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# Reporting SOFA in research: we should always present each of the SOFA subscores

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## Abstract

**Background:** The Sequential Organ Failure Assessment (SOFA) score is the sum of 6 components, each representing one organ system with dysfunction classified on a 4-point scale. In research, usually by default, the total SOFA score is taken into account, but it may not reflect the severity of the condition of the individual organs. Often, these values are expected to predict mortality.

**Methods:** In this study, we reanalysed 2 cohorts of critically ill elderly patients to explore the distribution of SOFA subscores and to assess the between-group differences. Both cohorts were adjusted to maintain similarity in terms of age and the primary cause of admission (respiratory cause).

**Results:** In total, 910 (non-COVID-19 cohort) and 551 patients (COVID-19 cohort) were included in the analysis. Both cohorts were similar in terms of the total SOFA score (median 5 vs. 5 points); however, the groups differed significantly in 4/6 SOFA subscores (respiratory, neurological, cardiovascular, and coagulation subscores). Moreover, the cohorts had different fractions of organ failures (defined as a SOFA subscore ≥ 3).

**Conclusions:** This analysis revealed significant differences in SOFA subscores between the COVID-19 and non-COVID-19 respiratory cohorts, highlighting the importance of considering individual organ dysfunction rather than relying solely on the total SOFA score when reporting organ dysfunction in clinical research.

**Key words:** Sequential Organ Failure Assessment, SOFA score, multiorgan dysfunction, organ failure.

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The Sequential Organ Failure Assessment (SOFA) score has been utilised as a primary tool to describe organ dysfunction in critically ill patients for over 25 years. The SOFA score is a sum of 6 components, each representing one organ system whose dysfunction is classified on a 4-point scale. Since its inception, the score has been validated across different critically ill populations and has often served as a prognosticator of mortality. Both total SOFA score as well as changes in total SOFA score have been widely used as an endpoint in clinical trials [1–3]. However, each case of multiorgan failure differs in terms of the degree of each organ's involvement; therefore, 2 seemingly similar total SOFA scores may reflect completely different clinical scenarios and prognoses. Hence, to promote comprehensive

**TABLE 1.** Characteristics of COVID-19 and non-COVID-19 cohorts

| Variable | Non-COVID-19 cohort (VIP-2 study) | COVID-19 cohort (COVIP study) | *P*-value |
|---|---|---|---|
| Number of patients (*n*) | 910 | 551 | – |
| Age (years) | 84 (81–86) | 83 (81–85) | < 0.0001 |
| Male sex (yes/no) | 458 (50.3) | 367 (66.6) | < 0.0001 |
| SOFA: total (points) | 5 (3–8) | 5 (3–8) | 0.5 |
| Clinical Frailty Scale (points) | 4 (3–6) | 3 (3–5) | < 0.0001 |
| Vasopressors (yes/no) | 394 (43.3) | 336 (60.9) | < 0.0001 |
| Invasive mechanical ventilation (yes/no) | 401 (44.1) | 315 (57.2) | < 0.0001 |
| Renal replacement therapy (yes/no) | 73 (8.3) | 67 (12.2) | 0.019 |

SOFA – Sequential Organ Failure Assessment
Continuous variables are presented as median (IQR); categorical variables are presented as *n* (%).

reporting of SOFA in clinical trials, we compared 2 critically ill, elderly cohorts in terms of differences in the distribution of each SOFA subscore.

## METHODS

We conducted a retrospective analysis by comparing 2 different, multicentre, prospectively enrolled cohorts: 1) VIP-2 (ID: NCT03370692), which was a cohort focused on the critically ill elderly (≥ 80 years old) and 2) COVIP (ID: NCT04321265), which was a population of critically ill, older COVID-19 patients [4, 5]. National coordinators were responsible for the recruitment of intensive care units (ICUs), coordinated the national and local ethical permission, and supervised patient recruitment at the national level. Ethical approval was mandatory for study participation in each country. Due to the diversity of ethical consent procedures, some countries could recruit patients without informed consent while the rest had to obtain it.

