Research

Sepsis-related organ failure assessment and withholding or withdrawing life support from critically ill patients

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Abstract

Background: We studied the incidence of withholding or withdrawing therapeutic measures in intensive care unit (ICU) patients, as well as the possible implications of sepsis-related organ failure assessment (SOFA) in the decision-making process and the ethical conflicts emerging from these measures.
Methods: The patients ($n = 372$) were placed in different groups: those surviving 1 year after ICU admission (S; $n = 301$), deaths at home (DH; $n = 2$), deaths in the hospital after ICU discharge (DIH; $n = 13$) and deaths in the ICU (DI; $n = 56$). The last group was divided into the following subgroups: two cardiovascular deaths (CVD), 20 brain deaths (BD), 25 deaths after withholding of life support (DWH) and nine deaths after withdrawal of life support (DWD).
Results: APACHE III, daily therapeutic intervention scoring system (TISS) and daily SOFA scores were good mortality predictors. The length of ICU stay in DIH (20 days) and in DWH (14 days) was significantly greater than in BD (5 days) or in S (7 days). The number of days with a maximum SOFA score was greater in DWD (5 days) than in S, BD or DWH (2 days).
Conclusions: Daily SOFA is a useful parameter when the decision to withhold or withdraw treatment has to be considered, especially if the established measures do not improve the clinical condition of the patient. Although making decisions based on the use of severity parameters may cause ethical problems, it may reduce the anxiety level. Additionally, it may help when considering the need for extraordinary measures or new investigative protocols for better management of resources.

Keywords: ICU, ethics, withhold, withdrawal, brain death, SOFA, APACHE III, TISS

Introduction

In 1990, Smedira *et al*[1] wrote that `life support is withheld or withdrawn from many patients especially those with critical illness, but the exact number is not known'. The terms `withholding of life support' and `withdrawal of life support' refer to the process according to which various medical interventions either are not given or are removed from patients with the expectation that they will die as a result.

The feeling that a patient admitted to the intensive care unit (ICU) should not be considered as a `terminal patient' [2] produces difficulties in rationalizing the use of new and costly technologies in a situation where resources are scarce, such as the modern healthcare systems [3]. This has led to the development of new systems for the assessment of severity for use in the ICU. These tools may be used to predict outcome, although their use has ethical and financial implications [4,5].

Over the last 15 years, several systems for the assessment of multiorgan failure have been developed [6–12], mainly because infections and multiorgan failure represent the main cause of mortality and morbidity among critically ill patients managed in the ICU [6]. This study was designed to combine severity scoring with information about the benefits and costs related to the use of the therapeutic intervention scoring system (TISS) [13–15].

The objectives of the study were:

1. To determine the incidence of withholding and withdrawing care in critically ill patients in a multidisciplinary adult Spanish ICU.

2. To evaluate whether decisions made about withholding or withdrawal of treatment and applying a pre-established protocol could be supported by the information obtained from the monitoring of indicators of severity, in other words sepsis-related organ failure assessment (SOFA) [6], TISS [16], and APACHE III [17].

3. To analyze the ethical conflicts emerging during the study period.

4. To decrease the level of anxiety among family members and the medical team responsible for the patient's care, at the time when the decision is taken to withhold or to withdraw therapeutic management [18].

Methods

Before the study was started, deaths among patients admitted to the ICU were defined in relation to the type of management before death [19].

Definitions

The patients were placed in groups according to the final outcome: those surviving 1 year after ICU admission (S); death at home after hospital discharge (DH); death in the hospital once discharged from the ICU (DIH); and death in the ICU (DI).

In the DI group, the cases were classified into the following subgroups according to the type of management decision taken at the time of death.

Cardiovascular death (CVD): those patients who died despite cardiopulmonary resuscitation (CPR) [20] for at least 30 min, according to hospital guidelines. This group represents a substantial investment in therapeutic resources at the time of death.

Brain death (BD): those patients where an irreversible loss of cerebral and brainstem function were found, following the guidelines of the Spanish Society of Neurology [21] and of Spanish law [22]. This group represents a large investment in diagnostic resources at the moment of death. Once BD was confirmed, mechanical ventilation was withdrawn or was continued until organ donation was authorized.

