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ORIGINAL ARTICLE

ADENI-UCI study: Analysis of non-income decisions in ICU as a measure of limitation of life support treatments☆

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KEYWORDS
Limitation of life support treatments;
Denial of income;
Futility;
Quality of life

Abstract:
Objective: To analyze the variables associated with ICU refusal decisions as a life support treatment limitation measure.
Design: Prospective, multicentrico.
Scope: 62 ICU from Spain between February 2018 and March 2019.
Patients: Over 18 years of age who were denied entry into ICU as a life support treatment limitation measure.
Interventions: None.
Main interest variables: Patient comorities, functional situation as measured by the KNAUS and Karnosfky scale; predicted scales of Lee and Charlson; severity of the sick person measured by the APACHE II and SOFA scales, which justifies the decision-making, a person to whom the information is transmitted; date of discharge or in-hospital death, destination for hospital discharge.
Results: A total of 2312 non-income decisions were recorded as an LTSV measure of which 2284 were analyzed. The main reason for consultation was respiratory failure (1080 [47.29%]). The poor estimated quality of life of the sick (1417 [62.04%]), the presence of a severe chronic disease (1367 [59.85%]) and the prior functional limitation of patients (1270 [55.60%]) were the main reasons for denying admission. The in-hospital mortality rate was 60.33%. The futility of treatment was found as a risk factor associated with mortality (OR: 3.23; IC95%: 2.62–3.99).
Conclusions: Decisions to limit ICU entry as an LTSV measure are based on the same reasons as decisions made within the ICU. The futility valued by the intensivist is adequately related to the final result of death.

PALABRAS CLAVE
Limitación de los tratamientos de soporte vital;
Negación de ingreso;
Futilidad;
Calidad de vida

Estudio ADENI-UCI: Análisis de las decisiones de no ingreso en UCI como medida de limitación de los tratamientos de soporte vital

Resumen
Objetivo: Analizar las variables asociadas a las decisiones de rechazo al ingreso en una Unidad de Cuidados Intensivos (UCI) como medida de limitación de tratamiento de soporte vital.
Diseño: Prospectivo, multicéntrico.
Ámbito: Sesenta y dos UCI de España entre febrero de 2018 y marzo de 2019.
Pacientes: Mayores de 18 años a los que se les negó el ingreso a una UCI como medida delimitación de tratamiento de soporte vital.
Intervenciones: Ninguna.
Variables de interés principales: Comorbilidades de los pacientes, situación funcional previa medida por la escala KNAUS y Karnosfky; escalas pronósticas de Lee y Charlson; gravedad del enfermo medida por las escalas APACHE II y SOFA, motivo que justifica la toma de la decisión, persona a la cual es trasmitida la información; fecha de alta o fallecimiento intrahospitalario, destino al alta hospitalaria.
Resultados: Se registraron un total de 2.312 decisiones de no ingreso como medida de limitación del tratamiento de soporte vital (LTSV), de las cuales se analizaron 2.284. El principal motivo de consulta fue la insuficiencia respiratoria (1.080 [47,29%]). La pobre calidad de vida estimada de los enfermos (1.417 [62,04%]), la presencia de una enfermedad crónica grave (1.367 [59,85%]) y la limitación funcional previa de los pacientes (1.270 [55,60%]) fueron los principales motivos esgrimidos para denegar el ingreso. La tasa de mortalidad intrahospitalaria fue del 60,33%. La futilidad del tratamiento se constató como factor de riesgo asociado a mortalidad (OR: 3,23; IC 95%: 2,62–3,99).

Conclusiones: Las decisiones para limitar el ingreso en UCI como medida de LTSV se basan en los mismos motivos que las decisiones tomadas dentro de la UCI. La futilidad valorada por el intensivista se relaciona adecuadamente con el resultado final de muerte.

Introduction

The limitation of life support treatment (LLST) is increasingly frequent in countries in our setting.[1] It is regarded as good medical practice, since therapeutic obstinacy and the maintenance of futile treatment measures lacks ethical or scientific justification.[2,3]

In some cases the decision not to admit a patient to the Intensive Care Unit (ICU) is considered to be a form of LLST, and multiple considerations may be involved in such a decision.[2,4] However, despite efforts to develop consensus documents and clinical practice guides with the aim of unifying criteria regarding patient admission to the ICU,[5] some authors have criticized the lack of information on the processes underlying the acceptance or refusal of admission to intensive care.[6,7] Few studies to date have focused on defining the main variables that influence the subsequent in-hospital mortality of these patients.[8,9]

The present multicenter study was carried out to describe the variables that intervene in the decision to reject admission to the ICU as an LLST measure; determine the frequency and types of such decisions; and analyze the factors associated to in-hospital mortality in these individuals, conducting patient follow-up for up to 90 days of hospital stay, until hospital discharge, or until the death of the patient — whichever occurs first.

