Severity scores should incorporate limitations on life support for predicting mortality

Las puntuaciones de intensidad deberían incorporar las limitaciones del soporte vital para predecir la mortalidad

Severity scores are routinely used in clinical practice for various purposes, including to predict mortality. Scores are updated periodically, mainly to take improved treatments into account. The latest versions of the most commonly used scores (SAPS3 and APACHE IV) were developed more than 15 years ago.[1,2]

Many patients are now admitted to intensive care units (ICUs) with orders to withhold some life-support measures. Our recent multicenter study found that more than 7% of all patients admitted to participating ICUs had limitations on life support; although nearly one-third survived more than 30 days, standard severity scores underestimated their high mortality.[3] The accuracy of severity scores' predictions within centers varies due to variations in performance or in case-mix. Advances in treatments since the most recent version of the score are associated with progressively reduced accuracy.[4]

Here we report a new analysis including all patients registered in the clinical database at our mixed ICU in a university-affiliated hospital from 2009 through 2017. The UCH Ethics Committee approved the study. Throughout this period, our ICU's admission criteria and case-mix remained unchanged. We admitted 6821 patients (mean age, 65.6 yr; ICU stay, 4.6 days). Hospital mortality was 16.2% and SAPS3-predicted mortality was 27.6%, yielding a standardized mortality ratio (SMR) of 0.59.

A total of 242 (3.5%) patients had limitations on life support at admission. In this subgroup, hospital mortality was 47.1% and SAPS3-predicted mortality was 46.5% (SMR 1.01); by contrast, in patients without limitations, hospital mortality was 15.1% and SAPS3-predicted mortality was 26.9% (SMR 0.56). We found no significant differences along the years of the study.

Multivariable logistic regression showed that hospital mortality was independently associated with SAPS3 (OR 1.05 [1.051–1.058]; $p < 0.001$) and limitations on life support at admission (OR 2.85 [2.11–3.85]; $p < 0.001$). The area under the receiver operating characteristic curve (AUROC) for the model including these variables was 0.85, similar to the original value for the APACHE IV.[2] Not including limitations on life support in the model yielded similar accuracy (AUROC 0.84), probably due to the small proportion of patients with limitations. Nevertheless, the mortality risk in patients with limitations on life support at admission was twice that predicted by standard severity scores (Fig. 1).

The results of our single center analysis are somewhat different from those of a recent multicenter trial. The rate of limitations on life support at admission was lower (3.5% vs. 7.8%) and hospital survival was better (53% vs. 41%), but severity scores' underperformance in patients with limitations was similar. Taken together, the two studies show the same trend in more than 10,000 patients.

Research networks focused on predictive models will probably update current severity scores in the near future, and we suggest they explore the possibility of including limitations on life support at admission in the new algorithms.
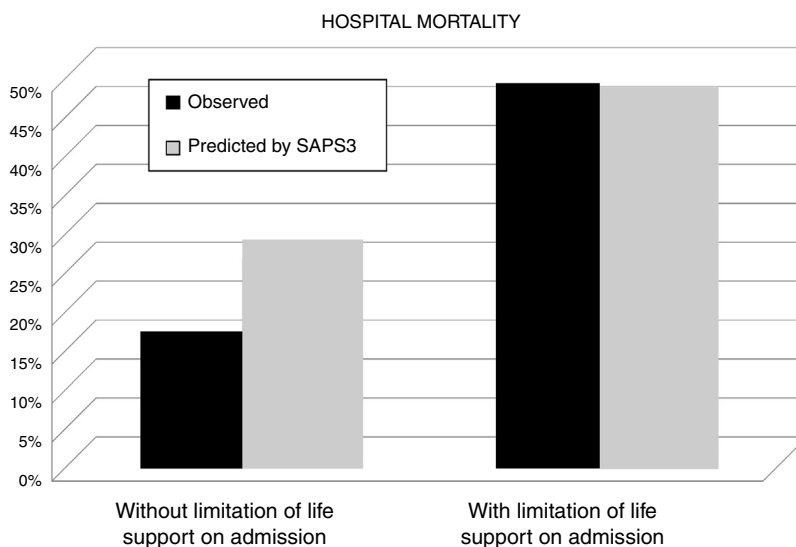

Figure 1 Comparison of observed and predicted hospital mortality in patients according to the existence or not of limitations of life-support on ICU admission.