Death after withholding of life support (DWH; patients in whom it was decided to limit therapy): the most common therapies withheld are CPR in the event of cardiac arrest and dialysis. Less frequently withheld therapeutic measures are mechanical ventilation, laboratory analysis, surgical procedures, administration of antibiotics, parenteral nutrition, blood transfusions, fluid therapy, antiarrhythmic drugs or vasopressors. In our ICU, the withholding of any therapeutic measure besides CPR and dialysis is rare, because either these cases would not be considered to be candidates for admission into the ICU [19], or the withdrawal of therapeutic measures of life support would be considered.

Death after the withdrawal of therapeutic life-support measures (DWD; patients in whom a gradual withdrawal of therapeutic resources of life support was carried out, after the previous establishment of withholding measures): initially, nutrition, vasopressor agents and dialysis were withdrawn. Finally, oxygen support was withdrawn and, if necessary, the respiratory frequency and the tidal volume were reduced [24]. The patient was never disconnected from mechanical ventilation, nor was sedation stopped in any case.

Decision-making process

The medical team considered the withholding or withdrawing of treatment in each patient without having knowledge of the analyzed severity parameters.

The ICU doctor responsible for the patient's care, on their own initiative or after considering a proposal from the patient's family or the head of the department, proposed the need to establish therapeutic restrictions or to withdraw treatment. This opinion was discussed with the other doctors of the service and the nursing staff responsible for the patient. If the proposal was accepted, the relevant doctors from other departments who had sought the patient's admission to the ICU were asked for their opinion and, once a consensus was reached, this was conveyed to the family by the ICU doctor directly responsible for the patient.

If at any time the decision was not accepted, the required life-support measures were continued. The ICU doctor on call always respected the decisions reached. Only in rare circumstances did the on-call doctor, in agreement with the admitting doctor, decide, with the family, to withhold treatment before group discussion. The decisions were documented in the patient's notes.

Once the patient was discharged to a general ward, the ICU doctor informed the ward doctor about the decisions taken, such as not to return to ICU in case of deterioration in the patient's clinical condition or not to perform CPR.

Data collected

Resource utilization was evaluated by measuring the use of mechanical ventilation and the daily TISS in the ICU. The APACHE III on the first day and the daily SOFA were used as indicators of severity. A SOFA score was calculated for

each organ system and all scores equal to or greater than 1 were added together to give an indication of the severity of the case. SOFA was not used in this case as an indicator of the severity of sepsis.

APACHE III and SOFA were recorded on the first day and also recorded were the mean SOFA value during ICU stay, maximum SOFA score, number of days with the maximum SOFA score, sum of all the SOFA points of the ICU stay, TISS at the first day, mean TISS value during the stay in ICU and sum of all the TISS points of the ICU stay.

Inclusion criteria

All patients with ICU stay longer than 24 h were included, as were those whose stay was less than 24 h but who needed mechanical ventilation.

Statistics

We compared the groups using the Kruskal-Wallis test and the Mann-Whitney rank-sum test, with the Tukey-B test and the Scheffe test correction for between-groups analysis. The qualitative variables were analyzed with the Chi-square test. Differences were considered significant at $P < 0.05$. Groups with small samples (< 5) were excluded from the statistical analyses. All statistical analyses were performed on a personal computer with the SPSS®7.5 (SPSS Inc, Chicago, Illinois, USA).

Results

A total of 623 patients were admitted to the ICU during the study period from March to December 1995, with an overall mortality rate of 9% (58 cases). Two hundred and fifty-one patients did not fulfill the inclusion criteria and were excluded.

A total of 372 patients were included: 68% were male, mean age (± SD) was 59 ± 17 years (range 14–92), mean average stay in ICU was 8 ± 10 days (range 1–81) and the 1-year mortality rate was 19% (71 cases). Table 1 shows mortality according to the patient's origin and Table 2 shows the analyzed parameters in relation to the 1-year mortality rate.

The 1-year mortality rate increased in relation to the length of ICU stay. It varied from 12% (15 out of 121 patients) for stays less than 2 days, to 22% (56 out of 251) for stays longer than 2 days ($P = 0.02$), and from 13% (35 out of 267) for periods shorter than 1 week to 34% (36 out of 105) for stays longer than 1 week ($P = 0.001$).

The mortality rate was also closely related to the need for mechanical ventilation. Of 203 cases (55%) who required mechanical ventilation, 66 died (32%) compared with a 3% mortality rate in cases where mechanical ventilation was not needed (5 out of 169; $P = 0.001$).

