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End of life decisions in immunocompromised patients with acute respiratory failure

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A B S T R A C T

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Pneumocystis

Purpose: To identify patient, disease and organizational factors associated with decisions to forgo life-sustaining therapies (DFLSTs) in critically ill immunocompromised patients admitted to the intensive care unit (ICU) for acute respiratory failure.

Material and methods: We performed a secondary analysis of the international EFRAIM prospective study, which enrolled 1611 immunocompromised patients with acute respiratory failure admitted to 68 ICUs in 16 countries between October 2015 and June 2016. Multivariate logistic analysis was performed to identify independent predictors of DFLSTs.

Results: The main causes of immunosuppression were hematological malignancies (50%) and solid tumor (38%). Patients had a median age of 63 yo (54–71). A pulmonologist was involved in the patient management in 38% of cases. DFLSTs had been implemented in 28% of the patients. The following variables were independently associated with DFLSTs: 1) patient-related: older age (OR 1.02 per one year increase, 95% confidence interval (CI) 1.01–1.03, $P < 0.001$), poor performance status (OR 2.79, 95% CI 1.98–3.93, $P < 0.001$); 2) disease-related: shock (OR 2.00, 95% CI 1.45–2.75, $P < 0.001$), liver failure (OR 1.59, 95% CI 1.14–2.21, $P = 0.006$), invasive mechanical ventilation (OR 1.79, 95% CI 1.31–2.46, $P < 0.001$); 3) organizational: having a pulmonologist involved in patient management (OR 1.85, 95% CI 1.36–2.52, $P < 0.001$), and the presence of a critical care outreach services (OR 1.63, 95% CI 1.11–2.38, $P = 0.012$).

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Conclusions: A DFLST is made in one in four immunocompromised patient admitted to the ICU for acute respiratory failure. Involving a pulmonologist in patient's management is associated with less non beneficial care.

1. Introduction

Over the last decades, advances in medical diagnoses and treatments have generated the possibility to improve survival in the face of critical illness. The consequence of this intensive medicalization has been the extensive Intensive Care Unit (ICU) utilization, especially around the end of life [1]. Nonetheless, as well as extending life, the use of ICU may also simply prolong the dying process and increase patient suffering, without altering the final outcome. In the majority of cases in the Western world, death most commonly results from limitation of life-sustaining treatment, a practice that is becoming more frequent in recent years [2-4]. Intensivists are faced with decisions to forgo life-sustaining therapies (DFLSTs), which are influenced by many factors, including the patient's prognosis, individuals' values and treatment preferences, cultural, philosophical, and religious beliefs [5,6].

Patients with immunosuppression associated with solid tumor or hematological malignancies, have poorer prognosis than immunocompetent patients with similar diagnoses [7]. Acute hypoxemic respiratory failure is the leading cause of ICU admission in immunocompromised patients and one of the most challenging conditions to manage, with mortality reaching up to 60% [7]. Nonetheless, outcomes in critically ill cancer patients have improved over the last decades, namely due to technological innovations and advances in understanding the pathophysiology of critical illness on one side, and implementation of precision medicine in cancer treatment and better management of side effects on the other [8,9]. In this context, life supporting therapy in ICU is increasingly offered to immunocompromised patients, as denying invasive interventions to this population can no longer be universally justified. Nonetheless, a high proportion of them will still die in ICU, with a significant number receiving aggressive treatment near the end of life [9-12].

When all interventions fail to reverse the critical illness, ICU clinicians are confronted with DFLSTs that can be ethically challenging. Accurate prognostication around end of life would ensure appropriate treatment decisions and facilitate palliative care provision and transition to terminal care [13]. Several prognostic factors have been identified as associated with increased risk of mortality but these were mainly 'bedside' factors after ICU admission [13]. Less is known about the potential impact of disease characteristics and organization on end-of-life practices in specific populations like immunocompromised patients [14-17].

