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End-of-life practices in 282 intensive care units: data from the SAPS 3 database

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Abstract *Objective:* To report incidence and characteristics of decisions to forgo life-sustaining therapies (DFLSTs) in the 282 ICUs who contributed to the SAPS3 database. *Methods:* We reviewed data on DFLSTs in 14,488 patients. Independent predictors of DFLSTs have been identified by stepwise logistic regression. *Results:* DFLSTs occurred in 1,239 (8.6%) patients [677 (54.6%) withholding and 562 (45.4%) withdrawal decisions]. Hospital mortality was 21% (3,050/14,488); 36.2% (1,105) deaths occurred after DFLSTs. Across the participating ICUs, hospital mortality in patients with DFLSTs ranged from 80.3 to 95.4% and time from admission to decisions ranged from 2 to 4 days. Independent predictors of decisions to forgo LSTs included 13 variables associated with increased incidence of DFLSTs and 7 variables associated with decrease incidence of DFLST. Among hospital and ICU-related variables, a higher number of nurses per bed was associated with increased incidence of DFLST, while availability of an emergency department in the same hospital, presence of a full time ICU-specialist and doctors presence during nights and week-ends were associated with a decreased incidence of DFLST. *Conclusion:* This large study identifies structural variables that are associated with substantial variations in the incidence and the characteristics of decisions to forgo life-sustaining therapies.

Keywords Intensive care · End-of-life · SAPS 3 · Treatment withholding · Treatment withdrawal

Introduction

The development of life-sustaining treatments over the last half century has resulted in some patients remaining dependent on life support until death [1]. In these patients, continued curative treatment is rarely the best option [2]. Prolonging non-beneficial treatments robs patients of their dignity and families of an opportunity to prepare for bereavement [3]. Intensivists have, therefore, limited the use of life-sustaining treatments in these situations. Presently, most deaths in the intensive care unit (ICU) occur after decisions to forgo life-sustaining treatment (DFLSTs) [4–6], and the incidence of decisions to forgo LSTs may be increasing [7]. Making DFLST, which may consist in withholding and/or withdrawing life support, marks a shift from curative care to comfort care. Patients with DFLSTs are closely monitored and given palliative care as needed to ensure optimal comfort.

DFLSTs must be ethically appropriate. Perceptions of what is ethical, however, may vary. Substantial variability in the decision making process has been documented in previous research. These variations concern the incidence of decisions to forgo LSTs, the characteristics of patients who receive these and the procedure that is followed for making decisions to forgo LSTs [4, 5, 8–12]. Variations were also identified in responses to ethical scenarios [6, 13]. There is widespread agreement that there is no ethical difference between withholding and withdrawal [6], although withdrawal has been described as more difficult for intensivists, and is not used in some countries [10]. A single large ICU study recorded practices in 37 ICUs from 17 European countries [10]. The results show considerable variability in decisions to forgo LSTs in Europe. However, no large study across widely disparate geographic areas has been reported to date. The objectives of this study were to collect data on decisions to forgo LSTs in 14,488 patients admitted to 282 ICUs in seven different regions, and to identify factors associated with decisions to forgo LSTs in ICUs.

Patients and methods

We used the prospective international cohort created for the SAPS 3 study [14, 15]. The organization of the project, data collection, and study cohort have been described in detail elsewhere [14, 15]. This is a pre-planed analysis of the SAPS 3 study. Participating countries can be seen from Table E10 of the ESM of the SAPS 3 cohort description [14, 15]. Definitions of major therapeutic limitation during ICU stay were collected at ICU discharge. The questions asked to researchers evaluates if major therapeutic limitations were used during the ICU stay. Only those limitations expected to have had a relevant impact on patient's morbidity and/or mortality were registered. Date where withholding or withdrawing therapy was first used was registered.

Database

The SAPS 3 hospital outcome cohort comprises 16,784 patients from 303 ICUs. We excluded the 2,296 patients for whom no data were available regarding decisions to forgo LSTs. This left 14,488 (86.3%) patients for the study. Among them, 1,239 (8.6%) received decisions to forgo LSTs.

Data quality

The database was evaluated for completeness and reliability. Independent raters rescored the data, and kappa coefficients and intra-class correlation coefficients were computed, as appropriate [16]. Data quality proved excellent, as shown by the detailed results reported in the ESM file of the SAPS 3 primary report [14, 15].

