sciendo

The Journal of Critical Care Medicine 2023;9(4):230-238

RESEARCH ARTICLE

DOI: 10.2478/jccm-2023-0028

# Limitation of Non-Beneficial Interventions and their Impact on the Intensive Care Unit Costs

Sotiria Koutsouki[1*], Dimitrios Kosmidis[2], Eva-Otilia Nagy[3], Alexandra Tsaroucha[4], Georgios Anastasopoulos[5], Ioannis Pnevmatikos[6], Vasileios Papaioannou[7]

[1] General Hospital of Kavala, Kavala, Greece

[2] Nursing Department, International Hellenic University, Didymoteicho, Greece

[3] General Hospital of Kavala, Kavala, Greece

[4] Postgraduate program on Bioethics, Laboratory of Bioethics, Medical School, Democritus University of Thrace, Alexandroupolis, Greece

[5] Medical Informatics Laboratory, Democritus University of Thrace, Alexandroupolis, Greece

[6] Faculty of Medicine, University of Cyprus, Lefkosia, Cyprus

[7] Faculty of Medicine, Democritus University of Thrace, Alexandroupolis, Greece

## Abstract

**Introduction**: Using a plan to limit non-beneficial life support interventions has significantly reduced harm and loss of dignity for patients at the end of life. The association of these limitations with patients' clinical characteristics and health care costs in the intensive care unit (ICU) needs further scientific evidence. **Aim of the study**: To explore decisions to limit non-beneficial life support interventions, their correlation with patients' clinical data, and their effect on the cost of care in the ICU. **Material and Methods**: We included all patients admitted to the general ICU of a hospital in Greece in a two-year (2019-2021) prospective study. Data collection included patient demographic and clinical variables, data related to decisions to limit (withholding, withdrawing) non-beneficial interventions (NBIs), and economic data. Comparisons were made between patients with and without limitation decisions. **Results**: NBIs were limited in 164 of 454 patients (36.12%). Patients with limitation decisions were associated with older age (70y vs. 62y; p<0,001), greater disease severity score (APACHE IV, 71 vs. 50; p<0,001), longer length of stay (7d vs. 4.5d; p<0,001), and worse prognosis of death (APACHE IV PDR, 48.9 vs. 17.35; p<0,001). All cost categories and total cost per patient were also higher than the patient without limitation of NBIs (9247,79€ vs. 8029,46€, p<0,004). The mean daily cost has not differed between the groups (831,24€ vs. 832,59€; p<0,716). However, in the group of patients with limitations, all cost categories, including the average daily cost (767.31€ vs. 649.12€) after the limitation of NBIs, were reduced to a statistically significant degree (p<0.001). **Conclusions**: Limiting NBIs in the ICU reduces healthcare costs and may lead to better management of ICU resource use.

**Keywords**: non-beneficial interventions, end-of-life, cost of care, intensive care units

Received: 29 May 2023 / Accepted: 30 September 2023

Published under CC BY 4.0 license

## Introduction

Intensive care units (ICUs) have contributed to increasing the survival of critically ill patients and prolonging the dying process. Providing futile treatment consumes scarce healthcare resources, delays the care of other patients, and can prolong suffering and deprive patients of dignity [1, 2, 3]. Avoiding ineffective treatment has led the international scientific community to establish practices of non-beneficial life support interventions, marking the transition from curative to palliative care [4, 5]. Using a plan to limit non-beneficial interventions (NBIs) reduces patient harm at the end of life, and its early adoption has been associated with fewer NBIs, less perceived suffering, and loss of dignity [6,7].

In addition, with the steady increase in life expectancy in many countries, the financial impact on health systems will be enormous, and the use of ICU resources will be valuable [8]. In the European Union, it is pro-

* Correspondence to: Sotiria Koutsouki, General Hospital of Kavala, Kavala, Greece. E-mail: sotiriak73@yahoo.gr

jected that 24.4 million people will be over 85 years of age in 2040. Rates of admission of elderly patients to the ICU accounted for 15% of ICU admissions, raising challenges in managing admitted patients and end-of-life decision-making [9].