The aim of this study was to describe the patient population receiving DFLSTs in a cohort of immunocompromised patients and to identify patient- and disease-related, as well as organizational factors associated with these decisions.

2. Patients and methods

2.1. Study design and participants

The full study methodology has been described elsewhere [18]. In brief, this was a preplanned ancillary analysis of the EFRAIM study that enrolled 1611 patients in 62 ICUs from 16 countries, between October 2015 and June 2016, with a 3-month follow up period [18]. The EFRAIM study was a multicenter, international, observational study on outcomes associated with acute respiratory failure in non-acquired immunodeficiency syndrome (AIDS) immunocompromised patients.

Inclusion criteria were adult patients with non-AIDS known immunosuppression (immunosuppressive drugs for >3 months or >0.5 mg. kg⁻¹ daily dose of corticosteroid, solid tumor, solid organ transplant, hematologic malignancies, hematologic stem cell transplantation) and acute hypoxemic respiratory failure (respiratory rate >30 breaths per minute, labored breathing, SpO₂ <90% or PaO₂ <60 mmHg on room air or need for >4 L/min oxygen, or need for mechanical ventilation). Patients were excluded if they were admitted to ICU after cardiac arrest, admitted only to secure bronchoscopy, had elective surgery within 6 days, or had respiratory failure occurring <7 days after organ transplantation. Physician participation was voluntary, without financial incentive. Participating providers obtained institutional review board (IRB) approval from their institutions, in accordance with local ethics regulations.

All management decisions were independently performed by the attending physicians according to standard practice in each ICU [18]. All diagnoses were reviewed by two study investigators for coherence and for alignment with established definitions [18]. Management of associated organ dysfunction and handling of immunosuppressive drugs or chemotherapy were done as per local preferences [18].

2.2. Data collection

Patient-related, disease-related and organizational factors were collected. There were previously described [18] and are presented in Tables 1, 2 and 3.

2.3. Outcomes

The main outcome was DFLSTs. Patients were classified depending on the presence of DFLSTs during ICU stay, which were left at the discretion of the physician. DFLSTs included patients with a do-not-resuscitate, do-not-intubate or no-escalation status, as well as any patient with withdrawing or withholding life-sustaining treatment decisions [4].

The secondary outcomes were ICU mortality and hospital mortality.

2.4. Statistical analysis

Continuous variables were described as medians [inter-quartile ranges (IQRs)] and categorical variables as proportions. Comparisons of proportions between groups were made using the χ^2 test. Comparisons of continuous variables between groups were made using the Wilcoxon rank-sum test. All variables associated with DFLSTs at a 20% threshold by logistic regression in univariate analysis were included in the multivariate logistic regression, and a *P* value-based backward selection was performed [19]. Only significant variables were kept in the final model. Odds ratio (OR) with corresponding 95% confidence intervals (CI) were computed. Interactions between variables and a center effect were tested [19]. Missing data were described in the tables and no imputation was made [20]. As it was a secondary analysis of the EFRAIM study [18], no sample size calculation was performed.

All reported *P* values are 2-sided; *P* < 0.05 was considered statistically significant. All analyses were performed using statistical software (SAS, version 9.4; SAS Institute; Cary, NC and R version 3.3.3).

Table 1
Decisions to forgo life-sustaining therapies according to patients baseline characteristics.

