

**SOFA score plus impedance ratio predict mortality in critically ill patients admitted to the emergency department: Retrospective observational study.**

Kammar-García Ashuin, MSc.<sup>1,2</sup>

Castillo-Martínez Lilia, PhD.<sup>3</sup>

Mancilla-Galindo Javier, MBBS.<sup>4,5</sup>

Villanueva-Juárez José Luis, MSc.<sup>3</sup>

Pérez-Pérez Anayeli, BSc.<sup>6</sup>

Rocha-González Héctor Isaac, PhD.<sup>2</sup>

Arrieta-Valencia Jesús, PhD.<sup>2</sup>

Remolina-Schlig Miguel, M.D.<sup>5</sup>

Hernández-Gilsoul Thierry, M.D.<sup>6</sup>

1. Dirección de Investigación. Instituto Nacional de Geriatría, Mexico City, México.

2. Sección de Estudios de Posgrado e Investigación, Escuela Superior de Medicina, Instituto Politécnico Nacional, México City, México

3. Department of Clinical Nutrition, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City, México

4. Facultad de Medicina. Universidad Nacional Autónoma de México, México City, México.

5. Facultad de Ciencias de la Salud. Universidad Autónoma de Tlaxcala, Tlaxcala, México.

6. Emergency Department, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City, México

### **Corresponding author**

Thierry Hernández-Gilsoul. Address: Vasco de Quiroga 15, Tlalpan, Col. Belisario Domínguez Sección XVI, CP 14080 Ciudad de México. Tel: 525554870900, ext. 5010, e-mail: thierry.hernandezg@incmnsz.mx; [doctorthierry@hotmail.com](mailto:doctorthierry@hotmail.com)

## Abstract

**Background:** The Sequential Organ Failure Assessment (SOFA) is a scoring system used for the evaluation of disease severity and prognosis of critically ill patients. The impedance ratio (Imp-R) is a novel mortality predictor.

**Aims:** This study aimed to evaluate the combination of SOFA + Imp-R in the prediction of mortality in critically ill patients admitted to the emergency department (ED).

**Methods:** A retrospective cohort study was performed in adult patients with acute illness admitted to the ED of a tertiary-care referral center. Baseline SOFA score and bioelectrical impedance analysis to obtain the Imp-R were performed within the first 24 hours after admission to the ED. A Cox regression analysis was performed to evaluate mortality risk of initial SOFA score plus Imp-R. Harrell's C-statistic and decision curve analyses (DCA) were performed.

**Results:** Out of 325 patients, 240 were included for analysis. Overall mortality was 31.3%. Only 21.3% of non-surviving patients died after hospital discharge, and 78.4% died during hospital stay. Of the latter, 40.6% died in the ED. SOFA and Imp-R values were higher in non-survivors and were significantly associated with mortality in all models. The combination of SOFA + Imp-R significantly predicted 30-day mortality, in-hospital mortality, and ED mortality with area under the curve (AUC) of 0.80 (95% CI: 74-0.86), 0.79 (95% CI: 0.74-0.86) and 0.75 (95% CI: 0.66-0.84) respectively. The DCA showed that combining SOFA + Imp-R improved the prediction of mortality through the lower risk thresholds.

**Conclusion:** The addition of Imp-R to baseline SOFA score at admission to the ED improves mortality prediction in severely acutely ill patients admitted to the ED.

**Keywords:** SOFA, impedance ratio, mortality, emergency department, critical care, prediction.

## Introduction

The emergency department (ED) is the first opportunity to generate therapeutic plans based on the severity and prognosis of disease of patients with acute illness. Different scoring systems have been designed to determine disease severity and to predict adverse outcomes in critically ill patients [1] and to improve the quality of therapeutic and preventive measures [2]. The Sequential Organ Failure Assessment (SOFA) is a scoring system used for the evaluation of disease severity and prognosis in critically ill patients [3]. It is based on the evaluation of six systems: respiratory, cardiovascular, neurological, hepatic, renal, and coagulation [4]. Although the SOFA score was not developed for the prediction of mortality, its usefulness to predict death has been observed in studies conducted in the intensive care unit (ICU), demonstrating a close relationship between organic failures and mortality [5,6]. Recently, the use of the initial SOFA score has been validated as a good predictor of mortality [7]. Despite these findings, few studies have used the SOFA score for the prediction of mortality in non-ICU settings, such as the ED [3]. This scoring system has characteristics that make it suitable for the ED since it requires laboratory data often routinely measured at ED admission [1]. Recent studies have suggested the inclusion of other mortality predictors in addition to the SOFA score could further improve the identification of high-risk patients [8], such as serum lactate levels [9], and C-reactive protein (CRP) [10].

On the other hand, fluid overload is an independent factor associated with worse prognosis in critically ill patients [11], which prolongs multiorgan dysfunction [12]. New markers of fluid overload such as the impedance ratio (Imp-R) have been associated with

a worse prognosis in critically ill patients [13,14]. The imp-R is the ratio between high- and low-frequency impedance values (200/5 kHz) obtained during bioelectrical impedance analysis (BIA). Imp-R has been previously evaluated as a predictor of mortality in critically ill patients [13-16].

Since multi-organic dysfunction and fluid overload are conditions associated with mortality in critically ill patients, their combination could possibly improve mortality prediction in patients admitted to the ED who develop critical disease. Therefore, the aim of this study was to evaluate the combination of initial SOFA score and Imp-R to predict mortality in critically ill patients admitted to the ED.

## Methods

This was a retrospective observational study performed in a cohort of patients [17] admitted to the ED of Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán—a tertiary care referral center in Mexico City—between September 2016 and September 2019. Adult ( $\geq 18$  years) patients with acute illness admitted to the emergency department who had been admitted within the last 24 hours until assessment for bioelectrical impedance measurement were eligible for inclusion in the study. Patients who had metal prostheses or who had errors on bioelectrical impedance measurements were excluded from the study. Patients without all clinical and laboratory variables needed to calculate SOFA score within the first 24 hours after admission or who had loss to follow-up were eliminated. The study protocol was approved by the Ethics Committee of the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán* under number 1977.