Because both cohorts were designed to analyse frailty in the context of critical illness, the cohorts were analogous in design and in data handling. To maximise the similarity between the groups, only respiratory admissions ($n = 910$) from the VIP-2 study (non-COVID-19 cohort) and only patients ≥ 80 years old ($n = 551$) from the COVIP study (COVID-19 cohort) were taken into account. Hence, both cohorts included only elderly patients (≥ 80 years old) with a primary respiratory cause of admission.

The baseline characteristics encompassed key details such as the patients' age, gender, frailty (by using the Clinical Frailty Scale), and the treatment details in the ICU. Within the initial 24 hours of ICU admission, we employed the SOFA score to evaluate the extent of organ dysfunction. The SOFA score encompasses 6 organ systems, namely cardiovascular, respiratory, renal, neurological, hepatic, and coagulation systems. Each system was assigned a score ranging from 0 to 4 points, with higher scores indicating more severe organ failure. The maximum score recorded within the first 24 hours was documented.

Rank-sum tests were used to analyse the differences in SOFA subscore distributions. Continuous variables are presented as median (IQR) and compared using rank-sum tests. Categorical variables were compared using the $\chi^2$ test. The SOFA score was approached from 2 perspectives: first as a categorical variable with assigned points (1, 2, 3, or 4) in each organ system, and secondly as a dichotomous indicator of organ failure (specifically, a SOFA score of 3 points or higher in each domain).

## RESULTS

There were 910 patients in the non-COVID-19 cohort and 551 patients in the COVID-19 cohort. Patient characteristics are shown in Table 1. Changes in the distribution of SOFA subscores are presented in Figure 1. Both groups had a similar median total SOFA score (5 vs. 5 points; $P = 0.5$); however, they differed significantly in respiratory, neurological, cardiovascular, and coagulation SOFA subscores (Table 1, Figure 1). As for the differences in organ failures (SOFA subscore ≥ 3 points), the non-COVID-19 cohort had significantly more patients with neurological failure, while the COVID-19 cohort had a higher fraction of respiratory and cardiovascular failures (Table 2).

## DISCUSSION

In this study, we compared 2 cohorts of critically ill elderly patients with respiratory cause of admission to investigate differences in SOFA subscores. Considering the variability in multi-organ failure, we aimed to emphasise the importance of reporting individual SOFA subscores in addition to the total score. Despite the seemingly similar total SOFA score (5 vs. 5 points, $P = 0.5$), both cohorts exhibited different degrees of organ failure.