	Absence of DFLSTs n = 1115	DFLSTs n = 433	P value
Age (years)	63 (53–71)	66 (57–74)	<0.001
Female gender	477 (41%)	169 (39%)	0.45
Comorbid conditions			
Cardiac	238 (22%)	101 (25%)	0.20
Chronic Obstructive Pulmonary Disease	183 (16%)	64 (15%)	0.61
Diabetes	217 (19%)	87 (20%)	0.68
Chronic kidney injury	167 (15%)	64 (15%)	0.95
Renal replacement therapy	31 (3%)	11 (3%)	0.83
Cirrhosis	43 (4%)	15 (4%)	0.79
Performance status (ECOG)			<0.001
Grade 0	259 (28%)	52 (14%)	
Grade 1	317 (34%)	105 (28%)	
Grade 2	214 (23%)	98 (26%)	
Grade 3	133 (14%)	123 (33%)	
Location before ICU admission			0.47
Emergency Department	268 (25%)	95/459 (21%)	
Hospital Ward	607 (56%)	281/459 (61%)	
Other ICUs	69 (6%)	34/459 (7%)	
Other hospital	111 (10%)	41/459 (9%)	
Hospice	7 (0.6%)	2/459 (0.4%)	
Other	24 (2%)	6/459 (1%)	
Underlying condition			0.85
Hematological malignancy			
Acute myeloid leukemia	152 (13%)	57 (13%)	
Acute lymphoid leukemia	39 (3%)	12 (3%)	
Non Hodgkin lymphoma	128 (11%)	53 (12%)	
Myeloma	108 (9%)	43 (10%)	
Hodgkin disease	23 (2%)	13 (3%)	
Chronic lymphocytic leukemia	38 (3%)	13 (3%)	
Chronic myeloid leukemia	21 (2%)	8 (2%)	
Other	89 (8%)	40 (9%)	
Solid tumor	407 (35%)	160 (36%)	0.52
Systemic diseases	212 (18%)	66 (15%)	0.15
Solid organ transplant	116 (11%)	26 (7%)	0.008
Disease status			<0.001
New diagnosis	238 (29%)	96 (30%)	
First line	144 (18%)	41 (13%)	
> First line	178 (22%)	88 (28%)	
Remission	140 (17%)	32 (10%)	
Uncontrolled	97 (12%)	42 (13%)	
Palliative	16 (2%)	17 (5%)	
Hematopoietic stem cell transplantation			0.73
No hematopoietic stem cell transplantation	988 (84%)	368 (84%)	
Autologous	77 (7%)	26 (6%)	
Allogeneic	107 (9%)	45 (10%)	

Variables are presented as n (%), or median (25–75%) percentiles. % were calculated according to the data recorded for each variable. Abbreviations: DFLSTs, Decisions to Forgo Life-Sustaining Therapies; ICU, Intensive Care Unit; ECOG, Eastern Cooperative Oncology Group.

3. Results

3.1. Patient characteristics and prevalence of DFLSTs

Among the 1611 patients included in the EFRAIM study, data about treatment escalation planning at admission and DFLSTs during ICU stay were available in 1548 patients (Fig. 1). Full code admission was documented for 1292 (83%) patients, 142 (9%) patients had an ICU trial, 58 (4%) patients had do-not-intubate decisions, whereas 56 (4%) patients had do-not-resuscitate decisions. Among each treatment escalation planning category, percentages of DFLSTs are described with respective ICU and hospital mortality (Fig. 1). Overall, 433/1548 (28%) patients had DFLSTs.

Table 2
Decisions to forgo life-sustaining therapies according to ICU disease characteristics.

