EDITORIAL

Age-adjusted Charlson Comorbidity Index: A Simple Tool, but Needs Further Validation in COVID-19 Patients

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Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global health crisis spreading rapidly across the world and was declared as a pandemic by the World Health Organization in March 2020. As of June 2021, globally it has infected more than 180 million people and has caused mortality of over 4 million and counting. This airborne disease tends to spread rapidly and can cause severe illness and high mortality rate in certain groups while having a relatively lesser impact on other groups of individuals.

The development of prognostic tools for an accurate prediction of COVID-19 prognosis will be beneficial for triaging and clinical management of patients and to improve outcomes.

Prognostic tools for severity and survival prediction for hospitalized COVID patients have been in development since the onset of the pandemic. In a recent systematic review and meta-analysis, comorbid conditions (chronic respiratory disease, cardiovascular disease, hypertension, and diabetes), clinical manifestations (dyspnea, fatigue, giddiness, and anorexia), and laboratory parameters (elevated WBC count, increased neutrophils, and lymphopenia) were associated with poor outcomes.[1] Similarly, several critical care scoring systems like APACHE II and SAPS II, were able to predict mortality in patients with COVID-19.[2]

The Charlson comorbidity index (CCI), first developed in 1984 to assess 1-year mortality by reviewing hospital charts and validated in a cohort study of nearly 700 patients affected by breast cancer.[3] It includes 19 medical comorbid conditions with a particular score assigned to each comorbid condition, to calculate the final total score without any laboratory values. Since then, CCI has become widely used scoring system to predict outcomes of variety of medical conditions and malignancies.[4,5]

Since age has been determined to be correlated with survival, the CCI was modified by Charlson et al. in 1994 with the addition of age to comorbid conditions. This modification, the age-adjusted Charlson comorbidity index (ACCI), includes the age of the patient as a correction variable of the final score of the CCI with the addition of one point for every decade over 40 years.[6] Similar to CCI, ACCI has been extensively validated and has been used for survival prediction in several medical and surgical conditions.[7–9]

The ability of CCI and ACCI to predict the outcome in hospitalized COVID patients has been tested recently in several clinical trials. In a systematic review and meta-analysis in hospitalized COVID-19 patients, CCI score of ≥3 was associated with increased mortality. Per point increase of CCI score increased mortality risk by 16%.[10] In another retrospective study by Kim et al.,[11] which included 5,621 hospitalized COVID-19 patients, the ACCI (≥3) group was an independent predictor of composite outcome (HR—3.63) and patient mortality (HR—22).

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In the current study by Shanbhag et al.,[12] the authors have studied the utility of ACCI as a predictor of need for invasive mechanical ventilation, length of hospital stay and mortality in Covid-19 patients treated with remdesevir. This was a single-center, retrospective study that included 122 patients aged between 18 and 90 years with moderate–severe COVID-19 patients. ACCI was calculated for all patients; the need for invasive mechanical ventilation, days of hospital stay, and in-hospital mortality were noted from the electronic data base. The primary outcome of the study was the ability of ACCI to predict in-hospital mortality whereas secondary outcomes was the ability of ACCI to predict length of hospital stay and requirement of invasive mechanical ventilation.

The results showed that out of 122 patients, 91 patients (68.6%) survived and 31 patients expired (25.4%). ACCI >4 was able predict hospital mortality with sensitivity and specificity of 68% and 62%, respectively. The area under receiver operating characteristic curve (AUROC) for predicting mortality was 0.709, $p = 0.001$. The ROC of ACCI for predicting the need for invasive mechanical ventilation was 0.696, $p = 0.001$ with a sensitivity of 67% and specificity 63%. However, ACCI was not able to predict prolonged length of stay (AUC 0.448, $p = 0.319$). The authors have concluded that ACCI was able to predict the need for mechanical ventilation and in-hospital mortality reliably.

The results of the study, however, should be interpreted with caution for the following reasons:

- The authors of the study had selected arbitrary cutoff (ACCI >4) to predict the outcomes. Ideally the outcomes should have been measured by using the optimum cutoff determined by ROC curve with best sensitivity and specificity. And one of these cutoffs would probably give a better result than the other.

- The current study is a single-center retrospective study. The performance of any predictive score often varies from one location to another and the interpretation of results might also differ. This needs to be considered when deciding the applicability of any research findings.
- The investigators who calculated the ACCI were not blinded to the outcomes and the investigator bias might have an effect on the outcomes.
- Finally, the sample size of the study is too small that can compromise the conclusions drawn from the study. Too small a sample may prevent the findings from being extrapolated.

This study suggests ACCI can be potentially used to predict outcome in hospitalized patients infected with COVID-19. Further prospective multicenter studies with adequate sample size are required to validate ACCI to predict outcome in hospitalized patients infected with COVID-19.

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