M.Varela[a], R.Asensio[b], G.García Navazo[b] M.D., D.D'Onofrio[c], M.Calvo[a], P.Galdos[b]

COMPLEXITY ANALYSIS OF THE TEMPERATURE CURVE IN CRITICALLY ILL PATIENTS: PROGNOSTIC IMPLICATIONS

[a] *Servicio de Medicina Interna, Hospital de Móstoles, Madrid, Spain*
[b] *Servicio de Cuidados Intensivos, Hospital de Móstoles, Madrid, Spain*
[c] *System analyst, Buenos Aires, Argentina*

Abstract

The complexity of the temperature curve was measured by means of ApEn (Approximate Entropy) in 16 critically ill patients, admitted to the Intensive Care Unit in multiorgan failure. ApEn was significantly lower (the temperature curve was less complex) in patients who died versus patients who survived. The predictive value of ApEn compares favourably with conventional scales of physiological status (Sepsis Organ Failure Assessment)

Key words: Complexity, temperature curve, multiorgan failure, Approximate Entropy .

Introduction

Although temperature is essentially quantitative, it is usually applied in clinical settings as a qualitative, dichotomic variable (febrile/afebril), with rather little prognostic implications, and usually not even considered in afebril patients. We aimed to investigate if a really quantitative approach, derived from complexity analysis, could overcome this febrile/ afebril dichotomy and perhaps provide some more prognostic information. In a previous paper[1] we analysed the temperature curve of healthy subjects, and found that the complexity of the temperature curve decreased with age. We now analyse the complexity of the temperature curve of patients admitted to an Intensive Care Unit (ICU) in multiple organ failure. We tried to find out:

1.- if the complexity of the temperature curve correlates with the severity of the clinical status, measured with conventional criteria

2.- if the complexity of the temperature curve has some prognostic value, and how does it compare with conventional clinical criteria.

Material and methods

16 successive patients in multiorgan failure admitted to the ICU of a general hospital in Madrid were studied. There were 8 men and 8 females. The mean age was 61.9 (range 36 – 84). In each patient a temperature probe was fixed to the right hipochondrium and connected to a data logger (Spectrum 1000, Veriteq Instruments Inc., Richmond, B.C., Canada). If the right hipochondrium was not accessible (because of surgical wounds, etc), the left hipochondrium was utilised. As long as possible, a measure was recorded each 10' to a precision of 0.05 ºC, until the patient died or was discharged (the last 4 hours of stay were not included in the analysis). The probe was disconnected for surgery or X-rays as needed. The mean length of stay in the ICU was 18 days (range 3-64).

In each patient, a SOFA (Sepsis Organ Failure Assessment)[2] score was obtained each other day. The SOFA score is obtained measuring the respiratory function (PaO2/FiO2 ratio), coagulation (platelet count), liver function (bilirrubin), cardiovascular function (arterial tension, use of vasoactive drugs), central nervous system (Glasgow coma score) and renal function (creatinine or urine output). It has a range of 0 to 20, with higher values indicating worse clinical status.

From the temperature time series, successive sets of 180 readings (30 hours) with a gap of 1 hour (and 29 hours of overlap) were analysed. The Approximate Entropy (ApEn) (m=2, r=0.15, N=180)[3] was calculated in each set. ApEn is a measure of complexity that essentially evaluates predictability. It states to what extent knowing a certain number of successive points (in our case, two lectures) allows a prediction of the next point. The more complex the time series, the less precise will be the prediction, and the higher will be ApEn. The ApEn algorithm was initially written in dBase III+ and later compiled with Clipper to obtain an executable file running on Windows.

The mean number of hours per patient from which ApEn could be calculated was 292 (range 33 – 918). We used the whole curve for comparison with the SOFA curve, and the

ApEn nadir (the minimum ApEn recorded) and peak SOFA for all other statistical analysis.

Results

Nine patients died (total mortality: 56.2%). There were no significant differences in mortality with regard to gender. There was a tendency to higher mortality with age, but it did not reach statistical significance (54.7 years in survivors, 67.5 in non-survivors, p=0.06).

Not surprisingly, there were significant differences in the SOFA peak between survivors and non-survivors (9.7 vs. 14.7, $p < 0.05$)

As previous observed[1], there was an inverse

relation between ApEn and age ($r = -0.54$, $p < 0.05$)

In all but 3 of the 16 cases there was a statistically significant negative correlation between ApEn and SOFA ($p < 0.000001$ in 11 patients, < 0.005 in 2 patients). Two of the three patients in whom a significant negative correlation could not be proved had < 40 ApEn determinations.

The nadir in ApEn was significantly lower in patients who finally died versus patient who survived (0.232 vs. 0.393, $p < 0.01$).

We used Proc GENMOD of the SAS package (SAS Institute 1999) to fit two logistic regression models on the response variable "survival". The models included age and either ApEn or SOFA as independent variables. Both ApEn and SOFA showed a significant effect on survival once corrected for the effect of age (Chi-sq=12.54, p=0.0004; Chi-sq=7.17, p<0.0074; respectively), but ApEn explained a higher percentage of deviance (48.75%) than SOFA did (32.67%). A receiver operating characteristics (ROC) curve was designed to compare the predictive power of ApEn vs. SOFA for survival. The area under the curve were, respectively, 0.873 for ApEn and 0.817 for SOFA

Discussion

Temperature control is a complex physiological process involving multiple structures. As in many other biological systems, it is reasonable to suspect that as a patient status deteriorates, the complexity of the system's output will decrease. To confirm this, we used ApEn, a robust and stable tool for measuring complexity in biological systems.

We found in most of the patients a significant negative correlation between clinical status, measured with the SOFA score, and complexity, measured with ApEn. All but one of the patients in which this negative correlation could not be observed had relatively short time series, which may explain the lack of correlation.

Furthermore, a loss in complexity implied a bad prognosis. The ApEn nadir was significantly lower in patients who finally died. The influence of a low ApEn on mortality can not be attributed to age, and probably reflects a deterioration of the clinical status.

The predictive value of ApEn compares favourably SOFA: it explains a higher percent of deviance in the logistic regression models, and its ROC curve includes a more surface under the curve.

ApEn may be continuously monitored, its measurement is harmless, inexpensive and does not require invasive procedures. If these results are confirmed, complexity analysis may help in decision making with critically ill patients.

References

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Correspondence: Manuel Varela:
e-mail: mvarela@arrakis.es