Material and methods

Study design

The ADENI-ICU is a prospective, multicenter observational study. The patient registry was opened in February 2018 — the first patient being recruited on 7 February and the last patient on 18 March. The follow-up period ended on 12 May 2019. The patients were recruited from 62 Departments of Intensive Care Medicine (DICMs) on a consecutive basis over a period of 6 months.

The limited literature on the refusal of admission to the ICU as an LLST measure complicated prior calculation of the study sample size. By extrapolating the results of the ADMISSIONREA study,[20] involving 11 French ICUs that recorded 51 patients considered ''too ill'' to benefit from admission to the ICU over a period of one month, an estimated sample size of approximately 1700 patients could be established.

The study included patients over 18 years of age and considered by the intensivist to not be candidates for admission to the ICU as an LLST measure. The latter was defined as the decision to refuse admission, made by the intensivist evaluating the patient, and supported by one or a combination of the following conditions: advanced patient age, the presence of serious chronic disease, previous functional limitation, estimated poor quality of life, treatment futility, the existence of a justifying living will or advance directives, or patient rejection in person.

Likewise, cases of in-hospital cardiac arrest in which the decision was made to suspend resuscitation as an LLST measure were also documented.

Data collection and study variables

A registry form in paper format was used to collect the study data, followed by entry of the information in an electronic database to create a single registry corresponding to all the participating centers.

The study variables included patient clinical and demographic data (age, gender, usual place of residency, associated comorbidities [supplementary material in electronic format], previous functional status as assessed by the KNAUS[10] and Karnofsky scores,[11] reason for hospital admission, previous hospital admissions and admissions to the ICU), parameters related to consultation (time, location of the patient at the time of consultation, consulting person, reason for consultation [supplementary material in electronic format] and time elapsed from admission to the time of consultation, and application of the Lee[12] and Charlson prognostic scales[13]), variables related to the decision to refuse admission (patient severity as assessed by the APACHE II[14] and SOFA scores,[15] the physician making the decision and his/her years of professional experience, time and reason justifying the decision made, the person to which the information was transmitted [relative or patient], degree of agreement and registry in the case history), and evolutive parameters (date of discharge or in-hospital death, patient destination at hospital discharge, and possible changes in the decision to refuse admission, with the corresponding reason).

Patient follow-up

The patients were subjected to follow-up for up to 90 days of hospital stay, until hospital discharge, or until the death of the patient — whichever occurs first.

The study was approved by the Clinical Research Ethics Committee (CREC) of the reference center. Subsequently, the required documentation was forwarded to the rest of the participating centers to allow approval to be obtained from their respective CRECs. The study only started once the required approval had been obtained from all the centers.

The study was endorsed by the Scientific Committee of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (*Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias* [SEMICYUC]).

Statistical analysis

A descriptive analysis of the study sample was made. The results were reported as percentages in the case of categorical variables and as the mean and standard deviation (SD) in the case of continuous quantitative variables.

Associations between the different variables and in-hospital mortality were analyzed, with a maximum follow-up of 90 days. Since patients admitted to the same hospital and to hospitals of the same province usually share similar procedures and protocols, we were unable to assume independence between patients. Consequently, triple-level nested logistic regression analysis was performed: province, hospital and patient. To summarize, usual logistic regression models the relationship between a variable such as for example the APACHE score and the probability of death expressed as:

$$Log\left(\frac{P(y_i)}{1-P(y_i)}\right) = \beta_0 + \beta_1 APACHE_i + \beta_2 age_i + \beta_3 sex_i + \beta_4 SOFA_i + \varepsilon_i$$

where P(yi) is the probability of death of the patient i; age, gender and the SOFA score take values for each patient; and ... is random error. In this formula, the natural logarithm provides the ratio of probabilities of death for each additional point of the APACHE score.

However, logistic regression requires independence between observations. Since this cannot be assumed in our study, we performed triple-level nested logistic regression analysis: province, hospital and patient. In this case, the relationship between the APACHE score and the probability of death included three random errors, one for each level of analysis:

$$Log\left(\frac{P(y_i)}{1-P(y_i)}\right) = \beta_0 + \beta_1 APACHE_i + \beta_2 age_i + \beta_3 sex_i + \beta_4 SOFA_i + u_j + v_k + \varepsilon_i$$

where uj is the random error for the interception due to the province and vk is the random error for the interception due to the hospital. The interpretation of the β parameters is the same as before.