	Absence of DFLSTs n = 1115	DFLSTs n = 433	P value
SOFA at admission	6 (4–9)	9 (5–12)	<0.001
Organ dysfunction and treatment in ICUs within Day 7			
Vasopressors	476/897 (53%)	341/485 (70%)	<0.001
Septic Shock	343/897 (38%)	260/485 (54%)	<0.001
Renal Replacement Therapy	194 (17%)	102 (23%)	0.002
Chemotherapy	146 (12%)	44 (10%)	0.18
Immunosuppressive drugs	342 (29%)	121 (28%)	0.52
Liver failure	225 (19%)	130 (31%)	<0.001
Reduced level of consciousness	256 (22%)	158 (36%)	<0.001
Use of non-invasive ventilation	349 (30%)	133 (30%)	0.83
Use of high-flow nasal cannula oxygen	370 (32%)	141 (32%)	0.83
Invasive mechanical ventilation	523 (45%)	276 (63%)	<0.001
Use of neuromuscular blocking agents	131 (11%)	98 (22%)	<0.001
Use of prone Position	44 (4%)	36 (8%)	<0.001
Use of nitric oxide	195 (18%)	67 (16%)	0.50
Extracorporeal membrane oxygenation	13 (1%)	3 (1%)	0.58
Acute respiratory failure etiology			
Bacterial infection	302 (27%)	118 (27%)	0.95
Viral infection	170 (15%)	79 (18%)	0.08
Pneumocystis pneumonia	45 (4%)	26 (6%)	0.07
Invasive pulmonary aspergillosis	45 (4%)	20 (5%)	0.52
Invasive fungal infection	159 (14%)	78 (18%)	0.03
Disease-related infiltrates	100 (9%)	48 (11%)	0.14
Cardiogenic pulmonary edema	83 (7%)	22 (5%)	0.13
Undetermined	151 (13%)	62 (14%)	0.51
More than one etiology	167 (14%)	71 (16%)	0.33
Rating from zero (very hard) to 10 (very easy)			
Complexity of medical management	8 (5–10)	7 (4–10)	<0.001
Complexity of ICU management	8 (6–10)	7 (5–10)	<0.001
Relationship with the primary physician	10 (8–10)	9 (8–10)	0.002
Relationship with colleagues/nurses	10 (9–10)	10 (8–10)	0.004
Was it easy to identify ARDS etiology?	8 (5–10)	8 (5–9)	0.031

Variables are presented as n (%), or median (25–75%) percentiles. % were calculated according to the data recorded for each variable. Abbreviations: DFLSTs, Decisions to Forgo Life-Sustaining Therapies; ICU, Intensive Care Unit; SOFA, Sequential Organ Failure Assessment; ARDS, Acute Respiratory Distress Syndrome.

The main causes of immunosuppression were hematological malignancies (50%) and solid tumor (38%). Patients had a median age of 63 yo (54–71).

DFLSTs according to patient's characteristics are presented in Table 1.

Patients with DFLSTs were older, had more advanced disease status, higher performance status Eastern Cooperative Oncology Group scale (ECOG), and higher Sequential Organ Failure Assessment (SOFA) score at admission by univariate analysis. Septic shock, liver failure and reduced level of consciousness were also related to DFLSTs in the univariate analysis (Table 1).

DFLSTs according to ICU disease characteristics are presented in Table 2. Invasive treatments related to DFLSTs by univariate analysis were: need of vasopressors, renal replacement therapy, invasive mechanical ventilation, prone position and the use of neuromuscular blocking agents (Table 2).

Complexity of medical and ICU management, relationship with the primary physician, with colleagues/nurses, and the ease of identifying acute respiratory failure etiology were considered slightly but significantly harder in patients with DFLSTs (Table 2).

3.2. Organizational factors

Participating hospitals were public university (82%), public general (12%) and private (6%). Hematologic, oncologic and transplant units were present in 95%, 64% and 82% of the hospitals, respectively.

Table 3
Decisions to forgo life-sustaining therapies according to organizational factors.