Analysis of the maximum SOFA score showed that patients with two or less organ-system failures had a 1-year mortality rate of 2% (3 out of 180). If 3–5 organ systems were involved, the mortality rate rose to 26% (38 out of 148). If the respiratory, cardiovascular and neurological systems were involved simultaneously, the mortality rate rose to 35% (35 out of 101). In patients where six organ systems failed, the mortality rate was found to be 68% (30 out of 44). In this last group, all 16 patients reaching a maximum SOFA score greater than 16 died.

Table 3 reflects the results of the analyzed parameters in relation to the final outcome. For the statistical analysis, patients from the CVD group and from the DH group were excluded, owing to the small size of the group. Table 3 shows that, in patients who died, APACHE III (BD: 91 ± 31, range 34–129; DWH: 84 ± 3, range 31–153; DWD: 81 ± 25, range 41–113; DIH: 91 ± 31, range 44–137) and SOFA score on the first day (BD: 9 ± 3, range 2–16; DWH: 9 ± 4, range 1–17; DWD: 9 ± 4, range 1–16; DIH: 10 ± 4, range 3-16) were significantly higher than in the S group (APACHE III: 38 ± 24, range 2–117; SOFA score on the first day: 4 ± 4, range 0–14; $P < 0.0001$). The CVD group (APACHE III: 41 ± 19, range 27–54; SOFA score on the first day: 2 ± 3, range 0–4) had similar results to the S group.

The TISS score on the first day is significantly higher in the BD (34 ± 10, range 15–53), DWH (34 ± 11, range 16–57) and DIH groups (34 ± 5, range 25–41) than in the S group (22 ± 13, range 4–54; $P < 0.0001$). There were no significant differences between the S group and the DWD (24 ± 13, range 8–46) and CVD groups (15 ± 1, range 14–16).

The mean SOFA of the S group (3 ± 3, range 0–12) and the CVD group (4 ± 5, range 0–7) was significantly lower than in the other groups (BD: 11 ± 3, range 5–19; DWH: 12 ± 4, range 4–18; DWD: 11 ± 4, range 7–19; DIH: 8 ± 3, range 3–11; $P < 0.0001$).

Similarly the mean TISS of the S group (21 ± 11, range 4–47) and the CVD group (21 ± 14, range 11–31) was significantly lower than in the other groups (BD: 35 ± 9, range 22–60; DWH: 37 ± 11, range 15–59; DWD: 33 ± 7, range 19–44; DIH: 31 ± 5, range 25–41; $P < 0.0001$).

ICU stay (days) was significantly shorter in the S (7 ± 8, range 1-58), CVD (4 ± 3, range 2–6) and BD groups (5 ± 6, range 1–20), compared with the DWH (14 ± 16, range 1–81) and DIH groups (20 ± 14, range 5–44; $P < 0.0001$). There were no significant statistical differences between the S and DWD groups (12 ± 10, range 3–29).

The accumulated SOFA of the groups with a shorter ICU stay (S: 31 ± 58, range 0–496; CVD: 11 ± 15, range 0–

Table 1
Mortality and origin

	Cases [*n* (%)]	Mortality rate
Admitted after surgical procedures	141 (38%)	13%
Referred from other medical center	105 (28%)	20%
Admitted from emergency room	63 (17%)	22%
Admitted from the general wards	63 (17%)	27%

Table 2
Indicators of severity in the population studied

	Total		Survivors		Death		
Age	59 ± 17	(14–92)	58 ± 17	(15–92)	62 ± 18	(14–86)	NSD
ICU stay (days)	8 ± 10	(1–81)	7 ± 8	(1–58)	12 ± 14	(1–81)	$P < 0.001$
APACHE III	48 ± 31	(2–153)	38 ± 24	(2–117)	86 ± 29	(27–153)	$P < 0.001$
TISS on first day	24 ± 13	(4–57)	22 ± 13	(4–54)	32 ± 11	(8–57)	$P < 0.001$
Accumulated TISS	232 ± 355	(5–2647)	185 ± 303	(5–2100)	434 ± 474	(22–2647)	$P < 0.001$
SOFA on first day	5 ± 4	(0–17)	4 ± 4	(0–14)	9 ± 4	(0–17)	$P < 0.001$
Maximum SOFA	6 ± 5	(0–24)	4 ± 4	(0–16)	13 ± 4	(0–24)	$P < 0.001$
Accumulated SOFA	49 ± 85	(0–619)	31 ± 58	(0–496)	129 ± 127	(0–619)	$P < 0.001$

Data are shown as mean ± SD (range). ICU, intensive care unit; TISS, therapeutic intervention scoring system; SOFA, sepsis-related organ failure assessment; NSD, not significantly different.

