EDITORIAL

Is it Time to Develop an Indian Sepsis-related Mortality Prediction Score?

Dedeepiya Devaprasad Vidyasagar

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Sepsis is among the leading causes of admissions into critical care units worldwide and an important cause of mortality as well. The global sepsis mortality rate in 2017 was 19.7% accounting for a total of 11 million deaths with 1 in every 5 deaths being sepsis related. In India, the sepsis incidence is 540–640 per 1 lakh population and the estimated total sepsis burden is 89.6 lakhs with a mortality of 25–30%.[1]

Mortality prediction scores are used by healthcare administrators to assess and compare ICU performances while researchers use them to design and evaluate trial outcomes more efficiently. These scores are used by critical care physicians to prognosticate patients and make treatment decisions, which sometimes may also include decisions not to escalate care based on the principles proposed by Beauchamp and Childress.[2] However, it may not be ideal to use these scores in any single patient since they perform poorly there.

The currently used standard severity scores are acute physiological and chronic health evaluation (APACHE II and III) and simplified acute physiology score (SAPS II). The APACHE IV and SAPS III are considered to be updated severity scores.

Acute physiological and chronic health evaluation-I first developed in 1981, by the American Intensivist William Knaus and Colleagues, was modified in 1985 as APACHE II, and again in 1991 as APACHE III. Acute physiological and chronic health evaluation IV was welcomed as the 'new kid on the block' in 2006 and could be possibly considered outdated in 2024.

The death of a young woman who was transferred to the ICU in septic shock following a major surgical procedure greatly troubled the treating physician and served as the immediate trigger for the idea of developing APACHE I. The physician treating this patient strongly felt that the quality of information gathered about a patient was most crucial to help in formulating treatment plans and helping betterment of outcomes. He went about listing important parameters whose information was critical for the care provided. APACHE I was subsequently developed from a sample of 582 patients admitted to a single centre–community hospital in the USA. That it could one day help to standardize care, assess ICU performance, and be used to determine in-hospital mortality was not envisaged at the time of its creation.[3]

Acute physiological and chronic health evaluation-II was needed to simplify this system by reducing the physiological parameters from 33 (listed in APACHE I) to the 12 most precise parameters. The focus was also to compare the predictive accuracy of in-hospital mortality between these scores. Improvement in software applications, increasing availability of funding, especially from venture capitalists, and expansion of commercialization of intellectual property rights to even medical decision systems helped improve APACHE II to III. A careful examination of the interaction of the physiological elements with different disease states was studied, and the best way to represent and compare them was determined and an appropriate weighting was introduced. Similarly, a distinct differential weighting of neurological assessment for a patient with traumatic coma vs non-traumatic causes of coma was also established. These improved the accuracy of prediction and the ROC curves of predictive accuracy improved from 0.86 with APACHE II to 0.90 with APACHE III.

Simplified acute physiology score II was developed as an alternative to APACHE II in 1984 and modified later as SAPS III in 2005. While SAPS II was felt to be inadequate in predicting mortality, SAPS III was criticized for being over-predictive of mortality.[4,5] The mortality probability model (MPM) score is the only validated score that has the advantage of being available at ICU admission rather than at 24 hours but is not widely used.[6]

While APACHE and SAPS scores included all patient population subsets, the sepsis severity score (SSS) was developed as a disease specific severity score for patients with sepsis in 2014. Data from 23,428 patients admitted to 218 hospitals from among the 18 countries enrolled in the Surviving Sepsis Campaign database helped to develop the score. Sepsis severity score has good discrimination comparable to APACHE II, SAPS II, and SAPS III but APACHE IV has the best discrimination and overall performance but, is not widely used yet.[7,8] In contrast to the above, a few authors claim that both APACHE II and APACHE IV have equal discriminating ability.[9]

Steady progress in diagnostic armamentarium, refinement and advances in therapeutic protocols have ensured that survivors

Department of Critical Care Medicine, Apollo Speciality Hospitals, Chennai, Tamil Nadu, India

Corresponding Author: Dedeepiya Devaprasad Vidyasagar, Department of Critical Care Medicine, Apollo Speciality Hospitals, Chennai, Tamil Nadu, India, Phone: +91 9444216333, e-mail: dedeepiya_76@yahoo.co.in

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of immune-suppressed states, hematological and solid organ malignancies are all represented in the ICU patient population. Better training of critical care personnel has also ensured that the sepsis related mortality is dipping.[10]

Preventing ICU mortality and in-hospital mortality were the initial goals of critical care physicians and was reflected in the early validation of these scores to predict the same. However, we subsequently realized that 30-day mortality was a more important outcome measure than in-hospital mortality. In the recent few years, the focus has been to look at 90-day mortality as they better reflect meaningful long-term outcomes.

