

# A novel index for trending sepsis and inflammatory response using processed EEG and Heart Rate Variability.

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## INTRODUCTION:

Sepsis is a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs. It is frequently a final common pathway to death for many infectious diseases worldwide.

Systemic inflammatory response syndrome (SIRS) is an exaggerated defense response of the body to a noxious stressor (infection, trauma, surgery, acute inflammation, ischemia or reperfusion, or malignancy, to name a few) to localize and then eliminate the endogenous or exogenous source of the insult. Dysregulation of proinflammatory and anti-inflammatory pathway homeostasis lies at the heart of the clinical scenario with the dysregulated release of acute and chronic phase reactants. This activity reviews the evolution of the definition and the clinical relevance of systemic inflammatory response syndrome. It outlines appropriate evaluation and management strategies for the syndrome and reviews the role of the interprofessional team in improving care and clinical outcomes for patients with this condition

Electroencephalography (EEG) has been employed to assess the hypnotic effect and the level of nociception/antinociception during general anaesthesia. Furthermore, Heart Rate Variability (HRV) has been put forth as a potential monitoring tool for the nociception/antinociception balance. A number of studies have indicated that a reduction in HRV is linked to an elevated level of systemic inflammation or sepsis (4, 5). Nevertheless, it has been demonstrated that certain HRV parameters, such as the Root Mean Square of Successive Differences (RMSSD), may also undergo a reduction during the induction of general anaesthesia or sedation. It is therefore essential to isolate the effects of inflammation on HRV by accounting for the level of sedation, as assessed by processed EEG.

## OBJECTIVE:

The objective of this study was to develop an index that would enable the accurate assessment of the inflammatory response based on processed electroencephalogram (EEG) and heart rate variability (HRV) data. The index was termed the "Trending Sepsis and Inflammation" (TSI) index.

## METHODS:

The Trending Sepsis and Inflammation (TSI) index was developed using data collected from patients at Hospital Quirón Salud in Barcelona, Spain, and Clínica Interhospital in Guayaquil,

Ecuador. Both hospitals had obtained the approval of their local ethics committee, and the CoreSys One monitor (CoreSys Health S.L., Barcelona, Spain) was employed to record two EEG channels and one ECG channel simultaneously. A total of 63 patients were included in the study, comprising 54 patients from surgical procedures of durations ranging from 45 minutes to five hours, 4 patients in the ICU with confirmed sepsis and 5 healthy volunteers for baseline estimation. In total, 1,279,557 readings were collected at 0.25-second intervals.

The dataset was categorized into three levels of increasing inflammation. The healthy awake volunteers were assigned to Level 1, the perioperative patients to Level 2, and the patients with confirmed sepsis to Level 3. Subsequently, an Adaptive Neuro-Fuzzy Inference System (ANFIS) model was employed to train the index, with heart rate, root mean square of the successive differences (RMSSD), the ratio between low and high frequency components of heart rate variability (LF/HF), and the brain activity index (BA) as inputs. Heart rate variability (HRV) parameters were calculated at 3-minute intervals, with a 20-second increment.

The TSI index provides real-time data on a patient's inflammatory status, facilitating prompt clinical decision-making. The index indicates that values ranging from 0 to 25 indicate a normal state, 25 to 50 suggest a mild inflammatory response, 50 to 75 denote a strong inflammatory response and risk of sepsis, and 75 to 100 indicate a severe inflammatory response and risk of sepsis and septic shock.

#### RESULTS:

The TSI index vs the reference inflammatory scale resulted in a  $P_k(SE)$  value of 0.9862(0.001) and an  $R^2$  Pearson correlation coefficient of 0.85. Figure 1 shows a boxplot of TSI vs the inflammatory scale.

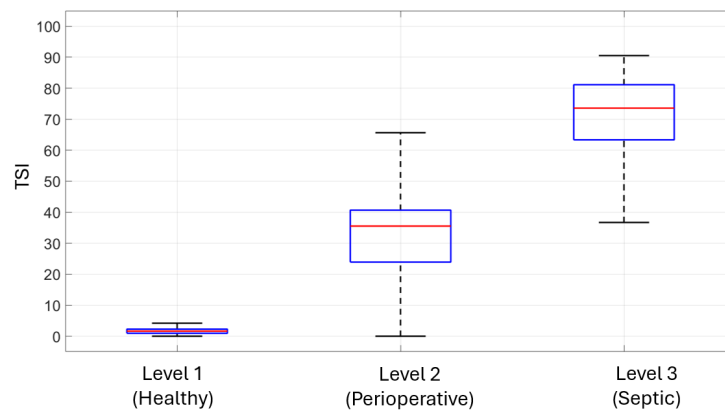


Figure 1 presents a boxplot depicting the distribution of TSI values among healthy volunteers, surgical cases, and septic cases.

#### CONCLUSIONS:

The prediction probability of the TSI of the reference inflammatory scale was high, however it should be taken into account that the  $P_k$  was calculated on the training data, the method should be validated in data set different from the training data. The TSI has the potential of detecting inflammatory states, however future studies, including inflammatory biomarkers, must be carried out to prove that the TSI is associated with systemic inflammation.

#### REFERENCES

- [1] Rudd, Kristina E., et al. "Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study." *The Lancet* 395.10219 (2020): 200-211.
- [2] Darbà, Josep, and Alicia Marsa. "Epidemiology, management and costs of sepsis in Spain (2008–2017): a retrospective multicentre study." *Current medical research and opinion* 36.7 (2020): 1089-1095.
- [3] Faix, James D. "Biomarkers of sepsis." *Critical reviews in clinical laboratory sciences* 50.1 (2013): 23-36.
- [4] D. P. Williams, J. Koenig, L. Carnevali, A. Sgoifo, M. N. Jarczok, E. M. Sternberg, and J. F. Thayer. Heart rate variability and inflammation: a meta-analysis of human studies. *Brain, behavior, and immunity*, 80:219–226, 2019.
- [5] B. Y. H. Wee, J. H. Lee, Y. H. Mok, and S. Chong. A narrative review of heart rate and variability in sepsis. *Annals of Translational Medicine*, 8(12), 2020.