21; BD: 65 ± 71, range 9–245) was significantly lower than in the groups with a longer stay (DWH: 161 ± 151, range 14–619; DWD: 139 ± 119, range 39–377; DIH: 168 ± 121, range 16–371; $P < 0.0001$).

The accumulated TISS of the groups with a shorter ICU stay (S: 185 ± 303, range 5–2100; CVD: 66 ± 5, range 62–69; BD: 207 ± 249, range 22–871) was significantly lower than in the DWH (516 ± 575, range 35–2647) and DIH groups (632 ± 437, range 123–1399; $P < 0.001$), but there were no statistically significant differences with the DWD group (396 ± 359, range 77–1036).

The maximum SOFA was significantly lower in the S (4 ± 4, range 0–16) and CVD groups (6 ± 8, range 0–12) compared with other groups (BD: 13 ± 4, range 8–24; DWH: 15 ± 4, range 4–22; DWD: 15 ± 4, range 9–23; DIH: 11 ± 4, range 3–16; $P < 0.0001$). There were also significant differences between the DWH and DIH groups ($P < 0.001$).

When the number of days with maximum SOFA was analyzed, significant differences were found between the DWD group (5 ± 9, range 1–29) and the S (2 ± 2, range 0–18), BD (2 ± 2, range 1–9) and DWH groups (2 ± 2, range 1–10; $P < 0.001$). No significant statistical differences were found with respect to the DIH group (3 ± 2, range 1–7).

Discussion

The aim of this study was to further the debate whether in the future, numerical data may be useful tools to help in the final decisions with respect to critical patients.

Leaving aside the `last bed' problem [25], this process normally implied a pre-admission interview with the patient and/or family, who accepted the use of the required procedures for the management of the critically ill patient.

The problems begin when the applied treatment does not improve the patient's clinical condition, and the severity of the illness and/or the use of sedation does not allow the patient's opinion to be obtained regarding life-sustaining treatment [26]. In this situation, communication with specialists and the family is of enormous importance [27], and it is vital to have a clear idea about the patient's clinical condition to obtain the necessary consent [1,28]. It should be noted that delegated consent was obtained in all cases.

Our study revealed that more than 65% of patients who died in the first year after admission to the ICU had treatment withheld or withdrawn. Unlike other studies [1,2,4,24], we differentiated between BD (28%) and DWD (13%), given that the medical care and ethical implications are very different in these two groups. The DWH group represented 35% of cases. While brain death caused only

Table 3
Indicators of severity according to the final outcome

Final outcome	S	DH	DIH	DWD	DWH	BD	CVD
Number of cases	301	2	13	9	25	20	2
ICU stay (days)*	7	24	20	12	14	5	4
APACHE III†	38	81	91	81	84	91	41
SOFA on first day†	4	12	10	9	9	9	2
Mean SOFA†	3	7	8	11	12	11	4
Maximum SOFA†	4	12	11	15	15	13	6
Days at max SOFA‡	2	4	3	5	2	2	1
Accumulated SOFA§	31	182	168	139	161	65	11
TISS on first day#	22	37	34	24	34	34	15
Mean TISS¶	21	38	31	33	37	35	21
Accumulated TISS**	185	914	632	396	516	207	66

S, survivors at 1 year; DH, death at home; DIH, death in the hospital once discharged from intensive care unit (ICU); DWD, death after the withdrawal of therapeutic life support measures; DWH, death after withholding of life support; BD, brain death; CVD, cardiovascular death. *The length of the ICU stay was significantly longer in the DWH and DIH groups than in the S and BD groups. †The APACHE III, sepsis-related organ failure assessment (SOFA) at the first day, mean SOFA and maximum SOFA scores were significantly smaller in the S group compared with the rest of the groups. ‡The number of days with a sustained maximum SOFA score was significantly higher in the DWD group than the S group and also greater than the BD and DWH groups, although this was not statistically significant. §The accumulated SOFA score was significantly greater in the DIH, DWH and DWD groups. #The therapeutic intervention scoring system (TISS) score at the first day was significantly higher in the DIH, DWH and BD groups. ¶The mean TISS score was significantly smaller in the S group. **The accumulated TISS score of the DIH and DWH groups showed statistically significant differences in relation to the S and BD groups.

occasional diagnostic difficulties, the greatest ethical conflicts among the medical team responsible for the patient were caused when deciding in which patients and at what moment should therapeutic restrictions or withdrawal of life-supporting measures be suggested and established. In our study, these ethical discussions arose in 48% of patients who died.

