Neuroanesthesia and Intensive Care

The logistic organ dysfunction score as a tool for making ethical decisions

[Le score logistique de dysfonction organique comme outil de prise de décisions éthiques]

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Purpose: We examined whether the change of the logistic organ dysfunction score (LOD) between the first and the fourth day in the intensive care unit (ICU) could be predictive of death in the ICU. The LOD could then be used to help make decisions concerning therapeutic limitations (TL).

Methods: One hundred fifty-four patients were included. Exclusion criteria were: discharge from the ICU or TL before the 72nd hr. Ninety-three patients remained for evaluation. The LOD was calculated on the day of admission (LOD1) and between the 72nd and 96th hr (LOD4). The $\Delta\text{LOD} = \text{LOD4} - \text{LOD1}$ index was calculated for survivors and non-survivors; sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.

Results: Sixteen patients died in the ICU, they had a higher ΔLOD (0 vs -2; $P = 0.0046$) than the survivors. After logistic regression, a high ΔLOD was associated with a higher risk of death in the ICU independent of the initial severity of disease. The PPV concerning death in the ICU was 0.66 for a $\Delta\text{LOD} \geq 4$ cut-off. The NPV was 0.89 for a cut-off of ≥ 1 .

Conclusion: ΔLOD appears to be a predictor of death in the ICU, independent of the initial severity of disease. The PPV is not high enough to assist with making individual TL decisions. The NPV can help to identify patients at low risk of death. The ΔLOD deserves to be evaluated in a population exhibiting greater severity of disease.

Objectif : Vérifier si le changement de score logistique de dysfonction organique (LDO) entre le premier et le quatrième jour à l'unité des soins intensifs (USI) peut être prédictif d'un décès à l'USI. Le LDO pourrait alors être utilisé pour aider à prendre des décisions concernant les limites thérapeutiques (LT).

Méthode : Cent cinquante-quatre patients ont participé à l'étude. Les critères d'exclusion étaient : un congé de l'USI ou une LT survenant avant la 72^e h. Quatre-vingt-treize patients sont restés pour l'évaluation. Le LDO a été calculé le jour de l'admission (LDO1) et entre la 72^e et la 96^e h (LDO4). L'index $\Delta\text{LDO} = \text{LDO4} - \text{LDO1}$ a été calculé pour les survivants et les non-survivants ; la sensibilité, la spécificité, la valeur prédictive positive (VPP) et la valeur prédictive négative (VPN) ont été calculées.

Résultats : Seize patients sont morts à l'USI, ils présentaient un ΔLDO (0 vs -2 ; $P = 0,0046$) plus élevé que les survivants. Après régression logistique, un ΔLDO élevé était associé à un plus grand risque de décès à l'USI indépendamment de la sévérité initiale de la maladie. La VPP de décès à l'USI a été de 0,66 pour une limite de $\Delta\text{LDO} \geq 4$. La VPN a été de 0,89 pour une limite ≥ 1 .

Conclusion : Le ΔLDO semble être un prédictif de décès à l'USI, indépendamment de la sévérité initiale de la maladie. La VPP n'est pas suffisamment élevée pour aider à prendre des décisions de LT individuelles. La VPN peut aider à reconnaître les patients à faible risque de décès. Le ΔLDO doit être évalué dans une population présentant des affections plus sévères.

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THERAPEUTIC limitations (TL) are involved in approximately 50% of deaths in the intensive care unit (ICU) and therefore concern about 10% of ICU patients.¹ Ethical decisions of TL are made in order to reduce the suffering of patients and families, when it is believed that continuing therapy would offer no possible benefit. In the event of low probability of short-term survival, invasive therapies probably do not offer any benefit. Therefore, identifying patients who will die in the ICU could help make decisions of TL. Therapeutic limitations also allow a better use of limited ICU resources. Nevertheless, TL decisions are predominately based on subjective criteria. For example, the physician's subjective prediction of survival, further cognitive function and perception that the patient would not want life support to be used are the factors most associated with mechanical ventilation withdrawal.² It would be of interest to have objective criteria clearly outlined to help make TL decisions in the ICU. Such a criterion could relieve the physician's conscience, reduce the bias associated with subjective decisions that lead to unequal treatment of the patients, speed up the decision process and limit the suffering of patients and families. It should accurately predict the death of individuals and should be available early on during the ICU stay in order to allow early TL. Response to treatment is often subjectively integrated by physicians when assessing a patient's prognosis, it also is a simple element which can easily be communicated to families. Therefore, it seems important to integrate it in the objective evaluation of the patient concerning TL.