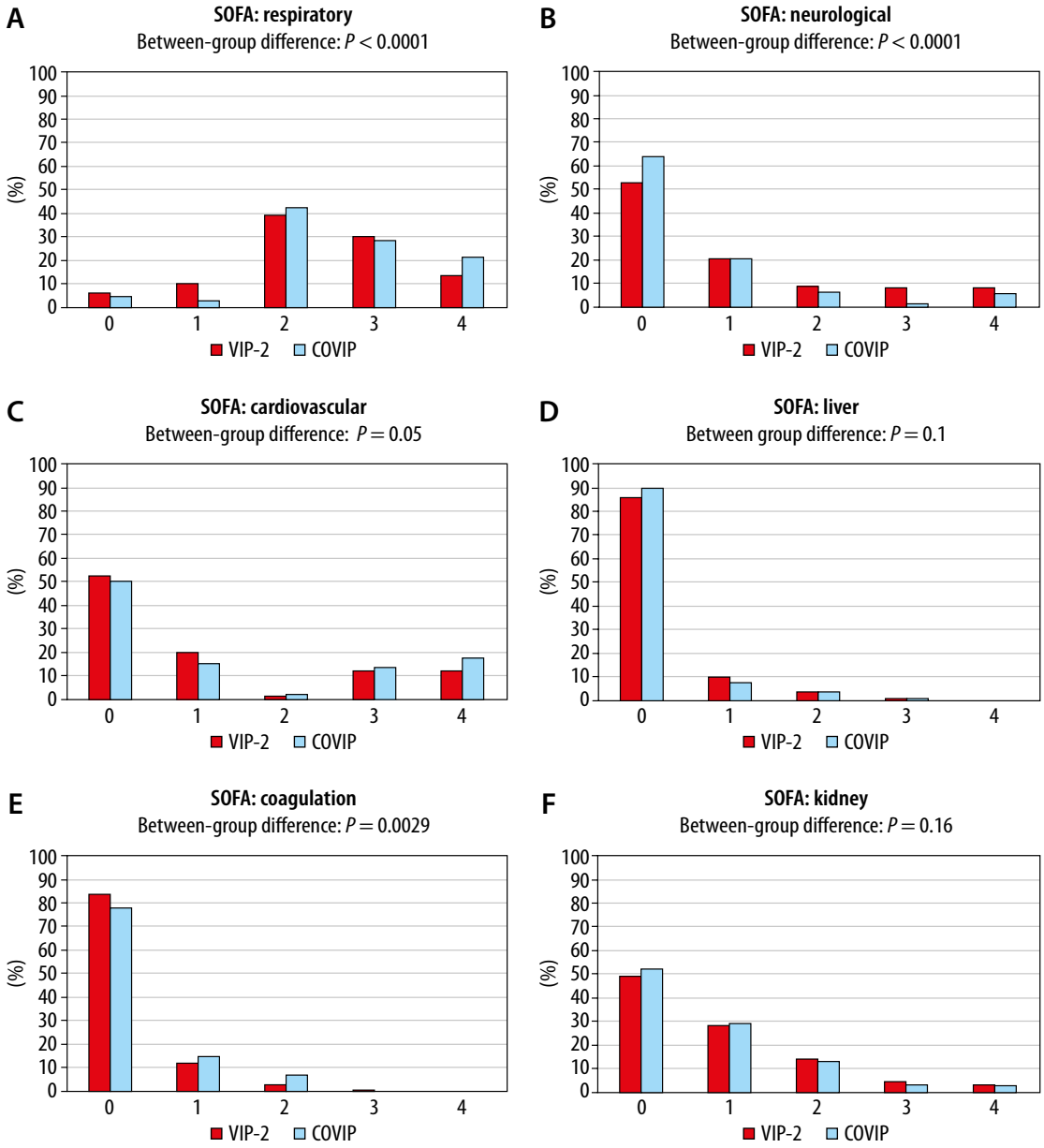


**FIGURE 1.** Distribution of SOFA subscores across the non-COVID-19 and COVID-19 cohorts

**TABLE 2.** Differences in organ failures (SOFA subscore ≥ 3 points) between the non-COVID-19 and COVID-19 cohorts

| Variable | Non-COVID-19 cohort (VIP-2 study) | COVID-19 cohort (COVIP study) | *P*-value |
|---|---|---|---|
| SOFA: respiratory failure ≥ 3 points (yes/no) | 400 (44.1) | 275 (49.9) | 0.0339 |
| SOFA: neurological failure ≥ 3 points (yes/no) | 157 (17.3) | 46 (8.3) | < 0.0001 |
| SOFA: cardiovascular failure ≥ 3 points (yes/no) | 227 (25.0) | 175 (31.8) | 0.0061 |
| SOFA: liver failure ≥ 3 points (yes/no) | 4 (0.4) | 2 (0.4) | 1 |
| SOFA: coagulation failure ≥ 3 points (yes/no) | 10 (1.1) | 3 (0.5) | 0.4 |
| SOFA: kidney failure ≥ 3 points (yes/no) | 72 (7.9) | 32 (5.8) | 0.16 |

SOFA – Sequential Organ Failure Assessment
Variables are presented as *n* (%).

The total SOFA score and its derivatives (such as delta SOFA, mean SOFA, maximum SOFA, etc.) are frequently employed as endpoints in clinical trials. De Grooth *et al.* [6] concluded that while fixed-day SOFA was the most frequently reported SOFA-based outcome, only delta SOFA showed any consistent as-

sociation with mortality. Meanwhile, Pölkki *et al.* [7] showed that each point of each of the SOFA subscores carries different, not necessarily proportional, information regarding the severity of organ failure and its relationship to mortality. Consequently, solely reporting the total SOFA values poses a risk of reduced statistical sensitivity and fails to provide readers with a comprehensive understanding of the patients' condition. Our analysis confirmed that if one were to adjust 2 different critically ill populations for organ failure, doing so by using total SOFA score would not suffice because these population differ in details.

## CONCLUSIONS

Our findings underscore the need to report individual SOFA subscores in clinical trials to provide a comprehensive understanding of organ dysfunction.

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