Statistical analysis

Statistical analysis was performed using the SAS system, version 9.1 (SAS Institute Inc., Cary, NC). All *P* values smaller than 0.05 were considered significant. Unless otherwise specified, results are expressed as median and quartiles. The chi-square test was used for categorical data. For continuous variables, ANOVA was used. Univariate logistic regression analyses were performed to identify patient- and ICU-related factors that might predict decisions to forgo LSTs. Factors that were significant in the univariate analyses were entered into a multivariate stepwise logistic regression analysis. These have been added in the footnote of Table 3. If regions were introduced into the model, significant differences could have been found. However, since participating countries were not representative samples in each country, we did not introduced this variable in the model.

Results

Figure 1 shows the patient flow chart of 14,488 patients admitted to 282 ICUs in seven geographic areas. ICU organizational and managerial characteristics were available for 271 ICUs (Table 1). Overall the median (quartile) number of admissions per year was 441.5 (267–723) patients per ICU.

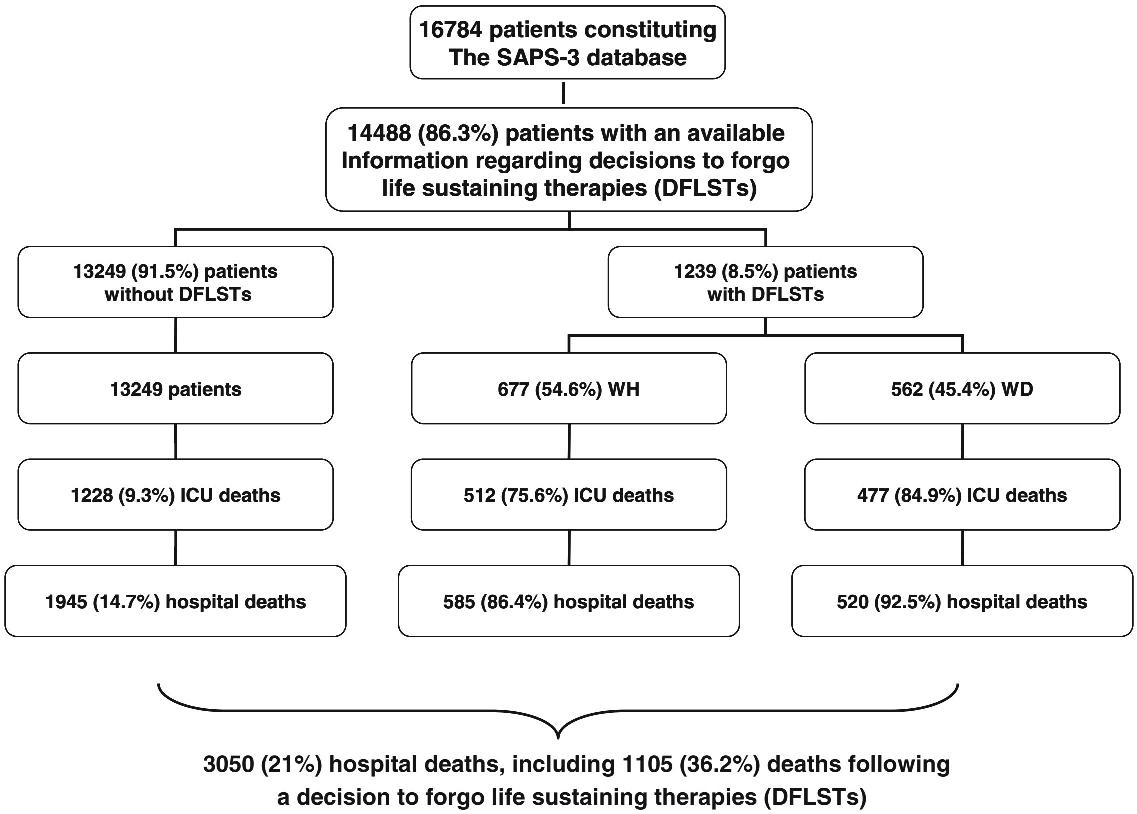

Fig. 1 Patient flow chart showing incidence and outcome of decisions to forgo life-sustaining therapies in patients included in the SAPS3 database