The results of the mentioned analysis of association are reported as odds ratios (ORs) with the corresponding 95% confidence interval (95%CI) corrected for age, gender, APACHE II score and the SOFA scale.

The Stata version 15.1 statistical package was used throughout.

Results

During the study we recorded 2312 decisions of non-admission to the ICU as an LLST measure among the 62 participating centers. The characteristics of the participating centers and Departments (5 failed to supply the required data) are reported in Table 1. Following review of the data, 28 decisions were excluded due to errors in data collection. The final number of analyzed decisions was therefore 2284.

The main clinical-epidemiological variables of the study sample are shown in Table 2.

Table 1 Characteristics of 57 of the 62 hospitals and Departments of Intensive Care Medicine participating in the study.

Variable	Value (n = 57)
Public hospital	52 (91%)
Healthcare expenditure per inhabitant (mean [SD])	1394.35 (166.71)
University hospital	43 (75%)
Number of hospital beds (mean [SD])	568 (878)
Hospitals with ≤200 beds	7 (12%)
Hospitals with 200–500 beds	23 (40%)
Hospitals with 501–1000 beds	20 (35%)
Hospitals with ≥1000 beds	6 (10%)
Number of ICU beds (mean [SD])	19 (11)
Number of annual ICU admissions (mean [SD])	998 (453)
Open ICU in visiting hours	30 (53%)
Mixed ICU according to treated disease	45 (79%)
IMCU facilities in DICM	12 (21%)
Existence of EICS in DICM	15 (26%)
Existence of LLST protocol in DICM	43 (75%)
Existence of NIMV outside DICM	48 (84%)
Existence of seriously ill patient detection scale	10 (17%)
CA registry	13 (23%)
Refusal of admission to ICU registry	10 (17%)

SD: standard deviation; ICU: Intensive Care Unit; IMCU: Intermediate Care Unit; EICS: Extended Intensive Care Service; LLST: limitation of life support treatment; DICM: Department of Intensive Care Medicine; NIMV: noninvasive mechanical ventilation; CA: cardiac arrest.

Variables related to DICM consultation

Department of Intensive Care Medicine consultation was carried out on 1064 occasions in the time window between 15:00 and 23:59 p.m. (47%), and took place in 1124 cases from the hospital emergency room (49%) and on the part of the physician on duty in 1117 cases (49%). The main reason for consultation was respiratory failure (n = 1080 [47%]), followed by altered level of consciousness (n = 911 [40%]) and hemodynamic instability (n = 741 [32%]). Assessment by the DICM in most cases was made by the specialist on duty (n = 1825 [81%]), with a professional experience of 6–15 years (n = 1040 [46%]). At the time of assessment, the mean APACHE II score was 20.38 (±8.52) with a mean SOFA score of 5.99 (±3.97). The mean Lee index was 12.73 (±4.07), while the mean Charlson score was 6.69 (±2.63).

Reasons for deciding non-admission to the ICU

The decision to refuse admission to the ICU was made at initial assessment in almost all cases (n = 2127 [93%]). Estimated poor patient quality of life (n = 1417 [62%]), the presence of serious chronic illness (n = 1367 [60%]), and prior functional limitation of the patients (n = 1270 [56%]) were the main reasons underlying the decision to refuse admission as an LLST measure.

Table 2 Main clinical-epidemiological characteristics of the 2284 patients analyzed in the study.

Characteristics	Value
Age (mean [SD])	75 (12)
Gender	
Male n (%)	1355 (59)
Origin	
Family home n (%)	1962 (86)
Institutionalized n (%)	275 (12)
Other n (%)	27 (1)
Reason for hospital admission	
Medical	1965 (86)
Surgical	271 (12)
Other	43 (2)
Knaus scale[a]	
A n (%)	166 (7)
B n (%)	725 (32)
C n (%)	877 (39)
D n (%)	473 (21)
Karnofsky scale	
Score ≤50	1022 (44)
Score >50	1262 (55)
Comorbidities	
HF n (%)	744 (32)
HF NYHA class III–IV n (%)	263 (11)
Neuromuscular disease n (%)	145 (6)
Neurodegenerative disease n (%)	299 (13)
COPD n (%)	595 (26)
COPD GOLD III–IV n (%)	203 (9)
Diabetes mellitus n (%)	750 (33)
Cancer n (%)	640 (28)
Renal failure n (%)	563 (25)
Liver cirrhosis n (%)	174 (8)
Cirrhosis CHILD C n (%)	75 (3)
Immunosuppression n (%)	333 (15)
Alcoholism n (%)	214 (9)
Lee index (mean [SD])	6.69 (2.63)
Charlson index (mean [SD])	12.73 (4.07)
Admission in last year[b] **n (%)**	1 (2)
Previous admission to ICU n (%)	336 (15)
Death as outcome n (%)	1378 (60)

SD: standard deviation; HF: heart failure.