	Absence of DFLSTs n = 1115	DFLSTs n = 433	P value
Type of hospital			0.78
Fully public university	792 (83%)	307 (81%)	
Fully public general	104 (11%)	46 (12%)	
Fully private for profit	59 (6%)	24 (6%)	
Type of ICU			0.10
Medical	261 (31%)	124 (35%)	
Mixed	528 (62%)	210 (60%)	
Specialized	61 (7%)	16 (5%)	
Presence of other units in hospital			
Hematology Unit in Hospital	891/944 (94%)	350/373 (94%)	0.89
Oncology Unit in Hospital	862/936 (92%)	322/363 (89%)	0.05
Transplantation Unit in Hospital	786/944 (83%)	303/373 (81%)	0.38
Number of beds			
Number of beds in ICU	20 (12–27)	21 (16–27)	0.031
Number of beds in Hospital	800 (630–1400)	1000 (650–1400)	0.762
Number of intensivists	12 (7–18)	11 (7–20)	0.16
Physicians characteristics			
Number of intensivists per day	5 (4–6)	5 (4–7)	0.52
Number of intensivists per night	1 (1–2)	1 (1–2)	0.13
Senior intensivists cover 24/7	889/944 (94%)	362/373 (97%)	0.03
Senior hematologists cover 24/7	580/852 (68%)	276/355 (78%)	<0.001
ICU organization			
Predefined admission criteria in ICU	211/944 (22%)	102/373 (27%)	0.06
Dedicated physiotherapist for the ICU	829/944 (88%)	325/373 (87%)	0.73
Critical care outreach services (CCOS)	738/944 (78%)	309/373 (83%)	0.06
Handover procedure			0.18
Informal	650/929 (70%)	241/364 (66%)	
Formal with checklist	121/929 (13%)	42/364 (12%)	
Varies according to intensivists	128/929 (14%)	65/364 (18%)	
High volume of hematology	835/889 (94%)	336/355 (95%)	0.62
High volume of solid organ transplant	554/944 (59%)	242/373 (65%)	0.04
High volume of oncology	913/944 (97%)	356/373 (95%)	0.27
High volume of internal medicine	798/944 (85%)	330/373 (88%)	0.07
High volume of acquired immunodeficiency syndrome patients	480/944 (51%)	196/373 (53%)	0.58
High volume of other immunocompromised patients	754/944 (80%)	273/373 (73%)	0.009
Ability to discharge dying patients	781/913 (83%)	327/373 (88%)	0.03
Use of checklists	440/939 (47%)	140/371 (38%)	0.003
Request of external advice for acute respiratory failure	217/1000 (21%)	118/393 (30%)	0.001
Pulmonologist involved in patient management	351/985 (36%)	174/389 (45%)	0.002

Variables are presented as n (%), or median (25–75%) percentiles.

% were calculated according to the data recorded for each variable.

Abbreviations: DFLSTs, Decisions to Forgo Life-Sustaining Therapies; ICU, Intensive Care Unit.

ICUs were medical (30%), mixed (64%) and specialized (6%). A pulmonologist was involved in the patient management in 38% of cases.

DFLSTs according to organizational factors are shown in Table 3. Center characteristics associated with DFLSTs by univariate analysis were a higher number of ICU beds, having a senior intensivist and a senior hematologist 24/7 in the hospital, more ability for discharge dying patients, less use of checklist (less protocolized treatment), request of external advice for acute respiratory failure management, management that involves a pulmonologist, and the presence of a critical care outreach services (CCOS, Table 3).

3.3. Factors associated with a decision to forgo life-sustaining therapies

The following patient characteristics were independently associated with increased incidence of DFLSTs after multivariate analysis: age (OR 1.02 per one-year increase, 95% CI 1.01–1.03; $P = 0.0002$) and poor performance status [3 or 4] measured by ECOG (OR 2.79, 95% CI 1.98–3.93; $P < 0.0001$, Fig. 2).

The following disease-related factors were independently associated with increased incidence of DFLSTs after multivariate analysis: need for invasive mechanical ventilation within Day 7 (OR 1.79, 95% CI 1.31–2.46; $P = 0.0003$), the presence of shock in ICU within Day 7 (OR 2.00, 95% CI 1.45–2.75; $P < 0.0001$) and liver failure in the ICU within Day 7 (OR 1.59, 95% CI 1.14–2.21; $P = 0.0058$ (Fig. 2).

The following organizational factors were independently associated with increased incidence of DFLSTs after multivariate analysis: the presence of a pulmonologist involved in patient management (OR 1.85, 95% CI 1.36–2.52; $P < 0.0001$) and the presence of a CCOS (OR 1.63, 95% CI 1.11–2.38; $P = 0.01$, Fig. 2). A center effect was not retained after multivariate analysis (Fig. 2).

