator of disease severity.
- It is important to account for disease severity when determining effectiveness of COVID-19 treatments in the inpatient setting.
- The World Health Organization (WHO) proposed the WHO Clinical Progression Scale, to classify COVID-19 patient outcomes according to disease progression and severity among ambulatory and hospitalized patients [WHO Working Group 2020].
- However, algorithms to examine COVID-19 severity in inpatient real-world data (RWD) are needed.

Objective

To develop an algorithm to determine COVID-19 severity based on use of O2/NIV and IMV in inpatient RWD and then to estimate the risk and incidence rate (IR) of death among these subgroups to attempt to confirm that patients with greater COVID-19 disease severity at hospital admission are at higher risk for severe outcomes.

Disclosures: This study is part of a research collaboration agreement between the U.S. Food and Drug Administration (FDA) and Aetion, Inc. to use real-world data to advance the understanding and the natural history of coronavirus disease (COVID-19) in specific patient populations, as well as treatment and diagnostic patterns during the COVID-19 pandemic.

This poster reflects the views of the authors and should not be construed to represent FDA's views or policies. EMG, ARW, SEV, and NMG are employees of Aetion, Inc., with stock options or existing equity.

Materials and Methods

Data source: HealthVerity data April 2020-January 2021 that comprises the following from all 50 US states and all major payer types (commercial, Medicaid and Medicare)

- medical and pharmacy claims
- laboratory data with results
- chargemaster records for inpatient and outpatient hospital encounters
- electronic medical record (EMR) data

Study cohort: Patients hospitalized with a COVID-19 diagnosis or positive SARS-CoV-2 laboratory results.

Subgroups: An algorithm based on a modified version of the WHO clinical progression scale (mWHO) was developed to categorize mutually exclusive COVID-19 severity levels at hospital admission according to respiratory support received including: no O2, O2/NIV, and IMV.

The algorithm included procedure and diagnosis codes indicative of need for respiratory support or procedure-related, and revenue codes indicating O2 use.

Statistical analyses: Patients were followed from hospital admission until death, discharge, or 28-days to report risks, IR, and corresponding 95% confidence intervals overall and for each severity level. Trends for heterogeneity in risk/IR of death across severity levels were evaluated. All analyses were conducted using the Aetion Evidence Platform® (2021).

Conclusion

Although performance of the mWHO COVID-19 severity algorithm remains to be validated, we observed a positive association between algorithm-defined COVID-19 severity level and 28-day mortality risk and IR. These findings provide assurance that our mWHO COVID-19 severity algorithm can be used for confounding control in studies of inpatient COVID-19 treatment effectiveness.

References: World Health Organization (WHO) Working Group on the Clinical Characterisation and Management of COVID-19 infection. A minimal common outcome measure set for COVID-19 clinical research. Lancet Infect Dis. 2020 Aug;20(8):e192-e197. doi: 10.1016/S1473-3099(20)30483-7. Epub 2020 Jun 12. Erratum in: Lancet Infect Dis. 2020 Oct;20(10):e250

Results and Discussion

- There were 88,967 COVID-19 positive patients identified who were hospitalized.
- The mWHO COVID-19 severity algorithm categorized:
  - 33,579 (37.7%%) as requiring no O2,
  - 47,691 (53.6%) as requiring O2/NIV, and
  - 7,697 (8.7%) as requiring IMV at hospital admission.
- Among **11,010 patients** who died, 1,294 received no O2, 6,060 received O2/NIV, and 3,656 received IMV at admission. The risk of death was 12.4% (12.2-12.6%) with an IR per 1000 person-days of 15.75 (15.46-16.05) over a median (IQR) of 5 (3-10) days.
- The risk of death among patients with no O2, O2/NIV, and IMV increased with increasing severity level ($p<0.001$). A similar trend was found for IR per 1000 person-days ($p<0.001$), despite an increase in median follow-up days. (Table 1).

Figure 1: Death rate in patients with and without respiratory support

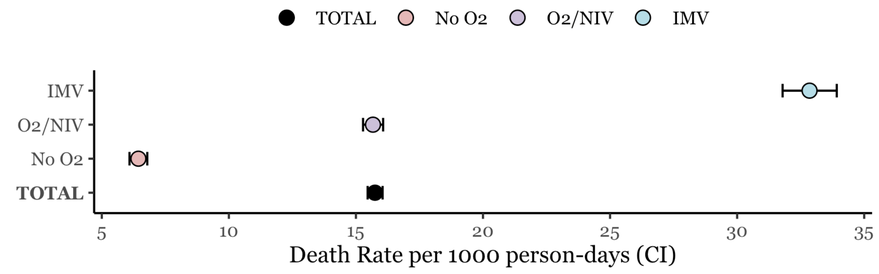

Table 1. Risk of death in patients with and without respiratory support

	TOTAL	NO O2	O2/NIV	IMV
Number of patients	**88,967**	**33,579**	**47,691**	**7,697**
mWHO category %	100.0%	37.7%	53.6%	8.7%
Total person days	698,906	200,974	386,649	111,283
Median (IQR) person days	5 (3-10)	4 (2-7)	6 (4-10)	13 (6-23)
Number of patients with an event	11,010	1,294	6,060	3,656
Death risk percent (CI)	12.4% (12.2-12.6%)	3.9% (3.7-4.1%)	12.7% (12.4-13.0%)	47.5% (46.4-48.6%)

*O2/NIV= supplemental oxygen or non-invasive ventilation, IMV= invasive mechanical ventilation, NO O2= neither of the above