Infection rate, mortality and characteristics of veterans with amyotrophic lateral sclerosis with COVID-19

Approximately 16,000 persons in the United States are affected by amyotrophic lateral sclerosis (ALS).1 Persons with ALS (PALS) have distinctive pathophysiological risks and health determinants that may increase their vulnerability for infection with severe-acute-respiratory-syndrome-associated-coronavirus (SARS-CoV-2) and severe Coronavirus-2019 (COVID-19) outcome.2,3 Data on the prevalence and impact of COVID-19 in this population is scarce.4

The Veteran Administration Informatics and Computing Infrastructure (VINCI) Resource Center and the Veteran Health Administration (VHA) Spinal Cord Injury/Disorders (SCI/D) Registry are operational tools which extract data from the Corporate Data Warehouse (a relational database which merges multiple VA data sources). VINCI utilizes data so that aggregate statistics can be accessed. In adjunct, the VHA-SCI/D Registry has specific inclusion criteria (i.e.: Veterans must be followed at an SCI/D Center) and the data extracted is validated. Both VINCI and VHA-SCI/D Registry have added the functionality for the identification of COVID-19-positive patients. Within this letter, the authors will describe the COVID-19 prevalence and case fatality rate (CFR), as reported by aggregate summaries from VINCI, as well as the characteristics and outcomes, as reported by the VHA-SCI/D Registry, for COVID-19-positive veterans with ALS.

From January 1st, 2020 to January 31st, 2021, VINCI identified 192,690 (3.6%) COVID-19-positive cases (excluding active, defined as patients tested or treated at a VA facility for known or probable COVID-19 who have neither died nor reached convalescent status) from a total of 5,295,285 Veterans. Of these positive cases, 8838 (4.6%; CI: 4.5%–4.7%) COVID-related deaths were recorded (within 30 days of diagnosis). Considering the 4086 PALS within VINCI, 138 COVID-19-positive cases were identified. Of these, 19 (13.8%; CI 8.5%–20.7%) died. Compared to the overall veteran population, veterans with ALS were 3.0 times more likely to die within 30 days of COVID-19 diagnosis (CI: 1.9–4.9, p < .001).

The VHA-SCI/D Registry includes 1910 of the 4086 (47%) Veterans with ALS. Of these, 699 (37%) were laboratory tested for COVID-19, and a total of 68 (10%) were found to be COVID-positive. Excluding three active cases, 48% had an uncomplicated course, 18% required hospitalization, 14% were transferred to an intensive care unit (ICU), and 20% died (Table 1). Outcomes more granular than 30-day mortality for the general VA population cannot be obtained without further regulatory approval. However, if compared to data available for the general population, the outcomes identified in the VHA-SCI/D Registry such as hospitalization, ICU care and death, highlight an exceptionally poor COVID-19 prognosis for patients with ALS.5

The 30-day mortality approach to determining CFR, which is the only practical method for large datasets such as VINCI, likely underestimates death due to COVID-19. Within the VHA-SCI/D Registry, eight PALS died within 30 days of diagnosis. However, an additional five were deemed to have died from COVID-19-related sequelae outside of the 30-day window. The ALS COVID-19-CFR is likely better estimated by the VHA-SCI/D Registry (20.0%; CI: 11.1%–31.8%), while the CFR comparison between PALS and the general VA population is more appropriately estimated by the within-VINCI 30-day mortality analysis (OR = 3.0; CI: 1.9–4.9; p < .001). To assess whether the COVID-19 related death rate for PALS was not artificially inflated by the fact that death is generally more likely to occur in these patients,6 we calculated the mortality rate for veterans with ALS in the 7 years prior to the COVID pandemic. The 2020 mortality rate was an outlier, and provides further evidence of the high potential of lethal SARS-CoV-2 infection for patients with ALS (Figure 1).

Multivariable binary logistic regressions, constructed using a forward-stepwise approach, were used to identify patient factors associated with increased risk of (1) contracting COVID-19 and (2) either dying from COVID-19 or requiring an ICU stay secondary to COVID-19. All variables in Table 1 were tested for association. The only factor adding predictive value was obstructive sleep apnea (OSA), which was associated with an increased chance of contracting COVID-19 (OR = 2.2; CI:1.2–4.0; p = .012). We could not extract more specific determinants of respiratory compromise than OSA, which has been shown to correlate with respiratory muscle weakness and disease progression.7 Though no factors proved to be associated with COVID-19 death or ICU stay in the present sample, efforts to find variables that can reliably identify at-risk sub-cohorts of COVID-positive ALS patients are ongoing.