Table 1 ICU characteristics

	ICUs		Patients		Univariate logistic regression analysis of explanatory variables		
	n	%	*n*	%	OR	95% CI	*P* value
Patient's geographic location							
South Europe and Mediterranean countries	139	51.3	5,533	38.2	0.88	0.78–0.99	0.04
Central and Western Europe	51	18.83	3,982	27.5			
Central and South America	30	11.1	1,678	11.6	0.78	0.64–0.954	0.01
Australasia	14	5.2	1,546	10.7	1.21	1.01–1.444	0.03
East Europe	26	9.6	767	5.3			
North America	5	1.8	662	4.7			
North Europe	6	2.2	320	2.2	3.48	2.67–4.54	<0.001
ICU characteristics (data are available for 271 ICUs)							
University hospitals	128	47.2			1.03	0.91–1.16	0.62
Availability of an emergency department in the same hospital	243	89.7			0.68	0.56–0.84	<0.001
Multidisciplinary meetings	125	46.1			1.06	0.94–1.20	0.30
Clinical rounds performed by nurses and doctors together	166	61.2			1.15	1.01–1.32	0.02
Availability of doctors in the ICU during weekdays	216	79.7			1.03	0.91–1.18	0.62
Availability of doctors in the ICU during nights and weekends	209	77.1			0.80	0.71–0.92	0.001
Number of staffed ICU beds (median, Q1–Q3)	9 (7–12)				0.98	0.97–0.98	<0.001
Number of physicians per bed (median, Q1–Q3)	0.8 (0.5–1.2)				1.09	0.98–1.22	0.09
Patient to nurse ratio (median, Q1–Q3)	3.0 (2.3–3.9)				1.03	1.02–1.05	<0.001
Full time specialist (median, Q1–Q3)	4 (4–7)				0.97	0.96–0.98	<0.001

As shown in Fig. 1, decisions to forgo LSTs were implemented in 1,239 (8.6%) patients, including 677 (54.6%) patients who received withholding decisions and 562 (45.4%) who received withdrawal decisions. Hospital mortality was 21% (3,050/14,488). Among the deaths, 1,105 (36.2%) occurred after decisions to forgo LSTs. Hospital mortality was 86.4% in patients with withholding decisions and 92.5% in patients with withdrawal decisions.

Table 1 shows that decisions to forgo LSTs were more common in hospitals without emergency departments, in smaller ICUs, and in ICUs with lower nurse-to-patient ratios and larger numbers of physicians per ICU bed. DFLSTs were also more common when intensivists were present only during weekdays (compared to ICUs where intensivists were present during weekdays and weekends), when multidisciplinary meetings were held, and when nurses and intensivists performed clinical rounds together. Conversely, DFLSTs were less common in ICUs that had at least one full time intensivist and in those with intensivists available at night and over weekends.

Among patients who died, the proportion with DFLSTs ranged from 26 to 63.5% according to the region where the patient was admitted. Moreover, the proportion of hospital survivors with withdrawal decisions ranged from 2.4 to 30.3% and the proportion with withholding decisions ranged from 4 to 40% according to the region. Table E1 and figure E1 describes significant differences across the participating regions. As shown in Table 2, overall patients with DFLSTs were older, and a larger proportion of them exhibited severe co-morbid conditions and immunosuppression. Admission from a ward and life-sustaining treatment before ICU admission were more common among patients with than without decisions to forgo LSTs. SAPS 3 and SOFA scores at ICU admission were 45 (36–57) and 3 (2–5) in patients without decisions to forgo LSTs compared to 67 (58–77) and 6 (4–9) in patients with decisions to forgo LSTs ($P < 0.0001$ for both scores), respectively.

Table 3 reports independent predictors of DFLST implementation identified by stepwise logistic regression. The following variables were associated with increased incidence of DFLST: higher age, hospital location before ICU admission, unplanned ICU admission, documented infection at admission, non-surgical status or emergency surgery, higher SOFA score at ICU admission, comorbidities such as NYHA-IV chronic heart failure, hematological malignancies and solid tumors; ICU admission for shock, ICU admission for neurological cause such as cerebrovascular accident, intracranial tumor or post-anoxic coma; pancreatitis and other digestive causes (excluding cholecistitis). The need for vasoactive agents and longer length of ICU stay were determinants of DFLST. Among ICU-related variables, a higher number of nurses per patient was associated with increased incidence of DFLST [odds ratio of 1.03 (1.005–1.058)/nurse per bed].