[a] Knaus scale: Class A: good previous health without functional limitations; Class B: mild/moderate limitation of activities due to chronic disease; Class C: severe but not disabling limitation due to chronic disease; Class D: severe restriction of activity due to disease.

[b] Hospital admission in the previous calendar year due to the disease causing current consultation of the Department of Intensive Care Medicine.

Variables related to the patient course following refusal of admission to the ICU:

Terminal sedation was started in 484 of the cases (21%) following the decision to refuse admission to the ICU.

The patient was informed of the decision in 368 cases (16%), while the family was informed in 1716 (75%). The decision was recorded in the patient case history in most cases (n = 2046 [90%]). Among the patients who were not informed of the decision to refuse admission to the ICU as an LLST measure (n = 1700 [81%]), the reason for consultation was altered level of consciousness in only 46% of the cases (n = 780).

Family disagreement with the decision was recorded in 54 cases (2%), while consulting physician disagreement was recorded in 138 cases (6%). In only 71 cases (3%) did posterior admission to the ICU take place once the decision had been made. Forty percent of these cases corresponded to patients with admission and care criteria as potential organ donors, while 18% corresponded to admissions decided as a consequence of external Department pressures.

The patient destination at hospital discharge was home in 65% of the cases, while in 20% of the cases the destination was a chronic care center.

Mortality analysis

Following the refusal of admission to the ICU as an LLST measure, the in-hospital mortality rate after 90 days in the study sample was 60.33%. The associations between the main clinical epidemiological parameters and mortality are reported in Table 3.

The assessment requests made from the emergency room were associated to lesser mortality (OR: 0.63; 95%CI: 0.52–0.76), taking as reference the consultations made from the conventional hospital wards. Apart from the cases of cardiac arrest in which the cessation of resuscitation was regarded as an LLST measure, consultation due to patient altered level of consciousness showed the strongest correlation to mortality (OR: 1.76; 95%CI: 1.44–2.15) (Table 4).

Patient severity at the time of consultation, as assessed by the APACHE II and SOFA scores, was associated to an increase in mortality (OR: 1.07 [1.05–1.08], p = 0.000 and OR: 1.28 [1.24–1.33], p = 0.000, respectively) for each point of increase in score. As can be seen in Fig. 1, the futility of treatment was the reason for refusing admission to the ICU with the strongest correlation to in-hospital mortality (OR: 3.23; 95%CI: 2.62–3.99).

No differences in survival were observed on analyzing the physician performing the assessment in terms of either physical location (destination unit, Extended Intensive Care Service [EICS] or physician on duty) or years of experience.

The time elapsed between patient admission to hospital and assessment by the DICM was significantly longer among the patients who subsequently died (7.04 [0.54] versus 3.58 [0.67] days, p < 0.000; OR: 1.02 [1.01–1.03], p < 0.001).

Discussion

The present study analyzes the decision to refuse admission to the ICU as an LLST measure, based on 2000 registries from 62 Spanish ICUs. It is the first study to adopt a systematic and exclusive approach in this field.

The results obtained highlight a low in-hospital mortality rate after 90 days (close to 60%) among those patients in which admission to the ICU was refused as an LLST measure. It is difficult to establish comparisons with other previous studies analyzing decisions against admission to the ICU in those patients considered to be too ill to benefit from admis-

Table 3 Differences in the characteristics of survivors and non-survivors in the study, and their association to mortality based on triple-level nested logistic regression analysis corrected for age and gender, and the APACHE II and SOFA scores.