## Data collection and management

All clinical (BMI, vasopressor assistance, mechanic ventilation, Glasgow coma scale) and biochemical (blood ureic nitrogen, creatinine, sodium, potassium, C-reactive protein, platelet count, bilirubin, albumin, lactate) variables, as well as cause of hospitalization and comorbidities were obtained directly from electronic medical records. Hospital stay was calculated from the first day of admission to the ED until the day of hospital discharge.

The initial SOFA score (range 0 to 24) was calculated and evaluated for each patient by using the first value of the physiological (Partial pressure of oxygen,  $\text{PaO}_2$ ; fraction of inspired oxygen,  $\text{FiO}_2$ ; mean arterial blood pressure, MAP; Glasgow Coma Scale and urine output) and laboratory (platelet count, bilirubin, and creatinine) parameters obtained within the first 24 hours after admission to the ED [7].

At the time of admission, all patients underwent a bioelectrical impedance analysis, using a tetrapolar device (BODYSTAT QuadScan 4000; BOSYSTAT LTD, Isle of Man, United Kingdom) with alternating current of 800 mA at four different frequencies (5, 50, 100, and 200 kHz). Clinicians with standardized knowledge and capacitance on the tetrapolar method performed BIA measurements [18]. The impedance values (Z) of all frequencies used in the BIA were obtained. The impedance ratio (Imp-R) was calculated as the quotient of Z at 200 kHz between Z at 5 kHz [16].

All patients were followed-up for 30 days from ED admission. The incidence of mortality was obtained directly from hospital records or through telephone interviews with family members. The primary endpoints of this study were 30-day all-cause mortality, in-hospital mortality, and ED mortality.

## Sample Size Calculation

The sample size was calculated according to an estimate of mortality risk according to increases in the SOFA score; previous studies showed a 9-fold higher risk for patients with an increase of 1 or more points at admission to the ICU from the ED [19]. Being more conservative in the increase in risk, we considered an estimate of 2 times higher risk for every 1-point increase in the SOFA score and considered a mortality of 15% in critical patients [19], which yielded a minimum sample size of 220 patients with an alpha error of 0.05 and power of 80%.

### Statistical analyses

All descriptive data are summarized as median with 25th–75th percentiles or as frequency with percentage. Comparisons between groups were performed by Mann-Whitney U test. Different Cox regression models were applied to estimate 30-day mortality risk, in-hospital mortality, and ED mortality, according to the initial SOFA score or Imp-R. Variables were entered into the models as continuous quantitative variables. The models were adjusted for: age, sex, BMI, invasive mechanical ventilation, creatinine, and lactate. Results of all models are summarized as Hazard Ratios with 95% confidence intervals (95%CI). Furthermore, models were plotted in cubic splines.

Other models were created in which the SOFA score and the Imp-R were included in the same model to determine if both variables could predict mortality better. The univariate and combined models were compared using Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC). The predictive value of each model was calculated by Harrell's C-statistic and expressed with the area under the curve (AUC). The evaluation and comparison of baseline SOFA score model and its combination with Imp-R was carried out through decision curve analysis.

The model assumptions were verified by residual analysis. All statistical analyses and figures were carried out in the statistical software SPSS version 21 and R v.3.6.1. A  $p<0.05$  was considered as statistically significant.

## Results

The flow of patients is shown in **Figure 1**. Out of 325 patients, 240 were included for analysis. Demographic and clinical characteristics of patients at ED admission are summarized in **Table 1**. Most patients admitted to the ED were women (58.3%) over 60 years (47.9%), with a median age of 60 (46–71.8) years. Most patients had normal BMI (47.1%). The main causes of admission to the ED were gastrointestinal (30%), infectious (21.7%), and cardiovascular (15.4%). The presence of kidney disease (16.3%) and cirrhosis (16.7%) were similarly frequent. Most patients (70.8%) did not require vasopressor support during their hospital stay, whereas 12.9% of patients required mechanical ventilation with an approximate duration of 2 (1–5) days. The median hospital stay was 6 (2–12) days. The incidence of mortality was 31.3% (n=75), with most deaths occurring in-hospital (78.4%, n=59) rather than after discharge (21.3%, n=16). Of all in-hospital deaths, 40.6% (n=24) died during their stay in ED.

Regarding SOFA scores, 58.3% of patients admitted to the ED had an initial SOFA score of 2 to 7, with a median score of 6 (4–9). In non-surviving patients, the initial SOFA score was higher (9, 6–11) than survivors (5, 3–7;  $p<0.0001$ ). A similar situation was observed in patients who died in-hospital (5, 3–7.5 vs. 9, 6–12;  $p<0.0001$ ) or in the ED (6, 4–9 vs. 9, 6–11.7;  $p=0.001$ ; **Table 2**).

The Imp-R on admission to the ED was 0.85 (0.81–0.88). When the values of the Imp-R were compared between survivors and non-survivors, higher values were observed in

non-survivors in the different mortality groups: 30-day mortality (0.84, 0.80–0.87 vs. 0.87, 0.83–0.90;  $p<0.0001$ ), in-hospital mortality (0.84, 0.80–0.87 vs. 0.87, 0.83–0.90;  $p<0.0001$ ), and ED mortality (0.84, 0.80–0.88 vs 0.88, 0.85–0.90;  $p<0.0001$ ). Of the other BIA parameters, only reactance and phase angle showed differences between survivors and non-survivors in all mortality groups (**Table 2**).