In order to have a tool to assist with making early TL in the ICU, we evaluated the performance of the logistic organ dysfunction score (LOD) evolution between the first and the fourth day in the ICU to predict death in the ICU.

Methods

As the study design was strictly observational, with no drug or technique being administered for the purpose of the study, nor requiring that any additional blood samples be drawn, and in accordance with French regulations on biomedical research, no informed consent was obtained. During April to June 2003 all patients admitted to a medical ICU were prospectively included in the study. Thereafter the patients who stayed < 72 hr in the ICU or who were subjects of a TL before the 72nd hr were excluded. For all patients the simplified acute physiology score (SAPS) II and the LOD (LOD1) were calculated during the first 24 hr in the ICU. For the final study sample (patients

not excluded before the 72nd hr) the LOD was calculated again between the 72nd and 96th hr in the ICU (LOD4). For patients leaving the ICU or who died in the ICU between the 72nd and 96th hr, LOD4 was calculated between the 72nd hr and the time of discharge or death.

The index $\Delta\text{LOD} = \text{LOD4} - \text{LOD1}$ was used to measure the evolution of the LOD between the first and the fourth day in the ICU. Thus a positive ΔLOD indicated that the patient's condition was worsening, and a negative ΔLOD indicated improvement. Other variables measured were: time and day of admission and discharge from the ICU, main admission diagnosis, Mc Cabe and Knaus score. All variables were recorded prospectively. The study endpoint was death in the ICU.

Sample size calculation assuming a 25% ICU mortality with a ΔLOD standard deviation of 3.8 (preliminary data) showed that 98 patients had to be analyzed in order to detect a 2.5-difference in ΔLOD between survivors and non-survivors with an α risk of 0.05 and a power of 80%. The study was therefore conducted over a three-month period to include about 150 patients in order to take into account exclusions and possible incomplete data collection.

Statistical analysis was performed by comparing ΔLOD between the patients who survived and the ones who died in the ICU using a univariate non-parametric test (Mann Whitney). To take into account the initial severity of disease two logistic regressions were performed, one using the SAPSII of the first day in the ICU and one using LOD1 as independent variables measuring the initial severity of disease. The prognostic performance of ΔLOD was evaluated by calculation of the specificity, the sensitivity, the positive (PPV) and negative (NPV) predictive values concerning death in the ICU for different cut-offs and construction of a receiver operating characteristics (ROC) curve. The different scores were calculated using the software Excel® (Microsoft Corporation, USA), the statistical analysis was performed using the software Statview® (SAS Institute Inc., USA).

Results are expressed as median [10th; 90th percentile]. A *P* value < 0.05 was considered significant.

Results

During the study period 154 patients were included, of whom 93 constituted the final study sample upon which further analysis was performed (Figure 1). The major characteristics of the final study patients are indicated in Table I. Sixteen patients (17.7%) died in the ICU, their SAPSII was significantly higher than that of survivors (47 [31; 61] *vs* 39 [19; 59];

FIGURE 1 Flow diagram depicting flow of patients through the study. ICU = intensive care unit; TL = therapeutic limitation.

$P = 0.05$). So was LOD4 (6 [2; 13] *vs* 2 [0; 6]; $P = 0.0005$). LOD1 values were not significantly different from values in the patients who died (6 [2; 10] *vs* 5 [2; 10]; NS).

Δ LOD was significantly higher in the patients who died in the ICU: 0 [-4; 4] *vs* -2 [-7; 0]; $P = 0.0046$.