4. Discussion

This secondary analysis of an international study of acute hypoxemic respiratory failure in immunocompromised patients is the first to describe the patient characteristics and organizational factors associated with DFLSTs. <20% of the admitted patients had any treatment escalation planning before ICU admission, and from those that did, the most frequent one was admission for a defined assessment period, the ICU trial [21] (Fig. 1). Overall, 28% of patients had DFLSTs. Organizational factors associated with the presence of DFLSTs were the presence of a pulmonologist involved in patient management and the presence of a CCOS (Fig. 2).

Decisions to forgo life-sustaining therapies had shown a substantial variability associated with geographic factors, on an ICU, regional, national and international level [22]. Furthermore, these differences might be related to physician and patient culture, religion, medico-legal factors and economic aspects [23]. Despite these differences, Lobo et al. [24] described a decision to withhold or withdraw life-

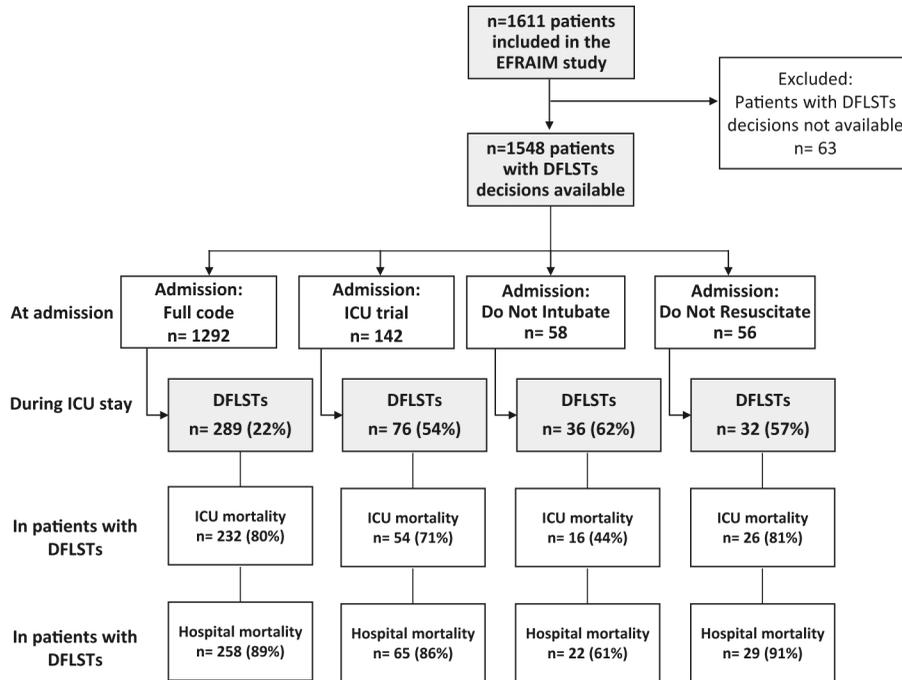


Fig. 1. Flow chart of the study: code status at the time of ICU admission, decision to forgo life-sustaining therapies during ICU stay and outcomes. Among the 1611 patients included in the EFRAIM study, data about treatment escalation planning and decisions to forgo life-sustaining therapies (DFLSTs) were available in 1548 patients. Full code admission was decided for 1292 (83%) patients, 142 (9%) patients had an intensive care unit (ICU) trial, 58 (4%) patients had do not intubate decisions, whereas 56 (4%) patients had do not resuscitate decisions. Among each treatment escalation planning category, percentages of DFLSTs are described with respective ICU and hospital mortality. Overall, 433 (28%) patients had DFLSTs. Abbreviations: DFLSTs, Decisions to Forgo Life-Sustaining Therapies.