**Table 3** shows the results of Cox regression analyses for the different mortality models. Increasing values of initial SOFA score and Imp-R were associated with higher mortality risk. Each additional point in the initial SOFA score increased 30-day mortality, in-hospital mortality, and ED mortality risks by 11%, 21%, and 18%, respectively. Likewise, each 0.01 unit increase in Imp-R led to larger 30-day mortality, in-hospital mortality, and ED mortality risks by 9%, 9%, and 12%, respectively. **Figure 2** shows the splines of each mortality model according to initial SOFA score and Imp-R; mortality risk begins to increase significantly at values higher than 5 points for initial SOFA score and 0.85 for Imp-R. The AUCs of initial SOFA score were 0.74 (95%CI: 0.68-0.81), 0.77 (95%CI: 0.70-0.83), and 0.71 (95%CI: 0.61-0.81) for the 30-day mortality, in-hospital and ED mortality, respectively (all  $p<0.0001$ ). Conversely, the AUC of the combination of initial SOFA score plus Imp-R were 0.80 (95%CI: 0.74-0.86), 0.80 (95%CI: 0.74-0.86), and 0.75 (95%CI: 0.66-0.84), respectively (all  $p<0.0001$ ). The comparison of models for the prediction of mortality by information criteria showed that for each mortality model, the combination of initial SOFA score with Imp-R improved outcome prediction (30-day mortality:  $\Delta AIC=11.46$ ,  $\Delta BIC=9.14$ , in-hospital mortality:  $\Delta AIC=4.73$ ,  $\Delta BIC=2.65$ , and ED mortality:  $\Delta AIC=4.81$ ,  $\Delta BIC=3.64$ ).

The decision curves for the different mortality models are shown in **Figure 3**. For the initial SOFA score and the combination with Imp-R, a slight superiority of the latter can be observed since it improves the prediction of mortality at the lower risk thresholds.

## Discussion

In this study, the combination of initial SOFA score and Imp-R at admission to the ED was accurate at predicting mortality in patients with acute illness admitted to the ED of a tertiary care referral center in Mexico City. The combination of SOFA plus Imp-R showed a better prediction of 30-day mortality, in-hospital mortality, and ED mortality than initial SOFA score alone.

To our knowledge this is the first study addressing the use of a marker of fluid overload in combination with the SOFA score. Our aim was to assess if the evaluation of fluid overload could aid the prediction of mortality of the SOFA score. To this end, we used imp-R as a marker of fluid overload, which has already been considered as a prognostic marker of mortality [14] and as a marker of fluid overload [16]. Imp-R and SOFA score were individually predictors of mortality in all the models evaluated (30-day mortality, in-hospital mortality, and ED mortality) similar to what has been reported previously [13].

In previous studies predictors of mortality in critically ill patients have been characterized, which include different biological parameters such as creatinine, lactate, bilirubin, and CRP, as well as clinical parameters such as heart rate, blood pressure, hospital stay, mechanical ventilation, and fluid overload [4,8,16,20]. Each of these parameters has a pathophysiological role in organic deterioration of the critically ill patient, although they do not allow the determination of multiorgan compromise by themselves, consequently, the

SOFA score takes a leading role in the evaluation of the prognosis of patients with severe acute illness. The SOFA score includes predictors of mortality such as creatinine, bilirubin, and mechanical ventilation, as well as other parameters like blood pressure instead of the heart rate or lactate. Some studies have shown that changes in the SOFA score can improve the prediction of mortality [4,21,22]. These changes are mainly substitutions of some parameters for others which are easier to obtain during in-hospital stay.

The SOFA score has been tested in multiple different contexts to predict [4,5,19,22]. For instance, by applying it at different times from admission to the ICU or by calculating average scores during a certain period of time. Recently, attempts to combine the SOFA score with other mortality risk factors have been done. For example, by combining it with CRP [23], procalcitonin [24], or lactate [25].

Studies that evaluated the prediction of hospital mortality through the SOFA score at ICU admission showed an AUC between 0.63 and 0.82 [1,4], whereas studies that evaluated the SOFA score after admission to the ICU (40-72 h) have shown higher AUC: 0.85-0.95 [5,18]. Nonetheless, these estimates may be biased since there is a risk that interventions performed after 24 hours could affect mortality risk and therefore scores, too [7], thereby altering predictive values. The results of this study are in line with the findings of others aiming at predicting in-hospital mortality [1], although our study has an additional strength since we evaluated 30-day mortality, in-hospital mortality, and mortality in the ED simultaneously.

Other studies have shown that combining the SOFA score with other mortality markers increases mortality prediction. With the combination of SOFA with procalcitonin (PCT), the single SOFA score had an AUC of 0.86, while its combination with PCT showed an AUC of 0.91 [24]. In the combination of SOFA score with lactate, the AUC was 0.83, which

was higher than SOFA alone and other prognostic scales [25]. The N-terminal pro-brain natriuretic (NT-proBNP) has also been used in combination with the SOFA score, being a stronger predictor of hospital mortality than either variable alone [26].

The combination of SOFA + imp-R are mutually complementary since there is a relationship between multi-organ dysfunction, increased adverse events, and fluid overload [12]. Other combinations of the SOFA score with markers such as lactate may present discrepancies, since the increase in lactate in critically ill patients can indicate hypoperfusion, something which is already considered by the SOFA score with mean arterial pressure, reason why adding lactate to the prediction could only modestly improve mortality prediction since patients with the lowest MAP could be the same with the highest lactate levels. Likewise, CRP has been shown in other studies to be an important marker of patient prognosis [27], although its combination with SOFA does not improve the mortality prediction in critically ill patients [22].

All studies that have evaluated combinations of SOFA scores with other mortality markers have been performed in patients admitted to the ICU, an approach which is different to ours since we performed evaluations of patients upon admission to the ED. This is relevant, since treatments throughout the hospital stay could affect the scores and mask true initial differences [7]. Thus, our findings could be generalizable to patients with acute illness who are admitted to the ED and who have these measurements performed upon admission. For these same reasons, our findings may not be generalized to patients who develop severe illness later during hospital stay.

The use of the initial SOFA score in combination with the imp-R for prognostic purposes is non-invasive, which could suggest that using these tools as predictors of mortality in the ED could be viable. Furthermore, determining fluid overload upon admission could be

relevant to guide management since the abuse of resuscitation fluids, due to poor evaluation of organic function and fluid volume status, could lead to the deterioration of severely ill patients [28, 29]. Our results contribute to continue improving common and widely used mortality predictions models such as the SOFA score.