We confirmed that SOFA as a marker of the evolution of severity may be of great help when these problems arise. This indicator of severity, associated with TISS, allowed us to make a quantitative evaluation of the patient's clinical response to the investment of resources. APACHE III and SOFA provided valuable information which facilitated approaches to the withholding or withdrawal of treatment, whether in the ICU itself or once the patient has been discharged to the general ward. TISS allowed an evaluation to be made of the investment of resources.

At this point, it would be easy to generalize decision making according to these markers, as they seem to be good indicators of bad prognosis [28]. However, decisions should be individualized for each patient, as the concepts of quality of life and dignity in death, new technologies, greater demand for health or the maintenance of sustainable or equitable medicine greatly influence the decision-making process [26,29,30].

With a follow-up based on objective and quantifiable data, the doctor is better informed. This is fundamental when the changes in the role of the doctor in the decision-making process are considered. The principles of autonomy and self-determination, and the new concepts of quality of life, are leading to consensual medical treatment and to written consents [28].

However, SOFA alone does not provide sufficient complementary information about the possible need to withdraw treatment, in particular when referring to the withdrawal of life support. Beginning a treatment is easy, but stopping it is much more difficult. The only analyzed data which may be of interest in this sense are the number of days with a maximum SOFA score despite an elevated TISS score. This could be considered as a sign of diagnostic or treatment failure.

In this sense, although it may be very difficult to accept a `feeling of failure' [29], the data afforded by daily TISS and SOFA may be very useful. Our study suggested that a patient suffering from the failure of six organs together with a SOFA score above 16 inexorably evolved to death. These data were reinforced when the increase in the patient's SOFA score was accompanied by an equally significant increase in the TISS. The worsening of the clinical situation was maintained despite the additional therapeutic resources used.

Undoubtedly, the withdrawal of life support reduces both ICU stay and the investment of therapeutic resources (lower accumulated TISS), which has corresponding economic repercussions. However, this reduction was not statistically significant among the patients in the DWH and DIH groups.

Analysis of the data showed that patients in the DWD group were in fact subject to therapeutic restrictions from the moment of admission. This can be explained by the fact that, with similar levels of severity (APACHE III and SOFA score on the first day), the TISS score on the first day was lower than in the other groups of deaths. Despite this, the mean TISS was very similar. It was surprising to note that, during ICU stay, an increase of resources used was observed for the DWD group which, in the end, reached the mean for the other groups of deaths.

Another noteworthy finding was the length of time that elapsed from the beginning of therapeutic restrictions until the decision to withhold life support. It was shown that patients in whom life-support measures were withheld had previously passed an average of 5 days with constantly high SOFA levels. This may be seen as a worryingly long period when costs and the optimal use of scarce resources are considered. It should also not be forgotten that, during this period, the patient is dying. It is not easy to define the `best moment' to withdraw life-support measures without overextending an `agonizing state' that leads to discomfort for the patient or the family. The withdrawal of all life-support measures except for mechanical ventilation may mean that the patient is maintained in a terminal situation for some time. If this situation is maintained for a few minutes or even hours it may facilitate contact between the patient and the family during the last moments, but if prolonged for more than a night or for days, it generates significant anxiety among both the family and the team caring for the patient [29].

In the DIH group, both the average and maximum SOFA scores were lower when compared with the other groups of deaths. The longer stay and higher accumulated TISS in this group are justified by an improvement in the severity markers, which enables these patients to be discharged from the ICU. However in these cases, the decision to discharge is usually accompanied by a specific order not to readmit in case of a new downturn in the patient's condition.

All these aspects imply cultural and social factors that should be respected. With time, new social and cultural factors will appear which will modify our behavior in these situations. These cultural changes cannot be expected to be equal for different countries, religions, social spheres, etc.

Finally, we should not forget that the parameters analyzed can also be used to evaluate the protocols used in each unit, and to help us determine in which cases extraordinary actions or research protocols should be considered. They may also lead to a better use of our resources.

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