After logistic regression, Δ LOD was associated with a higher risk of death in the ICU independent of the initial severity of disease, whether measured by the SAPSII of the first day (odd ratio [OR] = 1.41 [95% confidence interval [95CI] = 1.15–1.73]; $P = 0.0009$) or LOD1 (OR = 1.52 [95CI: 1.20–1.93]; $P = 0.0005$). A ROC curve was constructed by calculation of the sensitivity and specificity of Δ LOD for the prediction of death in the ICU (Figure 2). The area under the ROC curve was graphically small, the most informative cut-off was 1. Positive predictive value increased with higher values of cut-offs. For a cut-off of Δ LOD ≥ 1 the PPV was 53% (95CI: 23–77), the NPV was 89% (95CI: 62–99). At a cut-off of Δ LOD ≥ 0 the PPV was 33% (95CI: 15–49), the NPV was 88% (95CI: 64–96).

The highest PPV, 66% (95CI: 11–89), was observed for a cut-off of Δ LOD ≥ 4 , the highest NPV (100%; 95CI: 87–100) was observed for a cut-off of Δ LOD ≥ -4 .

FIGURE 2 Receiver operating characteristic curve. Performance of the change between day one and four in the intensive care unit of the logistic organ dysfunction score (Δ LOD) for predicting death in the intensive care unit. Diamonds represent data points; continuous line: $x = y$ straight line; dotted line represents third order polynomial regression curve.

Discussion

Δ LOD was significantly higher in patients who died in the ICU, and thus was independent of the initial severity of disease. According to logistic regression, when initial severity of disease was measured by LOD1, each 1 point increase in Δ LOD multiplied the risk of death in the ICU by a factor of 1.5. In the studied population the PPV appeared to be low, with the relatively small number of patients resulting in large 95CIs. At a cut-off of 1, the NPV was high (89%) indicating that patients with a Δ LOD of < 1 (inferring that their condition is improving or stable), have a probability of death of 11%, which is much lower than the probability of death of the whole study population (17%). A simple way of using Δ LOD is to consider the cut-off of 0: patients with a negative Δ LOD (whose condition is improving) have a probability of surviving their ICU stay of 88%.

The usual severity of disease scores (SAPS,³ Acute Physiology And Chronic Health Evaluation [APACHE],⁴ LOD)⁵ do predict accurately the risk of death on the level of a population of patients admitted

TABLE I Major characteristics of the final study patients

Variable	Non-survivors	Survivors	P **
Patients (n)	16 (17.2%)	77 (82.8%)	
Female	5 (31.2%)	31 (40.3%)	NS
<i>Main admission diagnosis</i>			
Multiple organ failure	0 (0%)	1 (1.30%)	NS
Septic shock	1 (6.25%)	12 (15.6%)	NS
Cardiogenic shock	1 (6.25%)	2 (2.60%)	NS
Shock (other)	0 (0%)	2 (2.60%)	NS
Acute respiratory failure	5 (31.2%)	16 (20.8%)	NS
Acute or chronic respiratory failure	0 (0%)	14 (18.2%)	NS
Acute renal failure	2 (12.5%)	4 (5.19%)	NS
Coma	6 (37.5%)	18 (23.4%)	NS
Trauma	1 (6.25%)	8 (10.3%)	NS
Age (yr)	61 (36; 76)	69 (40; 81)	NS
SAPS II*	47 (31; 61)	39 (19; 59)	P = 0.05
Mc Cabe†			NS
0:	9 (56.2%)	40 (51.9%)	
1:	5 (31.2%)	29 (37.7%)	
2:	2 (12.5%)	8 (10.4%)	
Knaus‡			NS
A:	7 (43.7%)	22 (28.6%)	
B:	6 (37.5%)	35 (45.4%)	
C:	3 (18.7%)	19 (24.6%)	
D:	0 (0%)	1 (1.30%)	
LOD1§	6 (2; 10)	5 (2; 10)	NS
LOD4¶	6 (2; 13)	2 (0; 6)	P = 0.0005
ΔLOD	0 (-4; 4)	-2 (-7; 0)	P = 0.0046