The main limitations of this study are its retrospective observational design, the fact that it was performed in a single tertiary care referral center, as well as the relatively small sample size because only patients that contained all laboratory results or clinical parameters for the calculation of SOFA score could be included in the study. Furthermore, we were unable to assess the time from onset of the illness to ED admission, which could be a relevant confounder since patients with delayed medical care could have higher mortality risk [30]. Similarly, a limitation of this study is the use of a single severity scale and not considering other scales that have been validated to be used in critically ill patients (APACHE, SAS, or MEXSOFA) or other common evaluation tools used in the in ED (qSOFA, NEWS, or MEDS). It would be interesting to carry out more research in the combination of these scales with the imp-R to determine if there is an improvement in the prediction of mortality of patients admitted to ED, mainly in the qSOFA scale that has become widely used since it is simpler to calculate [31]. Some studies have already began to explore the combinations of qSOFA with biomarkers in ICU patients [32,33] but more research is needed to better determine their use in ED.

## Conclusion

The initial SOFA score and Imp-R upon admission to the ED are independent predictors of 30-day mortality, in-hospital mortality, and ED mortality. The addition of Imp-R to baseline SOFA score at admission to the ED improves mortality prediction in severely

acutely ill patients admitted to the ED. This new assessment strategy could provide additional information to inform prognosis of patients admitted to the ED with severe acute illness.

### **Acknowledgments**

This work is part of the Ph.D. dissertation of Kammar-García Ashuin. He was also a CONACYT fellow (CVU number: 824658).

### **Conflict of interest statement**

The authors declare no conflict of interest

### **Funding information**

No funding or not able to provide at the moment.

### **Author contribution statement**

Ashuin Kammar-García: Conceptualization, Formal analysis, Writing - Original Draft, Funding acquisition. Lilia Castillo-Martínez: Validation, Software, Writing - Review & Editing. Javier Mancilla-Galindo: Methodology, Investigation, Writing - Review & Editing. José Luis Villanueva-Juárez: Supervision, Anayeli Pérez-Pérez: Data Curation, Resources. Héctor Isaac Rocha-González: Writing - Review & Editing, Visualization. Jesús Arrieta-Valencia: Supervision. Miguel Remolina-Schlig: Supervision. Thierry Hernández-Gilsoul: Project administration, Resources.

## References

1. Safari S, Shojaee M, Rahmati F, Barartloo A, Hahshemi B, Forouzanfar MM, et al. Accuracy of SOFA score in prediction of 30-day outcome of critically ill patients. *Turk J Emerg Med.* 2016;16(4):146-150. doi: 10.1016/j.tjem.2016.09.005.
2. Chawda M, Hildebrand F, Pape HC, Giannoudis PV. Predicting outcome after multiple trauma: which scoring system? *Injury.* 2004;35(4):347-358. doi: 10.1016/S0020-1383(03)00140-2.
3. Garbero RF, Simões AA, Martins GA, Cruz LVD, von Zuben VGM. SOFA and qSOFA at admission to the emergency department: Diagnostic sensitivity and relation with prognosis in patients with suspected infection. *Turk J Emerg Med.* 2019;19(3):106-110. doi:10.1016/j.tjem.2019.05.002.
4. Namendys-Silva SA, Silva-Medina MA, Vásquez-Barahona GM, Baltazar-Torres JA, Rivero-Sigarroa E, Fonseca-Lazcano JA, Domínguez-Cherit G. Application of a modified sequential organ failure assessment score to critically ill patients. *Braz J Med Biol Res.* 2013;46(2):186-93. doi: 10.1590/1414-431x20122308.
5. Minne L, Abu-Hanna A, de Jonge E. Evaluation of SOFA-based models for predicting mortality in the ICU: A systematic review. *Crit Care.* 2008;12(6):R161. doi: 10.1186/cc7160
6. de Groot HJ, Geenen IL, Girbes AR, Vincent JL, Parienti JJ, Oudemans-van Straaten HM. SOFA and mortality endpoints in randomized controlled trials: a systematic review and meta-regression analysis. *Crit Care.* 2017;21(1):38. doi: 10.1186/s13054-017-1609-1

7. Granholm A, Møller MH, Krag M, Perner A, Hjortrup PB. Predictive Performance of the Simplified Acute Physiology Score (SAPS) II and the Initial Sequential Organ Failure Assessment (SOFA) Score in Acutely Ill Intensive Care Patients: Post-Hoc Analyses of the SUP-ICU Inception Cohort Study. *PLoS One.* 2016;11(12):e0168948. doi: 10.1371/journal.pone.0168948.
8. Steele L, Hill S. Using sepsis scores in emergency department and ward patients. *Br J Hosp Med (Lond).* 2019;80(8):C120-C123. doi: 10.12968/hmed.2019.80.8.C120.
9. Haas SA, Lange T, Saugel B, Petzoldt M, Fuhrmann V, Metschke M, et al. Severe hyperlactatemia, lactate clearance and mortality in unselected critically ill patients. *Intensive Care Med.* 2016;42(2):202-10. doi: 10.1007/s00134-015-4127-0.
10. Basile-Filho A, Lago AF, Meneguetti MG, Nicolini EA, Rodrigues LAB, Nunes RS, et al. The use of APACHE II, SOFA, SAPS 3, C-reactive protein/albumin ratio, and lactate to predict mortality of surgical critically ill patients: A retrospective cohort study. *Medicine (Baltimore).* 2019;98(26):e16204. doi: 10.1097/MD.00000000000016204.
11. Malbrain ML, Marik PE, Witters I, Cordemans C, Kirkpatrick AW, Roberts DJ, et al. Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice. *Anaesthesiol Intensive Ther.* 2014;46(5):361-80. doi: 10.5603/AIT.2014.0060.
12. Chapalain X, Vermeersch V, Egretteau PY, Prat G, Alavi Z, Vicaut E, et al. Association between fluid overload and SOFA score kinetics in septic shock patients: a retrospective multicenter study. *J Intensive Care.* 2019;7:42. doi: 10.1186/s40560-019-0394-0.