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Lymphopenic hospital acquired sepsis (L-HAS): An immunological phenotype conferring higher risk of mortality[☆]

Sepsis nosocomial linfopénica: un fenotipo inmunológico que confiere un mayor riesgo de mortalidad

The clinical profile of Hospital Acquired Sepsis (HAS) is poorly known. In a recent work,[1] we found that patients suffering from HAS show many of the risk factors associated with cardiovascular disease and cancer.

Lymphopenia is a frequent finding in sepsis patients.[2–4] Sepsis affects the immune system by directly altering the lifespan, production and function of the effector cells responsible for homeostasis.[5] Lymphopenia is also found in other severe infections like pneumonia needing of hospitalization, and it is associated to an increased risk of mortality.[6]

The impact of lymphocyte counts on the prognosis of patients with HAS is unknown. The objective of the present study was to evaluate the association between lymphocyte counts and mortality risk of the patients suffering from HAS. The predictive ability of the other leukocyte subpopulations was also assessed.

The study was approved by the Clinical Research and Ethics Committee of our hospital. Informed consent was waived due to the observational nature of the study.

A total of 196 patients were included in the study. Hospital and 90 days mortality was 45.4%. The median age of HAS patients was of 73 years (IQR: 68.1–71.4), with 68.4% ($n = 134$) of them being male. Some serious comorbidities were: cardiac disease 63.8% ($n = 125$), cancer 34.2% ($n = 67$), chronic kidney disease 19.4% ($n = 38$), immunosuppression 17.9% ($n = 35$) and chronic hepatic disease 6.1% ($n = 12$) (Supplementary Table 1). Sepsis with organ failure (severe sepsis/septic shock) was present in 146 patients (74.5%) with 75 of these patients dying during the first 90 days.

HAS emerged 10 days following hospital admission in median (IQR, 11.4–14.5). The most frequent source of infection was the respiratory tract (29.1%), followed by bacteraemia (25%) (Supplementary Table 1). Microorganisms were isolated in one hundred and fifty patients (76.5%). Gram negative bacteria were the most common microorganisms (58.6%), followed by Gram positive cocci (46.0%).

We collected leukocyte subpopulations counts at hospital admission and also at HAS diagnosis. Patients with HAS showed a significant increase in the median values of neutrophil counts from admission to diagnosis: (5.3 [4.00–7.4] $\times 10^3/mm^3$) *vs* (10.9 [6.5–17.0] $\times 10^3/mm^3$) $p < 0.001$. On the contrary, median values of eosinophil and lymphocyte counts decreased from admission to diagnosis: (0.11 [0.04–0.22] $\times 10^3/mm^3$) *vs* (0.02 [0.00–0.11] $\times 10^3/mm^3$) for eosinophils and (1.6 [1.0–2.3] $\times 0^3/mm^3$) *vs* (0.8 [0.4–1.3] $\times 10^3/mm^3$]) for lymphocytes (with differences yielding a $p < 0.001$ in both cases). Median values of monocytes and basophil counts did not change in a significant manner between both moments.

Median values of lymphocytes at HAS diagnosis were higher in survivors than in non survivors. Survivors showed also higher median values of eosinophils at HAS diagnosis than non survivors. On the contrary, monocyte, basophil and neutrophil counts did not show differences between both groups (Supplementary Table 1).

Lymphocytes and eosinophil counts at HAS diagnosis showed significant AUCs for identifying survivors at hospital discharge (Supplementary Fig. 1), with an (AUC [CI95%], p) of (0.59 [0.59–0.67], 0.042) and (0.60 [0.52–0.68], 0.023) respectively. Other leukocyte subtypes failed to discriminate survivors from non survivors. The optimal operating point (OOP) was calculated for those leukocyte subpopulations showing an AUC $p < 0.05$ as previously described[7] for distinguishing between both kinds of patients in the AUC analysis was 775 cells/mm^3 for lymphocytes and 13 cells/mm^3 for eosinophils.

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