This report demonstrates an increased risk of COVID-19 related death in individuals with ALS. This finding, although limited, should be taken into consideration by relevant agencies during COVID-19 vaccine prioritization decision making processes.

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Abbreviations: ALS, Amyotrophic lateral sclerosis; PALS, Persons with ALS; SARS-CoV-2, Severe-acute-respiratory-syndrome-associated-coronavirus; COVID-19, Coronavirus-2019; VINCI, Veteran Administration Informatics and Computing Infrastructure; VHA, Veteran Health Administration; SCI/D, Spinal cord injury/disorders; CFR, Case fatality rate; ICU, Intensive Care Unit; OSA, Obstructive sleep apnea.
TABLE 1  Demographics and comorbidities of ALS patients in the SCI-D registry, by COVID-19 status

|                      | All patients with ALS | Not COVID tested | COVID tested | COVID - | COVID + | All | Death | ICU | Acute care | Uncomplicated course |
|----------------------|-----------------------|------------------|--------------|---------|---------|-----|-------|-----|------------|-------------------|
| N                    | 1910                  | 1211             | 699          | 631     | 68      | 13  | 9     | 12  | 34         |
| Age (mean, SD)       | 69 (11)               | 70 (11)          | 68 (11)      | 68 (11) | 69 (11) | 67 (13)| 72 (8) | 66 (12) |
| Race                 |                       |                  |              |         |         |     |       |     |            |
| White                | 1573 (82)             | 1005 (83)        | 568 (81)     | 512 (81)| 56 (82) | 10 (77)| 5 (5)  | 11 (9) | 30 (9)    |
| Black                | 144 (8)               | 84 (7)           | 60 (8)       | 54 (8)  | 6 (9)   | 2 (15)| 1 (2)  | 1 (8)  | 2 (6)     |
| Other                | 193 (10)              | 122 (10)         | 71 (10)      | 65 (10) | 6 (9)   | 1 (7) | 3 (3)  | 0 (0)  | 2 (6)     |
| Rural (vs urban)     | 589 (31)              | 406 (34)         | 183 (26)     | 160 (25)| 23 (34) | 6 (46)| 1 (11) | 4 (33) | 12 (35)   |
| Comorbidities        |                       |                  |              |         |         |     |       |     |            |
| Cardiovasculara      | 724 (38)              | 366 (30)         | 358 (51)     | 329 (52)| 29 (4)  | 2 (15)| 6 (70) | 7 (60) | 14 (40)   |
| Respiratoryb         | 186 (10)              | 94 (8)           | 92 (13)      | 8 (13)  | 10 (15) | 1 (8) | 3 (30) | 4 (30) | 2 (6)     |
| Diabetes             | 426 (22)              | 248 (20)         | 178 (25)     | 162 (27)| 16 (23) | 2 (15)| 3 (30) | 4 (30) | 7 (20)    |
| CKD                  | 64 (3)                | 26 (2)           | 38 (5)       | 33 (5)  | 5 (7)   | 0 (0) | 0 (0)  | 3 (25) | 2 (6)     |
| OSA                  | 212 (11)              | 89 (7)           | 123 (17)     | 105 (17)| 18 (26) | 2 (15)| 4 (40) | 4 (30) | 2 (6)     |
| Tobacco use          | 140 (7)               | 56 (5)           | 84 (12)      | 80 (13) | 4 (6)   | 1 (8) | 0 (0)  | 2 (20) | 1 (3)     |

Note: Data reported as N (%), unless otherwise specified.

a Including cerebrovascular accident, heart failure, hypertension, and ischemic heart disease.

b Including asthma and chronic obstructive pulmonary disease.

FIGURE 1  Mortality rate presented as deaths per 1000 persons for veterans with ALS, comparing 2020 to monthly averages from the prior 7 years [Color figure can be viewed at wileyonlinelibrary.com]

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

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DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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