13. Demirci C, Aşçı G, Demirci MS, Özkahya M, Töz H, Duman S, et al. Impedance ratio: a novel marker and a powerful predictor of mortality in hemodialysis patients. *Int Urol Nephrol.* 2016;48(7):1155-62. doi: 10.1007/s11255-016-1292-1.

14. Lukaski HC, Kyle UG, Kondrup J. Assessment of adult malnutrition and prognosis with bioelectrical impedance analysis: phase angle and impedance ratio. *Curr Opin Clin Nutr Metab Care.* 2017;20(5):330-339. doi: 10.1097/MCO.0000000000000387.

15. Kammar-García A, Castillo-Martínez L, Villanueva-Juárez JL, Pérez-Pérez A, Rocha-González HI, Arrieta-Valencia J, et al. Comparison of Bioelectrical Impedance Analysis Parameters for the Detection of Fluid Overload in the Prediction of Mortality in Patients Admitted at the Emergency Department. *JPEN J Parenter Enteral Nutr.* 2021;45(2):414-422. doi:10.1002/jpen.1848.

16. Mulasi U, Kuchnia AJ, Cole AJ, Earthman CP. Bioimpedance at the bedside: current applications, limitations, and opportunities. *Nutr Clin Pract.* 2015;30(2):180-193. DOI: 10.1177/0884533614568155

17. Kammar-García A, Pérez-Morales Z, Castillo-Martinez L, Villanueva-Juárez JL, Bernal-Ceballos F, Rocha-González HI, et al. Mortality in adult patients with fluid overload evaluated by BIVA upon admission to the emergency department. *Postgrad Med J.* 2018;94(1113):386-391. doi: 10.1136/postgradmedj-2018-135695.

18. Ronco C, Kaushik M, Valle R, Aspromonte N, Peacock WF 4th. Diagnosis and management of fluid overload in heart failure and cardio-renal syndrome: the "5B" approach. *Semin Nephrol.* 2012;32:129–141. doi: 10.1016/j.semephrol.2011.11.016.

19. García-Gigorro R, Sáez-de la Fuente I, Marín Mateos H, Andrés-Esteban EM, Sanchez-Izquierdo JA, Montejo-González JC. Utility of SOFA and Δ-SOFA scores for predicting outcome in critically ill patients from the emergency department. *Eur J Emerg Med* 2018;25(6):387-393. doi: 10.1097/MEJ.0000000000000472.

20. Gessolo Lins PR, Carvalho Padilha WS, Magalhaes Giradin Pimentel CF, Costa Batista M, Teixeira de Gois AF. Risk factors, mortality and acute kidney injury outcomes in cirrhotic patients in the emergency department. *BMC Nephrol* 2018;19(1):277. doi: 10.1186/s12882-018-1061-8.

21. Jones AE, Trzeciak S, Kline JA. The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. *Crit Care Med* 2009;37:1649-1654. doi: 10.1097/CCM.0b013e31819def97.

22. Demandt AMP, Geerse DA, Janssen BJP, Winkens B, Schouten HC, van Mook WNKA. The prognostic value of a trend in modified SOFA score for patients with hematological malignancies in the intensive care unit. *Eur J Haematol* 2017;99(4):315-322. doi: 10.1111/ejh.12919.

23. Suberviola B, Castellanos-Ortega A, Ruiz Ruiz A, Lopez-Hoyos M, Santibañez M. Hospital mortality prognostication in sepsis using the new biomarkers suPAR and proADM in a single determination on ICU admission. *Intensive Care Med* 2013;39(11):1945-1952. doi: 10.1007/s00134-013-3056-z.

24. Matsumura Y, Nakada TA, Abe R, Oshima T, Oda S. Serum Procalcitonin Level, and SOFA Score at Discharge from the Intensive Care Unit Predict Post-Intensive Care Unit Mortality: A Prospective Study. *PLoS ONE* 2014;9(12):e114007. doi: 10.1371/journal.pone.0114007.

25. ffrench-O'Carroll R, Frohlich S, Murphy N, Conlon N. Predictors of outcome in decompensated liver disease: validation of the SOFA-L score. *Ir Med J* 2015;108(4):114-116.

26. Ju MJ, Zhu DM, Tu GW, He YZ, Xue ZG, Luo Z, et al. Predictive value of N-terminal pro-brain natriuretic peptide in combination with the sequential organ failure assessment score in sepsis. *Chin Med J (Engl)* 2012;125(11):1893-1898.

27. Wang X, Jiao J, Wei R, Feng Y, Ma X, Li Y, et al. A new method to predict hospital mortality in severe community acquired pneumonia. *Eur J Intern Med.* 2017;40:56-63. doi: 10.1016/j.ejim.2017.02.013.

28. Payen D, de Pont AC, Sakr Y, Spies C, Reinhart K, Vincent JL. Sepsis Occurrence in Acutely Ill Patients (SOAP) Investigators. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. *Crit Care.* 2008;12(3):R74. doi: 10.1186/cc6916.

29. Sakr Y, Vincent JL, Reinhart K, et al. High tidal volume and positive fluid balance are associated with worse outcome in acute lung injury. *Chest* 2005;128:3098–3108.

30. Mancilla-Galindo J, Kammar-García A, Martínez-Esteban A, Meza-Comparán HD, Mancilla-Ramírez J, Galindo-Sevilla N. COVID-19 patients with increasing age experience differential time to initial medical care and severity of symptoms. *Epidemiol Infect.* 2021;149:e230. doi: 10.1017/S095026882100234X.

31. Askim Å, Moser F, Gustad LT, Stene H, Gundersen M, Åsvold BO, et al. Poor performance of quick-SOFA (qSOFA) score in predicting severe sepsis and mortality - a prospective study of patients admitted with infection to the emergency

department. Scand J Trauma Resusc Emerg Med. 2017;25(1):56. doi: 10.1186/s13049-017-0399-4.