Variable	Survivors 912 (40%) n (%)	Non-survivors 1372 (60%) n (%)	OR (95%CI)	p
Age	75 (12)	75 (13)	1.01 (1.00–1.02)	0.044
Gender Male n (%)	519 (58)	828 (60)	1.03 (0.85–1.25)	0.749
Origin				
Family home n (%)	755 (85)	1195 (88)	0.90 (0.39–2.06)	0.807
Institutionalized n (%)	122 (14)	153 (11)	1 (ref.)	
Others n (%)	12 (1)	15 (1)	0.79 (0.59–1.05)	0.108
Reason for hospital admission				
Medical n (%)	809 (90)	1145 (84)	1 (ref.)	
Surgical n (%)	87 (10)	184 (13)	1.43 (1.05–1.94)	0.022
Other n (%)	4 (0)	39 (3)	5.02 (1.67–15.06)	0.004
Knaus scale				
A n (%)	41 (5)	125 (9)	1 (ref.)	
B n (%)	267 (30)	450 (34)	0.61 (0.40–0.92)	0.020
C n (%)	368 (41)	506 (38)	0.47 (0.31–0.71)	0.000
D n (%)	210 (24)	262 (19)	0.43 (0.28–0.66)	0.000
Karnofsky scale				
Score ≤50 n (%)	353 (39)	661 (48)	1 (ref.)	
Score >50 n (%)	547 (61)	711 (52)	0.70 (0.58–0.85)	0.000
Comorbidities				
Heart failure n (%)	314 (35)	424 (31)	0.75 (0.62–0.93)	0.007
NYHA Class III–IV n (%)	106 (12)	156 (11)	0.96 (0.72–1.29)	0.781
Neuromuscular disease n (%)	70 (8)	74 (5)	0.66 (0.45–0.97)	0.036
Neurodegenerative disease n (%)	136 (15)	163 (12)	0.84 (0.64–1.11)	0.217
COPD n (%)	269(30)	323(23)	0.66 (0.53–0.82)	0.000
GOLD III–IV n (%)	105 (12)	96 (7)	0.56 (0.41–0.78)	0.001
Diabetes mellitus n (%)	278 (31)	468 (34)	1.10 (0.90–1.35)	0.347
Cancer n (%)	226 (25)	410 (30)	No-data	No-data
Renal failure n (%)	210 (23)	350 (25)	0.87 (0.69–1.09)	0.216
Liver cirrhosis n (%)	62 (7)	111 (8)	No-data	No-data
CHILD C n (%)	20 (2)	54 (4)	0.99 (0.55–1.77)	0.963
Immunosuppression n (%)	117 (13)	215 (16)	No-data	No-data
Alcoholism n (%)	87 (10)	125 (9)	0.65 (0.47–0.91)	0.012
Lee index (mean [SD])	12.95 (0.14)	12.58 (0.11)	0.97 (0.95–1.00)	**0.031**
Charlson index (mean [SD])	6.45 (0.09)	6.85 (0.07)	1.03 (1.00–1.08)	0.085
Admission in last year n (%)	560 (62)	779 (57)	0.75 (0.62–0.91)	0.004
Previous admission to ICU n (%)	133 (15)	201 (15)	1.01 (0.77–1.33)	0.923

SD: standard deviation.
*Knaus scale: Class A: good previous health without functional limitations; Class B: mild/moderate limitation of activities due to chronic disease; Class C: severe but not disabling limitation due to chronic disease; Class D: severe restriction of activity due to disease.
**Hospital admission in the previous calendar year due to the disease causing current consultation of the Department of Intensive Care Medicine.

sion, though the reported mortality rates range between 80%–100%.[16–19] Despite our high survival rate, however, it cannot be discarded that these survivors were free of disabilities or showed progression of their functional limitation. In effect, up to 20% of the patients discharged from hospital were referred to chronic care centers.

On the other hand, our patients were older on average than the populations analyzed in other studies of similar characteristics,[20–23] and only 7.4% had no limitations due to disease.

The results referred to the benefit of admitting or not admitting critically ill elderly patients to the ICU are discordant.[24] Although our data show older age to be associated to increased in-hospital mortality following the refusal of admission, it has been postulated that frailty may be a more robust predictor of vulnerability and ''recoverability'' than chronological age in itself — particularly in the context of serious disease.[25,26]

The FRAIL-ICU study underscored the association between mortality and frailty in the critically ill. These

Table 4 Associations between the variables related to consultation of the Department of Intensive Care Medicine and mortality based on multilevel nested logistic regression analysis corrected for age and gender, and the APACHE II and SOFA scores.