Seven variables were independently associated with a decreased incidence of DLST, namely, ICU admission for diabetic complication, rhythm disturbances, acute lung injury, or cholecistitis. Among ICU and hospital-related variables, availability of an emergency department in the same hospital, presence of a full time ICU-specialist and doctors presence during nights and week-ends were also associated with a decreased incidence of DFLST.

Discussion

Decisions to forgo LSTs in adult ICU patients have been a focus of increasing research over the last two decades. Descriptive studies were performed at local, national, [4, 5, 8–10] and multinational levels [5, 8, 10]. Using the SAPS 3 database of 14,488 patients in 282 ICUs, we found that in addition to previously identified predictors (case-mix, severity, co-morbidities and nature of the acute medical disease), organizational variables were independently associated with the incidence of DFLSTs. Namely, the number of nurses, availability of an ED in the same hospital, the presence of full time intensivist including doctors who make the rounds during the week-end days were independently associated with incidence of DFLSTS.

We decided not to study the impact of geographic area on the incidence of DFLSTs. Indeed, center participation to the SAPS 3 database included criteria to minimize heterogeneity in terms of outcome in homogeneous groups of patients.

A major strength of this study is the large sample of patients. In addition, we collected information on ICU characteristics. Very little is known about the potential impact of ICU characteristics and critical-care organization on end-of-life practices. The status of the institution, e.g., private versus public and teaching versus non-teaching, has been reported to affect end-of-life practices [17–19]. As expected, DFLSTs were made in the sickest ICU patients [4, 5, 8–10]. However, the impact of organizational factors on the incidence of DFLSTs suggests that these substantially influence the end-of-life decision-making procedure. Indeed, these results suggest that in ED-patients who were admitted from another hospital, DFLSTs were more likely to occur. Along this line, presence of a full time ICU-specialist and availability of doctors making rounds during weekend days is associated with decrease in incidence of DFLST. These findings must be integrated in a strategy to better understand factors that influence end-of-life care.

This finding of significant impact of organizational factors on DFLSTs invite qualitative studies into factors that determine the incidence, pattern, and outcomes of

Table 2 Patient characteristics

	No DFLST (*n* = 13,249)		DFLST (*n* = 1,239)		*P* value
	n	%	*n*	%	
Patient's age (median, quartiles)	63 (48–73)		70 (58–78)		<0.0001
Comorbidities					
Chronic pulmonary failure	509	3.8	79	6.4	<0.0001
COPD	1,652	12.5	184	14.9	0.01
Class IV NYHA chronic heart failure	137	1	28	2.3	0.0001
Cirrhosis	379	2.9	65	5.2	<0.0001
Chronic renal failure	730	5.5	113	9.1	<0.0001
Hematological cancer	174	1.3	59	4.8	<0.0001
Cancer	370	2.8	61	4.9	<0.0001
Cancer therapy (chemotherapy, immunosupression radiotherapy, steroids)					<0.0001
Intra-hospital location before ICU admission					
Operative room	5,561	42	188	15.2	<0.0001
Emergency room	3,613	27.3	360	29.1	0.17
Ward	2,178	16.4	413	33.3	<0.0001
Intermediate care unit/high dependency unit	326	2.5	78	6.3	<0.0001
Other	311	2.3	32	2.6	0.60
Other ICU	449	3.4	66	5.3	0.0004
Surgical status					
No surgical procedure, miss	6,080	45.8	845	68.2	<0.0001
Scheduled surgery	4,986	37.6	130	10.5	<0.0001
Emergency surgery	2,183	16.5	264	21.3	<0.0001
Patient's case-mix					
Scheduled surgery	4,986	37.6	130	10.5	<0.0001
Emergency surgery	2,183	16.5	264	21.3	<0.0001
Unplanned ICU admission	8,126	61.3	1,067	86.1	<0.0001
Use of major therapeutic options before ICU admission					
CPR	536	4	181	14.6	<0.0001
Mechanical ventilation	5,872	44.3	631	50.9	<0.0001
Vasoactive drugs	2,239	16.9	395	31.9	<0.0001
Acute infection at ICU admission					<0.0001
No infection	10,623	80.2	725	58.5	<0.0001
Clinically improbable/colonization	197	1.5	22	1.8	0.42
Clinically probable/documented	1,673	12.6	331	26.7	<0.0001
Microbiologically documented	747	5.6	161	13	<0.0001
Missing	9	0.1	0		0.35
Reasons for ICU admission					
Basic monitoring	4,553	34.4	149	12	<0.0001
Neurological					
Coma	610	4.6	97	7.8	0.01
Focal neurological deficit	245	1.8	35	2.8	<0.0001
Intracranial mass effect	266	2.0	53	4.3	<0.0001
Hepatic					
Liver failure	146	1.1	48	3.9	<0.0001
Renal					
Acute renal failure	527	4	163	13.1	<0.0001
Respiratory					
Acute lung injury and ARDS	679	5	179	14.4	<0.0001
Acute respiratory failure in COPD patients	874	6.6	139	11.2	<0.0001
Acute respiratory failure (not ALI or ARDS)	1,222	9.2	152	12.3	0.0005
Cardiovascular					
Septic shock	389	2.9	145	11.7	<0.0001
Non septic shock	188	1.4	42	3.4	<0.0001
Chest pain with ECG changes	811	6.1	25	2	<0.0001
Hypovolemic or hemorragic shock	454	3.4	64	5.2	0.0016
Anaphylactic, mixed and undefined shock	234	1.8	70	5.7	<0.0001
Digestive					
Severe pancreatitis	86	0.6	21	1.7	<0.0001
Hematological					
Severe hemolysis	8	0.1	6	0.5	<0.0001