32. Dimitrov E, Minkov G, Enchev E, Halacheva K, Yovtchev Y. A combination of C-reactive protein and quick sequential organ failure assessment (qSOFA) score has better prognostic accuracy than qSOFA alone in patients with complicated intra-abdominal infections. Acta Chir Belg. 2019;16:1-5. doi: 10.1080/00015458.2019.1642579.

33. Yu H, Nie L, Liu A, Wu K, Hsein YC, Yen DW, et al. Combining procalcitonin with the qSOFA and sepsis mortality prediction. Medicine (Baltimore). 2019 Jun;98(23):e15981. doi: 10.1097/MD.00000000000015981.

**Table 1.** Demographic and clinical characteristic at ED admission

Variables	Total sample n=240
Sex, n (%)	
Female	140 (58.3)
Male	100 (41.7)
Age, years	60 (46-71.8)
BMI, kg/m <sup>2</sup>	24.5 (21.5-28.3)
Causes of hospitalization, n (%)	
Neurology	12 (5)
Cardiovascular	37 (15.4)
Respiratory	23 (9.6)
Gastrointestinal	72 (30)
Oncology	7 (2.9)
Endocrinology	9 (3.8)
Nephrology	19 (7.9)
Rheumatology	2 (0.8)
Infection	54 (21.7)
Hematology	7 (2.9)
Comorbidity, n (%)	
Diabetes	74 (30.58)
Hypertension	74 (30.8)
Renal failure	39 (16.3)
Hepatic cirrhosis	40 (16.7)
Malignancy	49 (20.4)
VIH	8 (3.3)
Use of Vasopressors, n (%)	70 (29.2)
Use of a mechanical ventilator, n (%)	
Yes	31 (12.9)
No	209 (87.1)
Initial SOFA score, n (%)	6 (4-9)
0-1	17 (7.1)
2-7	140 (58.3)
8-11	56 (23.3)
>11	27 (11.3)
30-days mortality, n (%)	75 (31.3)
In-hospital mortality, n (%)	59 (24.6)
In-ED mortality, n (%)	24 (10)

Data are expressed by median (25<sup>th</sup>-75<sup>th</sup>) or frequency and percentage (%)  
 BMI: Body mass index, SOFA: Sequential Organ Failure Assessment, ED: Emergency department.

**Table 2.** Comparison of clinical data, bioimpedance analyses, and biochemical analyses at admission to ED in survivors and non-survivors

	30-days Mortality			In-Hospital Mortality			In-ED Mortality		
	No n=165	Yes n=75	p value	No n=181	Yes n=59	p value	No n=216	Yes n=24	p value
Age, years	57 (40.5-67)	64 (51-76)	0.005	58 (42.5-69)	64 (50-76)	0.04	59 (44.3-69)	73 (54-80.1)	0.009
BMI	24.6 (21.7-28.1)	24.1 (20.8-24.1)	0.7	24.6 (21.6-28.1)	24 (20.9-28.7)	0.9	24.2 (21.4-27.7)	26.9 (21.9-30)	0.2
Initial SOFA score	5 (3-7)	9 (6-11)	<0.0001	5 (3-7.5)	9 (6-12)	<0.0001	6 (4-9)	9 (6-11.7)	0.001
Z to 5 kHz, Ω	604 (512.5-724.5)	557 (462-651)	0.03	596 (494-711)	559 (478-677)	0.2	596 (499-704)	495.5 (378-683)	0.05
Z to 50 kHz, Ω	545 (467.5-654)	520 (432-599)	0.08	541 (455.5-650.5)	520 (432-626)	0.3	543 (466-649)	446 (368-614)	0.03
Z to 100 kHz, Ω	512 (447-626.5)	510 (417-581)	0.2	511 (442-625.5)	511 (418-609)	0.5	513 (442-621)	430.5 (392-597)	0.04
Z to 200 kHz, Ω	489 (425.5-604.5)	493 (399-562)	0.3	488 (419.5-600)	496 (399-588)	0.6	494 (423-595)	412.5 (343-576)	0.05
Resistance	539 (464.3-650)	517 (429-596)	0.07	536.4 (536.4-647.1)	517 (429.7-619.2)	0.3	538.8 (459-644)	442.6 (361-607)	0.02
Reactance	49.5 (29.9-64.7)	28.8 (19.8-48.5)	<0.0001	46.7 (28.7-63.4)	31.9 (19.8-48.5)	<0.0001	43.8 (27.8-62.1)	23.8 (16.3-38.4)	0.001
Phase angle	4.7 (3.6-6.1)	3.3 (2.5-4.9)	<0.0001	4.5 (3.4-6)	3.2 (2.5-5.1)	<0.0001	4.4 (3.2-5.9)	3.2 (2.2-4.3)	0.001
Impedance ratio	0.84 (0.8-0.87)	0.87 (0.83-0.9)	<0.0001	0.84 (0.8-0.87)	0.87 (0.83-0.9)	<0.0001	0.84 (0.8-0.88)	0.88 (0.85-0.9)	0.002
Creatinine, mg/dL	1.1 (0.72-2)	1.6 (0.81-2.68)	0.1	1.1 (0.73-2.08)	1.62 (0.87-2.75)	0.09	1.21 (0.75-2.1)	2.06 (1-4.3)	0.07
CRP, mg/L	5.2 (0.84-15.9)	10.7 (5.5-15.3)	0.06	5 (1.1-15.7)	11.9 (6.7-15.5)	0.03	7.1 (1.6-15.5)	14.1 (11.3-21.9)	0.02
Bilirubin, mg/dL	0.69 (0.47-1.5)	1.66 (0.64-6.7)	<0.0001	0.7 (0.48-1.51)	1.95 (0.64-8.67)	<0.0001	0.76 (0.5-1.81)	3.39 (0.82-6.6)	0.004
Lactate, mg/dL	1.7 (1.2-2.8)	3.4 (1.9-6.2)	<0.0001	1.8 (1.3-2.8)	4.1 (2.2-6.7)	<0.0001	2 (1.4-3.8)	3.3 (2-6.9)	0.005

Data are expressed by median (25<sup>th</sup>-75<sup>th</sup>)