Variable	Survivors 912 (40%) n (%)	Non-survivors 1372 (60%) n (%)	OR (95%CI)	p
Consultation time window				
8:00/14:59	280 (31)	467 (34)	1 (ref.)	
00:00/7:59	202 (22)	323 (24)	0.91 (0.70–1.20)	0.518
15:00/23:59	413 (46)	573 (42)	0.84 (0.68–1.04)	0.105
Patient location				
Ward	367 (41)	723 (53)	1 (ref.)	
Emergency room	511 (57)	608 (44)	0.63 (0.52–0.76)	**0.000**
Operating room	8 (1)	19 (1)	0.84 (0.34–2.10)	0.715
Others	13 (1)	18 (1)	0.69 (0.31–1.55)	0.372
Consulting professional				
Resident	84 (9)	133 (10)	1 (ref.)	
Staff physician	370 (41)	528 (38)	0.84 (0.60–1.19)	0.330
Physician on duty	436 (48)	679 (49)	0.90 (0.64–1.27)	0.547
Others	9 (1)	32 (2)	1.85 (0.77–4.45)	0.170
Reason for consultation				
Hemodynamic instability	263 (29)	476 (35)	1.04 (0.85–1.28)	0.690
Respiratory failure	417 (46)	657 (48)	0.98 (0.81–1.19)	0.846
Altered level of consciousness	274 (30)	633 (46)	1.76 (1.44–2.15)	**0.000**
Sepsis	139 (15)	228 (17)	0.93 (0.72–1.21)	0.585
Laboratory test alterations	254 (28)	375 (27)	0.90 (0.72–1.11)	0.319
Family request	5 (1)	19 (1)	No-data	No-data
Interrupted CA	11 (1)	178 (13)	5.20 (2.72–9.97)	**0.000**
Others	2 (15)	3 (10)	4.35 (0.22–87.26)	0.337
No. available beds in ICU (mean [SD])	3.58 (1)	3.76 (0)	0.98 (0.94–1.02)	0.389

SD: standard deviation.

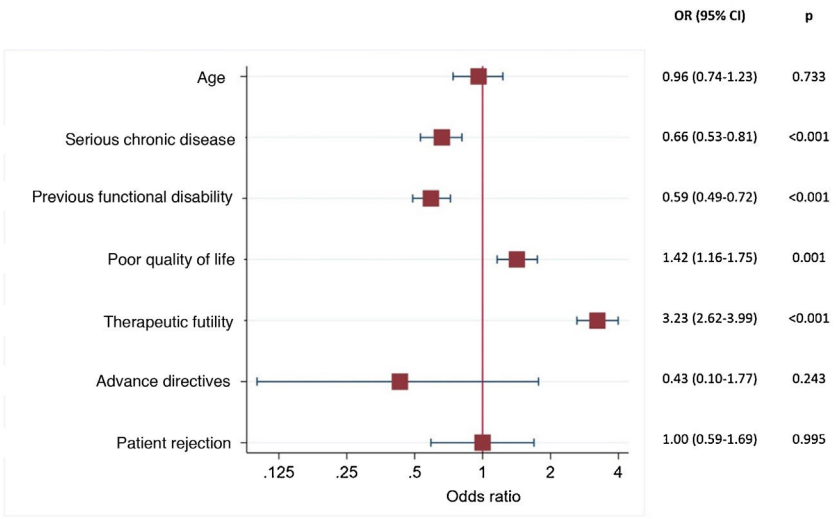

Figure 1 Associations between the reasons for refusing admission to the ICU as an LLST measure and in-hospital mortality based on multilevel nested logistic regression analysis corrected for age and gender, and the APACHE II and SOFA scores.

patients were characterized by a greater percentage of LLST decisions in the ICU.[27] This could suggest that lesser mortality in such frail subjects could be explained simply by the fact of avoiding those factors inherent to the intensive care setting that could worsen their prognosis.[28]

Likewise, and although there are no publications allowing for the comparison of results, we found the percentage of patients proposed for admission to the ICU from the emergency room to have significantly lower mortality than those patients proposed for admission to the ICU from the hospital ward. The fact that such patients came from the emergency

room where first assessment was made, with possibilities for clinical improvement, could in part explain the observed low mortality.

Based on our results, the reasons of the intensivist for refusing admission to the ICU as an LLST measure were not significantly different from the LLST decisions described upon admission to the ICU in our setting. The main reasons were the presence of previous serious chronic illness, compliance with advance directives of the patient, prior functional limitation, and qualitative futility.[29] Likewise, the INSTINCT study recently reported the impossibility of restoring autonomy, the presence of advanced stage chronic disease and poor quality of life to be the main reasons given for considering admission to the ICU as affording no benefit for the patient.[30]

Only 16% of the patients were informed about the decision. In this regard, it is true that critically ill patients are often characterized by circumstances that complicate or impede their full participation in the process.[31] However, it must be considered that perceived quality of life among elderly ICU stay survivors (as in the case of our series of patients) is no different from that found in younger age groups, and moreover increases over time despite a decrease in activities of daily living.[6]

In three out of every four cases the decision was agreed with the patient relatives or representatives. However, studies have evidenced that the opinion of the relatives is not a reliable indicator of the wishes of the patient,[32] and it has even been reported that the relatives may be unaware of the wishes of the patient in this respect.[33] In any case, the level of agreement between the decision of the patient and that of the relatives in a hypothetical case is close to 70%.[34] Likewise, the prognosis contemplated by the relatives is based not only on the information they receive from the medical team but also on other imponderable factors such as the robustness of the patient and his/her ability to overcome past diseases, as well as the impression gained from the physical appearance of the patient, etc.[35]