Categorical variables are expressed as *n* (%), quantitative variables are expressed as median (10th, 90th percentile). *SAPS II = Simplified acute physiology score II; †Mc Cabe score; ‡Knaus score; §Logistic organ dysfunction score at day 1; and ¶day 4 ||LOD4-LOD1;

**Univariate analysis. NS = not significant (NS : *P* > 0.05).

to the ICU. However, they poorly predict the individual likelihood of death,⁶⁻⁸ they are not well suited for patients staying more than three days in the ICU,⁹ and they do not take into account the patient's response to treatment. It has been shown that the assessment of scores (APACHE, LOD, Sequential Organ Failure Assessment, Mortality Probability Model) on any day during the first week in the ICU provides a better prediction of the individual likelihood of death,¹⁰⁻¹⁴ but this method of evaluating the probability of death does not take into account the response to treatment. The evaluated indices which take into account the patient's response to treatment are based on the maximum value of a score during the first week in the ICU,^{15,16} or on the calculation of composite scores with weighting coefficients.¹⁷⁻¹⁹ The available objective methods to measure a patient's prognosis (taking into account the response to treatment) are therefore difficult to use in clinical practice, as they require relatively complex calculation. The indices which require determination of the maximal value of a score can only be used retrospectively, in general after one week, and

therefore are of little help for ethical discussion early on during the ICU stay.

The ΔLOD is an interesting prognostic factor in the ICU, as it is easy to calculate, it can be used after 72 hr in the ICU, allowing physicians to consider early TL, and it takes into account patient response to treatment. The ΔLOD is an easy way to objectively assess the patient's response to treatment, and therefore could be used by physicians to complement subjective evaluation of the clinical condition. When communicating to families and caregivers the rationale of TL, ΔLOD can serve as a numerical objective support to the overall ethical discussion, with a ΔLOD value ≤ 0 being associated with an overall good prognosis.

This study presents several limitations. First, the final study population was a selected subgroup of the initial population. Patients with TL before the 72nd hr, due to their survival probability being considered very low by the physician in charge, were excluded. Exclusion of these patients, who would have had high ΔLOD values and probably have died, does not influence the positive results of the study, but could have

contributed to the low PPV observed. Another limitation could have been that patients underwent implicit TL before the 72nd hr without notification in the study protocol. This was unlikely to happen as the study ICU has a standard procedure for making TL that has been in use for many years, and includes a staff discussion and the completion of a standard form. The patients who left the ICU between the 72nd and 96th hr were a possible source of bias, as they were susceptible to show very extreme Δ LOD values, particularly in case of death. This was not the case as the Δ LOD of these patients were close to the values in the overall sample: one patient died within this period (Δ LOD = 2) and ten were discharged (Δ LOD = -2.5 [-7; 0]). This study was performed in only one ICU and included a limited number of patients, therefore the results may not necessarily apply to other ICU settings.

The LOD, which is a score constructed objectively through logistic regression, has been chosen for this study because it quantifies organ dysfunction and is therefore well suited for sequential assessment during the ICU stay, in contrast to scores which include age or chronic health status. Furthermore, there is a growing body of evidence suggesting that acute organ failures are the major determinant of prognosis in the ICU, chronic health status being of less prognostic value.²⁰⁻²² However, TL decisions will always be made considering the whole patient, and particularly his/her health status prior to ICU admission. We chose to measure the evolution of the LOD in an additive model (Δ LOD = LOD4 - LOD1), as preliminary analysis showed that in our population LOD4 and LOD1 exhibited a linear relationship (data not shown).

Accordingly to the Bayes' theorem the PPV for a given issue is linked positively to the prevalence of this issue in the population. The prevalence of death in the study sample was low (17.7%) and explains partly the low PPV for death observed. This low mortality rate reduced the power of the study as compared to the sample size calculation.

In conclusion, a high Δ LOD is associated with death in the ICU. The Δ LOD can be used in daily clinical practice to assess objectively the patient's response to treatment. A negative Δ LOD or no change is associated with a low probability of death in the ICU, and therefore could constitute an argument against TL within a global ethical discussion. However Δ LOD should only be considered as one tool to help within the global clinical and ethical evaluation of critically ill patients.

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