ED: Emergency department, BMI: Body mass index, SOFA: Sequential Organ Failure Assessment, Z: impedance, CRP: C-reactive protein

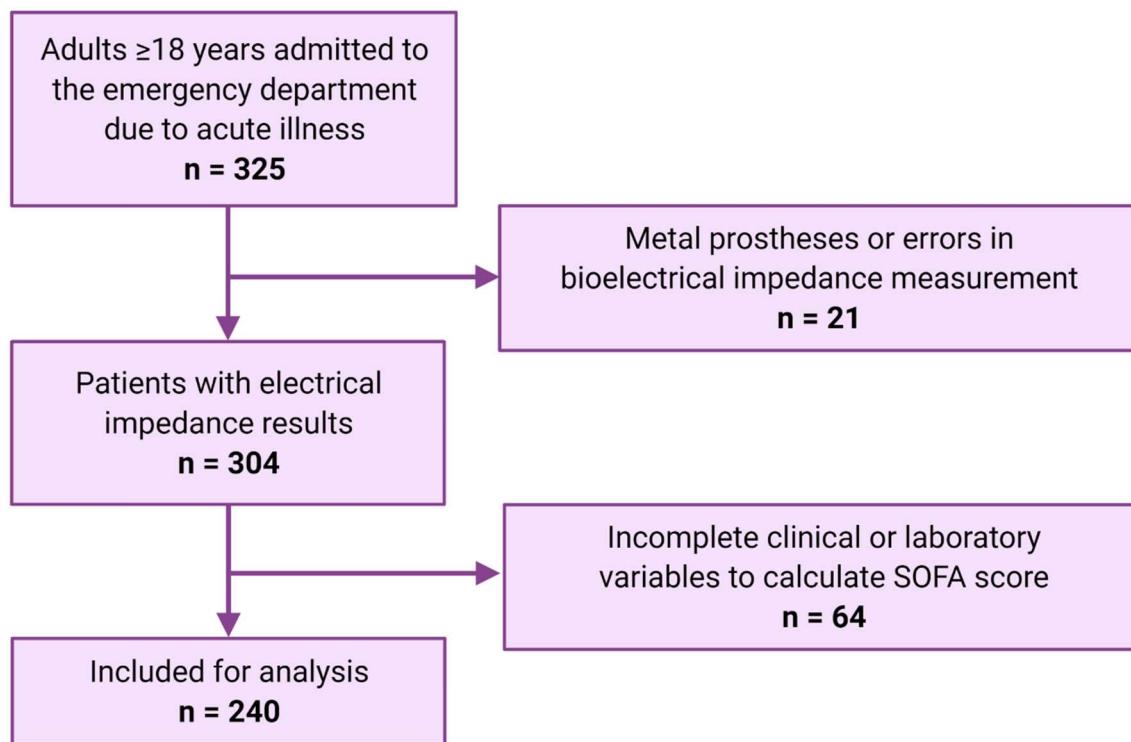
**Table 3.** Unadjusted and adjusted Cox's regression models for prediction of mortality by initial SOFA score and impedance ratio.

	Unadjusted model			Adjusted model		
	$\beta$ coefficient	HR (95% CI)	p Value	$\beta$ coefficient	HR (95% CI)	p Value
30-days mortality model <sup>a</sup>						
Initial SOFA score	0.16	1.18 (1.10-1.27)	<0.0001	0.11	1.12 (1.03-1.22)	0.01
Impedance ratio	0.10	1.11 (1.05-1.17)	<0.0001	0.09	1.10 (1.04-1.16)	0.002
In-hospitality mortality model <sup>b</sup>						
Initial SOFA score	0.22	1.25 (1.16-1.34)	<0.0001	0.21	1.23 (1.14-1.33)	<0.0001
Impedance ratio	0.10	1.10 (1.05-1.17)	<0.0001	0.09	1.10 (1.03-1.16)	0.002
In-ED mortality model <sup>c</sup>						
Initial SOFA score	0.19	1.20 (1.09-1.34)	<0.0001	0.18	1.20 (1.08-1.33)	0.001
Impedance ratio	0.14	1.15 (1.05-1.25)	0.002	0.12	1.13 (1.03-1.24)	0.01