Table 2 continued

	No DFLST		DFLST		*P* value
	(*n* = 13,249)		(*n* = 1,239)		
	n	%	*n*	%	
Metabolic					
Hypo and hyperthermia, Hypo and hyperglycemia (includes diabetic comas), Other	262	2	17	1.4	0.1381
Other					
Severe trauma patient	654	4.9	40	3.2	0.0071
Acute medical disease					
Cardiovascular					
Myocardial infarction	825	6.2	98	7.9	0.02
Rhythm disturbances	608	4.6	47	3.8	0.19
Digestive					
Esophageal or gastric varices rupture	71	0.5	13	1	0.02
Cholecystitis	71	0.5	4	0.3	0.31
Other (includes esophageal, gastric varices, Other)	741	5.6	102	8.2	0.0001
Trauma					
Isolated brain trauma	209	1.6	36	2.9	0.0005
Neurological					
Cerebrovascular accident	694	5.2	169	13.6	<0.0001
Post-anoxic coma	55	0.4	41	3.3	<0.0001
Intracranial tumor	380	2.9	19	1.5	0.006
Other	465	3.5	23	1.9	0.002
ICU mortality	1,228	9.3	989	79.8	<0.0001
Hospital mortality	1,945	14.7	1105	89.2	<0.0001
Length of ICU stay (median, quartiles)	2 (1–5)		5 (2–13)		<0.0001
SOFA score (median, Q1–Q3)	3 (2–5)		6 (4–9)		<0.0001
SAPS 3 score (median, Q1–Q3)	45 (36–57)		67 (58–77)		<0.0001
Destination at ICU Discharge					
Unplanned discharge	1,293	9.7	54	4.4	<0.0001
Home	303	2.3	21	1.7	0.17
Other hospital	729	5.5	20	1.6	<0.0001
Same hospital (ward)	9,057	68.3	178	14.4	<0.0001
Same hospital (high dependency unit or other ICU)	2,070	15.6	24	1.9	<0.0001

DFLSTs. Studies have shown variations in decisions to forgo LSTs with personal physician characteristics, experience [20], gender [21], specialty [19] or time working in ICUs [22]. Religious beliefs and cultural background play a role [6, 10, 21, 23]. The current study suggests that, in addition, ICU resources, case-mix, co-morbidities, patterns of ICU may also influence decisions to forgo LSTs. Along this line, the fact that the presence of full time intensivist was associated with lower risk of decisions to forgo LST may be ascribed to a less opened ICU admission policy when each single admission is discussed with the senior intensivist rather than commanded by the primary physician.