The present study has limitations. Firstly, the ICUs were not randomly selected but participated voluntarily in the study. Secondly, there are variable criteria among the professionals regarding the decision to admit a patient to the ICU. On the other hand, the 6-month study period might not be representative of the screening procedures over time in each ICU — giving rise to potential bias derived from the seasonal behavior of certain disease conditions. Nevertheless, we consider that the many participating Units and the total duration of the study adequately reflect daily practice in Spanish ICUs. In turn, some decisions might not have been duly recorded (weekends, holidays, etc.). Other possible sources of bias such as variable case registry, the absence of homogeneous protocols, the difference in proactive or upon-demand follow-up of the patients, and the different levels of implication of the hospitals may be considered to have been partially or fully resolved by the statistical analysis made.

It can be concluded that one of the main strengths of our study is the many decisions that have been recorded. This allows us to evidence that the decisions to limit admission to the ICU as an LLST measure are based on the same criteria as the decisions made within the ICU, and that in most cases refusal of admission does not lead to the death of the patients. This raises the hypothesis that the decisive factor in refusing admission was not the seriousness of the disease condition in itself but that the decision was influenced by the procedure and the comorbidities of the patient at the time of assessment. On the other hand, we wish to underscore the viability of the evaluations made by the intensivists in terms of therapeutic futility and the association to posterior mortality.

Author's contributions

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medine.2022.02.008.

References

1. Sprung CL, Ricou B, Hartog CS, Maia P, Mentzelopoulos SD, Weiss M, et al. Changes in end-of-life practices in European Intensive Care Units from 1999 to 2016. JAMA. 2019;2:1–12.
2. Bosslet GT, Pope TM, Rubenfeld GD, Lo B, Truog RD, Rushton CH, et al. An official ATS/AACN/ACCP/ESICM/SCCM policy statement: responding to requests for potentially inappropriate treatments in Intensive Care Units. Am J Respir Crit Care Med. 2015;191:1318–30.
3. Estella Á, Saralegui I, Rubio Sanchiz O, Hernández-Tejedor A, López Camps V, Martín MC, et al. Update and recommendations in decision making referred to limitation of advanced life support treatment, Puesta al día y recomendaciones en la toma de decisiones de limitación de tratamientos de soporte vital. Med Intensiva. 2020;44:101–12.
4. Grupo de Estudios de Ética Clínica de la Sociedad Médica de Santiago. La reanimación cardiorespiatoria y la orden de no reanimar. Rev Med Chil. 2007;135:669–79.
5. Nates JL, Nunnally M, Kleinpell R, Blosser S, Goldner J, Birriel B, et al. ICU admission, discharge, and triage guidelines:

a framework to enhance clinical operations, development of institutional policies, and further research. Crit Care Med. 2016;44:1553–602.
6. Boumendil A, Somme D, Garrouste-Orgeas M, Guidet B. Should elderly patients be admitted to the intensive care unit? Intensive Care Med. 2007;33:1252.
7. Capuzzo M, Moreno RP, Alvisi R. Admission and discharge of critically ill patients. Curr Opin Crit Care. 2010;16:499–504.
8. Escudero-Acha P, Palomo Navarro M, Leizaola Irigoyen O, Vidal Tegedor B, González Romero D, Misis Del Campo M, et al. Grupo de Trabajo de Bioética de la SEMICYUC, preliminary results of the ADENI-ICU trial: analysis of decisions of refuse admission in intensive care units as a limitation of life support treatments; multi-center, prospective, observational study. Med Intensiva. 2019;43:317–9.
9. Bassford C. Decisions regarding admission to the ICU and international initiatives to improve the decision-making process. Crit Care. 2017;21:174.
10. Knaus WA, Zimmerman JE, Wagner DP, Draper EA, Lawrence DE. APACHE-acute physiology and chronic health evaluation: a physiologically based classification system. Crit Care Med. 1981;9:591–7.
11. Crooks V, Waller S, Smith T, Hahn TJ. The use of the Karnofsky Performance Scale in determining outcomes and risk in geriatric outpatients. J Gerontol. 1991;46:139–44.
12. Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a prognostic index for 4-year mortality in older adults. JAMA. 2006;296:801–8.
13. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
14. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13:818–29.
15. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996;22:707–10.
16. Reignier J, Dumont R, Katsahian S, Martin-Lefevre L, Renard B, Fiancette M, et al. Patient-related factors and circumstances surrounding decisions to forego life-sustaining treatment, including intensive care unit admission refusal. Crit Care Med. 2008;36:2076–83.
17. Louriz M, Abidi K, Akkaoui M, Madani N, Chater K, Belayachi J, et al. Determinants and outcomes associated with decisions to deny or to delay intensive care unit admission in Morocco. Intensive Care Med. 2012;38:830–7.
18. Bouneb R, Mellouli M, Dardouri M, Soltane HB, Chouchene I, Boussarsar M. Determinants and outcomes associated with decisions to deny intensive care unit admission in Tunisian ICU. Pan Afr Med J. 2018;29:176.
19. Vanhecke TE, Gandhi M, McCullough PA, Lazar MH, Ravikrishnan KP, Kadaj P, et al. Outcomes of patients considered for, but not admitted to, the intensive care unit. Crit Care Med. 2008;36:812–7.
20. Garrouste-Orgeas M, Montuclard L, Timsit JF, Reignier J, Desmettre T, Karoubi P, et al. French ADMISSIONREA Study Group. Predictors of intensive care unit refusal in French intensive care units: a multiple-center study. Crit Care Med. 2005;33:750–5.
21. Reignier J, Dumont R, Katsahian S, Martin-Lefevre L, Renard B, Fiancette M, et al. Patient-related factors and circumstances surrounding decisions to forego life-sustaining treatment, including intensive care unit admission refusal. Crit Care Med. 2008;36:2076–83.
22. Joynt GM, Gomersall CD, Tan P, Lee A, Cheng CA, Wong EL. Prospective evaluation of patients refused admission to an intensive care unit: triage, futility and outcome. Intensive Care Med. 2001;27:1459–65.
23. Iapichino G, Corbella D, Minelli C, Mills GH, Artigas A, Edbooke DL, et al. Reasons for refusal of admission to intensive care and impact on mortality. Intensive Care Med. 2010;36:1772–9.
24. Fuchs L, Novack V, McLennan S, Celi LA, Baumfeld Y, Park S, et al. Trends in severity of illness on ICU admission and mortality among the elderly. PLoS One. 2014;9:e93234.
25. Montgomery C, Bagshaw SM. Frailty in the age of VIPs (very old intensive care patients). Intensive Care Med. 2017;43:1887–8.
26. Bagshaw SM, Stelfox HT, McDermid RC, Rolfson DB, Tsuyuki RT, Baig N, et al. Association between frailty and short- and long-term outcomes among critically ill patients: a multicentre prospective cohort study. CMAJ. 2014;186:95–102.
27. López Cuenca S, Oteiza López L, Lázaro Martín N, Irazabal Jaimes MM, Ibarz Villamayor M, Artigas A, et al. Fragilidad en pacientes mayores de 65 años ingresados en cuidados intensivos (FRAIL-ICU). Med Intensiva. 2019;43:395–401.
28. Rothschild JM, Landrigan CP, Cronin JW, Kaushal R, Lockley SW, Burdick E, et al. The Critical Care Safety Study: the incidence and nature of adverse events and serious medical errors in intensive care. Crit Care Med. 2005;33:1694–700.
29. Rubio O, Sánchez JM, Fernandez R. Criterios para limitar los tratamientos de soporte vital al ingreso en unidad de cuidados intensivos: resultados de una encuesta multicéntrica nacional. Med Intensiva. 2013;37:333–8.
30. Quenot JP, Large A, Meunier-Beillard N, Pugliesi PS, Rollet P, Toitot A, et al. INSTINCT study group. What are the characteristics that lead physicians to perceive an ICU stay as non-beneficial for the patient? PLoS One. 2019;14:e0222039.
31. Rigaud JP, Giabicani M, Meunier-Beillard N, Ecarnot F, Beuzelin M, Marchalot A, et al. Non-readmission decisions in the intensive care unit under French rules: a nationwide survey of practices. PLoS One. 2018;13:e0205689.
32. Tillyard AR. Ethics review: «Living wills» and intensive care. An overview of the American experience. Crit Care. 2007;11:219.
33. Sharma RK, Hughes MT, Nolan MT, Tudor C, Kub J, Terry PB, et al. Family understanding of seriously-ill patient preferences for family involvement in healthcare decision making. J Gen Intern Med. 2011;26:881–6.
34. Shalowitz DI, Garrett-Mayer E, Wendler D. The accuracy of surrogate decision makers. A systematic review. Arch Intern Med. 2006;166:493–7.
35. Boyd EA, Lo B, Evans LR, Malvar G, Apatira L, Luce JM, et al. «It's not just what the doctor tells me»:' factors that influence surrogate decision-makers' perceptions of prognosis. Crit Care Med. 2010;38:1270–5.