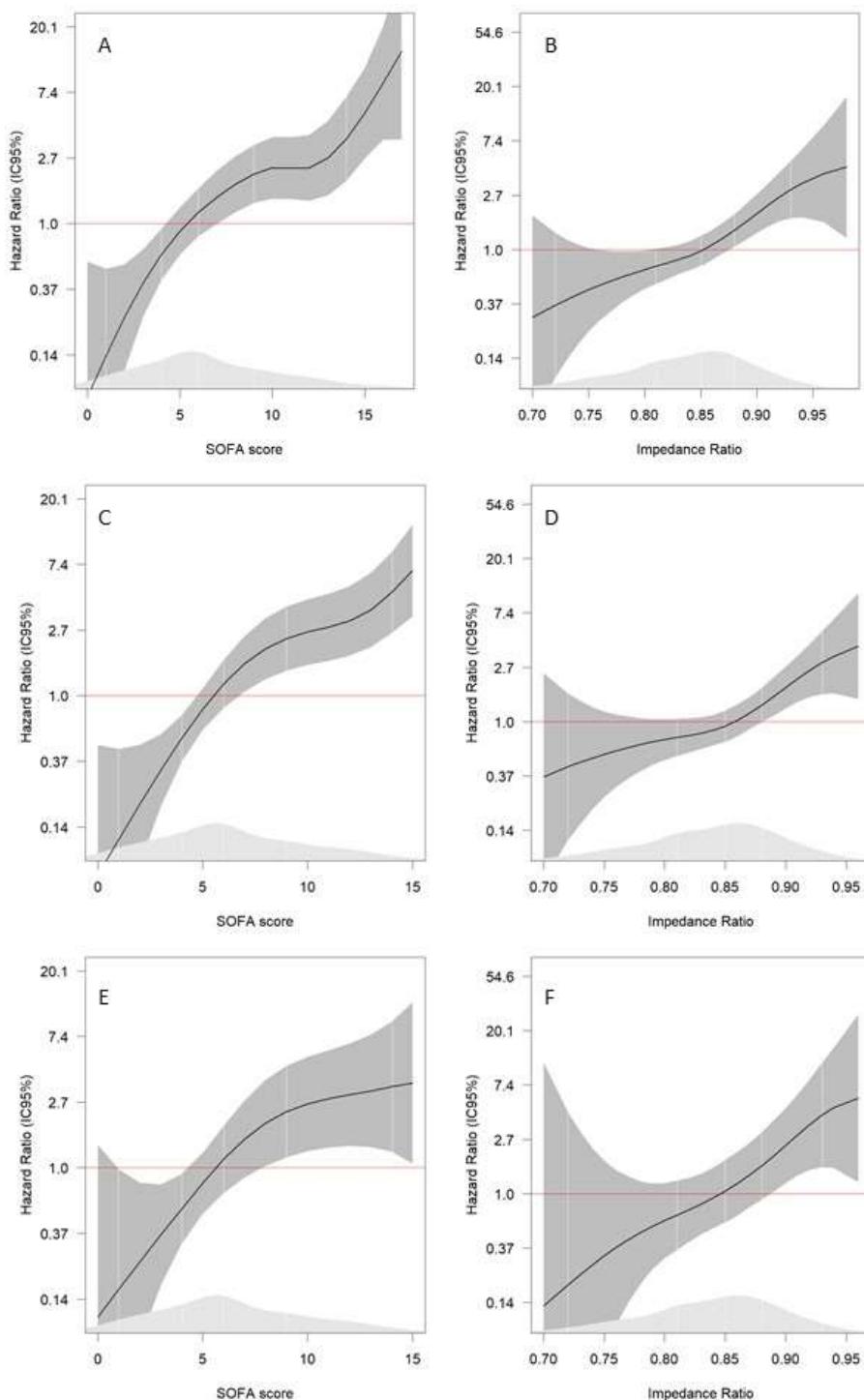
Adjusted model for: a: age, sex, and body mass index, invasive mechanic ventilation, creatine, lactate; b: age, sex, and body mass index, invasive mechanic ventilation; c: age, sex.

SOFA: Sequential Organ Failure Assessment, ED: Emergency department.

**Figure 1.** Flow of patients assessed for eligibility.



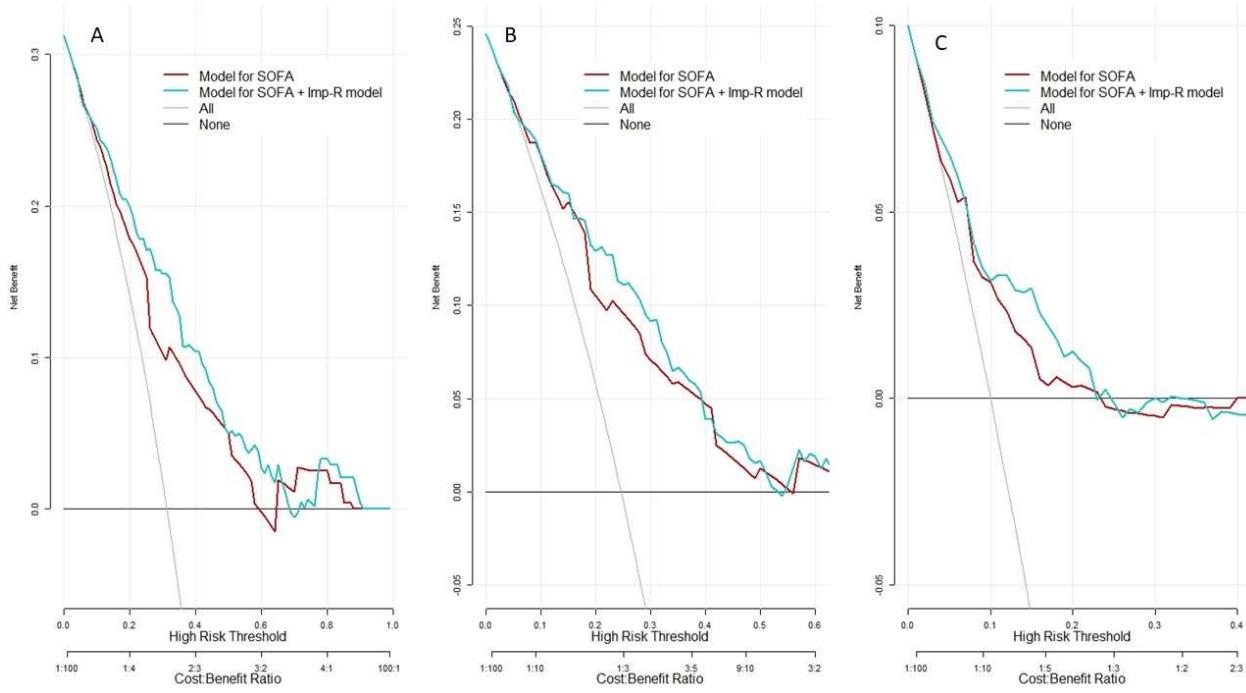
**Figure 2.** Splines of initial SOFA score and impedance ratio for prediction of mortality.



A: Prediction of 30-day mortality by initial SOFA score. B: Prediction of 30-day mortality by Impedance ratio. C: Prediction of In-hospital mortality by initial SOFA score. D:

Prediction of In-hospital mortality by Impedance ratio. E: Prediction of In-ED mortality by initial SOFA score. F: Prediction of In-ED mortality by Impedance ratio. 30-day mortality model adjusted by: age, sex, and body mass index, invasive mechanic ventilation, creatine, lactate. In-hospital mortality model adjusted by: age, sex, and body mass index, invasive mechanic ventilation. In-ED mortality model adjusted by: age, sex

**Figure 3.** Decision curve analyses for initial SOFA score model and the combination with impedance ratio in the prediction of mortality.



A: Models for prediction of 30-day mortality, B: Models for prediction In-hospital mortality, C: Models for prediction of In-ED mortality.