Our study has several limitations. First, the database used for the study was not designed for an investigation of decisions to forgo LSTs. Nevertheless, a sub-study on decisions to forgo LSTs was planned early in the designing of the SAPS 3 study, so that investigators were aware of the need to collect accurate data on treatment withholding and with withdrawal decisions. Second, we did study whether the country or the region were potential determinants of DFLSTs. Beyond the lack of representative sample of each country or region, we also may hypothesize that the variability across geographic areas demonstrated in our study may mask variability within each country and within each ICU, as previously reported [13]. Last, information on DFLSTs was missing for about 15% of the patients in the database. The patients did not differ from the rest of the cohort in terms of severity or mortality, suggesting that missing data did not indicate absence of decisions to forgo LSTs but instead reflected failure to record information on decisions to forgo LSTs.

In summary, this multicenter international study documents variables that influence significantly the procedure of end-of-life decisions. The finding that organizational factors may have significant impact on incidence of DFLST raises crucial questions about the determinants of DFLSTs and the definition of optimal DFLST practice.

Table 3 Results of multivariate stepwise logistic regression on decision to forgo life-sustaining therapies

Variables	Odds ratio	95% CI	*P*
Patients age (years)	1.030	1.024–1.035	<0.0001
Intrahospital location before ICU admission			
Emergency room	1.674	1.234–2.270	0.0009
Other ICU	2.457	1.881–3.208	<0.0001
Unplanned ICU admission	1.653	1.245–2.195	0.0005
Documented infection at admission	1.337	1.104–1.618	0.0030
Surgical status			
No	1.858	1.375–2.511	<0.0001
Emergency surgery	1.708	1.258–2.318	0.0006
Length of stay in the ICU	1.016	1.010–1.021	<0.0001
Mechanical ventilation at ICU admission	1.391	1.148–1.685	0.0008
SOFA Score at ICU admission	1.160	1.131–1.190	<0.0001
Co-morbidities			
Chronic heart failure (NYHA IV)	2.054	1.242–3.397	0.0050
Hematological malignancy	2.053	1.327–3.175	0.0012
Cancer	3.203	2.216–4.629	<0.0001
Reason(s) for ICU admission			
Cardiovascular			
Hypovolemic or hemorrhagic shock	1.508	1.054–2.157	0.0245
Septic shock	1.949	1.458–2.605	<0.0001
Anaphylactic or mixed and undefined shocks	2.198	1.533–3.153	<0.0001
Severe pancreatitis	2.595	1.389–4.850	0.0028
Diabetic complications	0.480	0.243–0.946	0.0339
Acute lung injury	0.734	0.571–0.944	0.0158
Use of major therapeutic option before ICU admission			
Vasoactive drugs	1.327	1.095–1.609	0.0040
Acute medical disease			
Neurologic			
Cerebrovascular accident	3.007	2.313–3.910	<0.0001
Intracranial tumor	2.349	1.213–4.548	0.0113
Post-anoxic coma	2.757	1.568–4.848	0.0004
Cardiovascular			
Rhythm disturbances	0.630	0.425–0.932	0.0209
Digestive			
Cholecistitis	0.232	0.064–0.848	0.0272
Other (includes esophageal, gastric varices, other)	1.480	1.103–1.987	0.0091
Isolated brain trauma	2.100	1.272–3.468	0.0037
Other	0.515	0.295–0.902	0.0202
ICU-related variables			
Full time specialist	0.967	0.947–0.988	0.0025
Nurse per bed	1.031	1.005–1.058	0.0173
Emergency department available in the same hospital	0.658	0.499–0.869	0.0031
Doctors presence during nights and weekends	0.725	0.596–0.881	0.0012

The following variables were entered in the multivariate stepwise logistic regression: ICU-related variables (staffed beds, full time specialists, number of nurse per bed, availability of an emergency department in hospital, daily clinical rounds and presence of doctors during night and weekends), patient's age, location before ICU admission, intrahospital location before ICU admission, unplanned ICU admission, documented infection at ICU admission, surgical status, length of ICU stay, mechanical ventilation on admission day, area, SOFA score on admission day, comorbidities, reasons for admission, use of mechanical ventilation, vasopressors or CPR before ICU admission and acute medical disease

In the future, guidelines may help spread excellence in end-of-life care. However, certain types of cultural variations are permissible and should not be perceived as incorrect practices. In addition, organizational factors should be recognized as factors potentially influencing ICU end-of-life care.

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