sustaining treatment in 13% of 9524 patients from 730 ICUs in 84 countries. Likewise, in the large Ethicus study [25] conducted in 1999–2000 in 17 European countries, a decision to limit life-sustaining treatment was made in 10% of all ICU admissions. The present study found a higher prevalence of DFLSTs, which are in accordance with those reported by Cesta et al. [26] in a similar cancer population. Several factors could explain the higher prevalence in DFLSTs in our study compared with other critically ill populations. The present study evaluated treatment limitation decisions in immunocompromised patients, who have been

shown to receive more hospital care, more ICU care, and to have a higher likelihood of dying in the hospital than other patient populations [9,27]. Cancer is recognized as an independent factor associated with DFLSTs [28]. As the ICU admission rate of this vulnerable population has increased in the last decades, the increase in the number of DFLSTs is to be expected. Another contributing factor could be that our study included predominantly ICUs from high gross national income countries. Decisions to withhold or withdraw life-sustaining treatment are less frequent in low/lower-middle than in high gross national income

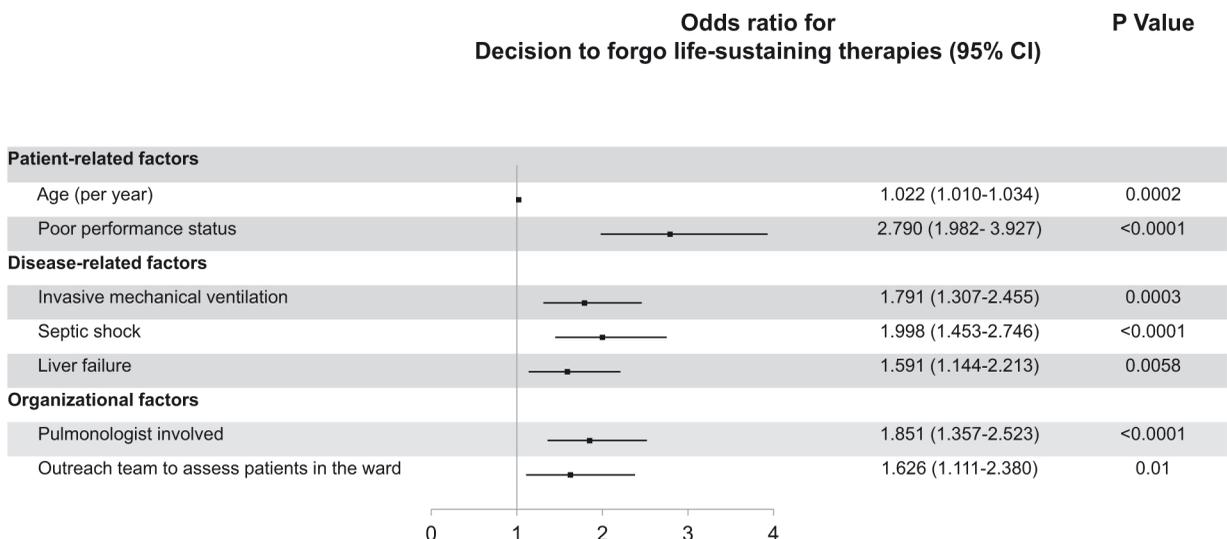


Fig. 2. Final multivariate logistic regression model of the factors associated with decision to forgo life-sustaining therapies. Abbreviations: ICU, Intensive care unit; CI, Confidence interval.

countries, possibly due to lack of policies to support the provision of withholding/withdrawing care, uncertainty around legislative support, and fewer opportunities for staff training [22].

It is interesting to note that, although patients with cancer increasingly undergo more aggressive treatments, they also have a higher number of DFLSTs than other populations. In our study, from the 81% of patients with a full admission code, 22% had a DFLSTs made. This may represent an initial misinterpretation of the real needs of this cohort of patients.