Simplified mortality score (SMS) developed in 2017 is truly simple as it employs only 7 readily available variables–(2 numeric parameters and 5 dichotomous parameters). The major strength of the SMS is the use of 90-day mortality while the inherent limitation is that the data variables used in the study for external validation were drawn from SUP-ICU; AID-ICU cohort studies and the 6S, TRISS, and CLASSIC trials. These studies were all performed in Europe and hence the generalizability may be limited outside Europe.[11]

The sepsis-induced organ failure assessment (SOFA) score was developed in 1994 by the European Society of Intensive Care and Emergency Medicine to objectively describe organ failure in sepsis. It has now been renamed as sequential organ failure assessment score and applied to patients without sepsis as well. The incremental increase in SOFA score in the ICU is now being used as a predictor of mortality.[12]

The article by Natthaka Sathaporn et al. published in the current issue of IJCCM is a comparative assessment of the predictive accuracies for the 90-day mortality of sepsis patients using the SMS, SSS, APACHE II, APACHE IV, and SAPS II scores. However, the SOFA score was not included.[13]

In this well-done study that looked at data from 1,161 patients with sepsis, about 55% met the criteria for septic shock. The authors claim that this is likely the first external validation study comparing the performance variability of the various severity scores in the prediction of 90-d mortality in septic critically ill patients. The authors have concluded the SAPS II was simpler to use and had the best overall performance with comparable discrimination to APACHE IV.

However, this is a single-center study and 17.4% of the population studied had a background of hematological or solid organ malignancies and 7.8% of patients had other immunocompromised states. This high proportion of patients with malignancy and immunocompromised states may limit its use to other ICUs. This study was done in Thailand—an Asian country and there are others who point out that the applicability of SAPS II to Asian cases of sepsis needs more clinical research and validation.[8] Trop ICS scores that have been tested claim to outperform APACHE II in the Asian population.[14]

The ISCCM has now completed 30 years of caring for critically ill patients in the most trying circumstances across the country. We have always realized that our disease patterns, patient characteristics, and health care delivery capabilities are so different from the Western world. Tropical infections account for an important proportion of sepsis patients in India as is the case in the rest of South-East Asia.[15] We have far fewer MRSA than in the West.[16] Our gram-negative infection-resistant mechanism patterns are also different from those described in Western literature. Yet we continue to apply validated scores drawn from the Western population to predict the mortality of septic patients in our Indian population.

The lack of adequate personnel, whose major worktime was dedicated to providing clinical care, leaving them with very little time for data entry, analysis, and research was a barrier of the past. The expected increase in nurses and physicians with the current explosion in nursing and medical seats in India will improve the nurse-patient and doctor-patient ratio freeing up clinician's time for clinical research. We now are increasingly using electronic medical records and have options for automated data entry in certain hospitals. The availability of trained medical researchers, better databases, easy availability of trained big data analysts, and improvements in artificial intelligence (AI) and machine learning (ML) offer more than a glimmer of hope for better research.[17]

Apart from medical, technical, and financial challenges that were inherent barriers to the development of such a scoring system, researchers should also be cognizant of the fact that potential legal barriers as well as criticism of ethical and moral integrity may arise. The 4 founders of APACHE I were subjected to investigation by the federal funding agency for possible inappropriate use of research grants to promote commercial applications. When the team had to withhold the equation and coefficient needed to calculate prediction due to propriety intellectual property rights, their morality and ethical behavior were questioned by their colleagues. The above notwithstanding, it is important for us to realize that without pain there is no gain.

The scores that were generated from a Western critically ill population from a general ICU with varied diagnoses are now expanded to assess the severity of 'septic patients' in the Indian ICU. What were originally designed as severity scores and only later found to be useful for mortality prediction are now predominantly used for that purpose. The scores used for in-hospital mortality are now extrapolated to predict 90-day mortality for which they were not initially intended.

For all the above compelling reasons, I firmly believe that under the auspices of ISCCM, developing a 90-day mortality prediction score for sepsis patients admitted to Indian ICUs is an idea whose time has truly come.

Orcid

Dedeepiya Devaprasad Vidyasagar https://orcid.org/0000-0003-3457-0143

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