Patient- and disease-related factors have been well described in relation to DFLSTs [13,27,28]. We demonstrated that age, poorer performance status measured by the ECOG, need for invasive mechanical ventilation, presence of shock and liver failure were independently associated with DFLSTs (Fig. 2). These findings substantiate previous research that demonstrates critical illness and the need for aggressive life supporting measures are associated with increased risk of mortality for patients with a cancer diagnosis. Age remains a contentious factor, with a recent systematic review concluding that 30% of studies identified that increasing age was significantly associated with increased risk of mortality in both univariate and multivariable analyses, in a combined sample of 10,027 people [13].

An important finding of this study was the identification of ICU and hospital factors influencing DFLSTs, such as the involvement of a pulmonologist in patient management and the presence of a CCOS. In non-selected ICU patients, organizational factors have been shown to be related to patient outcomes – for example, staffing models are associated with acquired infections in ICU and hospital mortality, as well as human resources and the time working in ICU are linked to limitation of life-sustaining treatment decisions [14–17]. Quill et al. [29] analyzed results from 153 ICUs in the United States and described that, when patients are unable to participate in decision-making, the characteristics of ICUs and hospitals may hold greater importance over the decisions that are made.

Recent studies have described the role of CCOS in the triage and management of immunocompromised ward patients [30,31]. Our study reports an increase in DFLSTs in hospitals with a CCOS. The contribution of CCOS in end-of-life discussions and terminal care has been identified previously, with as much as 20% of the team's time devoted to reviewing patients around the end of their lives [30]. In approximately 30% of patients with hematological malignancies, the CCOS initiated or participated in discussions at the end of life and therefore instigated more frequent referrals to palliative care teams [30]. Although CCOS involvement is associated with most DFLSTs, the majority of immunocompromised patients in the current study were admitted for full escalation. This highlights the difficulty in addressing appropriateness of engaging a non-parent team in DFLSTs, especially when these occur out-of-hours or when prognosis is not well established.

The differing perceptions between non-ICU physicians and intensivists around end-of-life decisions have been shown for patients with chronic obstructive pulmonary disease [32]. Conversely, our reported results show an increase in DFLSTs when a pulmonologist was present in the hospital. The experience in the care of immunosuppressed patients with acute respiratory failure can explain the association with a greater frequency in end-of-life decisions. Multi-disciplinary involvement assumes greater knowledge of the patient, and their wishes and preferences around future care. This may explain the higher frequency of decisions in centers with greater involvement of several specialties [33–35].

Our study has several limitations. Although this study includes units from various parts of the world, most of them are European. Since DFLSTs are influenced by cultural and legal factors, our results may reflect the practice of European units and may not be representative of other parts of the world. Furthermore, although this was a pre-planned study, several important information was not collected. For example, the rationale behind the decision-making process, any association with patient trajectory or the time spent in ICU before DFLSTs

were made, were not explored. We cannot exclude residual confounding including a more severe cause of acute respiratory failure, that could be linked to the involvement of a pulmonologist. However, the final model was adjusted on several potential confounding factors, such as age, poor performance status, shock, liver failure and invasive mechanical ventilation, that could be closely related to severe causes of acute respiratory failure. Finally, this study focused on patients admitted in ICU, so any decision-making around treatment escalation before admission was not taken into account.

5. Conclusions

The current study suggests that, in addition to patient-related factors, the presence of a pulmonologist and an outreach team, involved in patient management on the ward, increased the number of DFLSTs in ICU. A DFLST was made in one in four immunocompromised patient admitted to the ICU for acute respiratory failure. Involving a pulmonologist in patient's management was associated with less non beneficial care. Further mixed method studies that evaluate the reasons behind the decision-making process and assess the association between these and patient outcomes will enable further conclusions to be drawn.

Ethics approval

Participating providers obtained institutional review board approval from their institutions in accordance with local ethics regulations.

Consent for publication

Not applicable.

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Author statements

All authors substantially contributed to the design of the study, acquisition, analysis, and interpretation of data, drafted and revised the manuscript for important intellectual content, approved the final version, and agreed to be accountable for all aspects of the work.

Declaration of Competing Interest

Authors declare no conflict of interest in relation with this study.

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