Although capturing the economic impact of changing standards of care in ICUs is complex, the need for more studies to measure the actual cost of care is urgent [10]. Healthcare professionals and policymakers will need results from economic analyses to make better-informed decisions about allocating resources to healthcare [11]. In this context, studies on cost savings in ICUs based on alternative models of care have already started to be documented in the international literature. Bouttell et al. concluded that implementing a plan to limit NBIs for all expected deaths in Scottish hospital ICUs would save $3.1 million [12]. In the study by Chin-Yee et al., palliative care over full support in the ICU was an independent factor in reducing costs in older patients [13]. However, overusing aggressive care and underusing palliative care at the end of life are common in high and low-income countries [14]. Although there has been an international emphasis on research into issues related to the limitation of NBIs, studies investigating their impact on the cost of care for these patients have been rare. This study investigated decisions to limit non-beneficial life support interventions, their correlation with patients' clinical data, and their impact on ICU care costs.

## Material and Methods

The study was a prospective single center observational study conducted in the general adult ICU of the General Hospital of Kavala, Greece. The study was approved by the hospital's Ethics committee (no. 2o/14/11-6-2019). All patients 18 years or older admitted to the participating ICU were eligible. The data collection period was two consecutive years (from 1/7/2019 to 30/6/2021).

The demographic and clinical characteristics of the patients, as well as ICU data, were collected by daily recording in a specialized database maintained in the ICU. Cost data were obtained from the hospital's information system and data from the above database.

Data collection included patient demographic and clinical data (age, sex, reason for admission, disease severity, length of stay), outcome (ICU mortality and 60-day mortality), variables related to clinical decisions to limit NBIs (day and type of decision, length of ICU stay before and after the decision, type of interventions that limited) and variables related to economic data (variable and fixed costs).

All decisions to limit non-beneficial interventions were at the discretion of the treating physician(s) on each shift based on international recommendations. They were validated by the entire medical team at their daily meeting. A nurse extracted information about limitations from clinical sessions and medical records and entered them into the ICU database. A non-beneficial intervention was defined as an intervention that did not achieve stabilization or reversal of the patient's clinical condition. Non-beneficial interventions included administration of vasoactive/inotropic drugs, mechanical ventilation, noninvasive ventilation, and renal function replacement therapies. The decision to limit NBIs included the application of withholding (WH) or withdrawal (WD) of one or more interventions. WH was the decision not to initiate or increase one or more interventions, and WD was to discontinue one or more.

Disease severity was calculated using the APACHE IV scale in the first 24 hours after admission. The standardized Mortality Ratio (SMR) was based on APACHE IV predicted death rate.

The microcosting (bottom-up) methodology with a combination of attributable (top-down) was used to calculate costs [15, 16]. Variable costs included costs that depended on the number of inpatients and related to direct patient care (imaging and laboratory tests, drugs, patient consumables). Imaging and laboratory tests were calculated based on the current government prices. Fixed direct costs were defined as those independent of the number of inpatients and related to direct patient care (staff salaries). Fixed indirect costs were those independent of the number of inpatients and do not relate to indirect patient care (cleaning materials, linen, technical materials, stationery, purchase and maintenance of equipment, hospital support services, and depreciation of fixed capital). Direct variable costs were calculated using the microcosting (bottom-up) method by counting each activity performed (imaging and laboratory tests, drugs, consumables) at the patient level. However, the costs of the variable subcategories (drugs, consumables, and tests) of the daily costs were calculated cumulatively for each patient and then allocated according to the length of stay.

Furthermore, for patients with NBIs, limitation decisions were calculated before and after the decision

date and then distributed according to the days of stay of each patient, before and after the decision date. In contrast, indirect fixed costs (hospital support services, purchase and maintenance of equipment) were calculated using the top-down costing method for the specified period and allocated proportionally to each patient's length of stay (number of days). Direct fixed costs were calculated by counting the monthly salary for each personnel of the ICU, summarized, and then distributed according to the length of stay of each patient. The total cost per patient was obtained by summing each patient's three categories (variable, fixed direct, and fixed indirect costs). All costs were calculated based on the prices of the starting year of the study in the current European common currency (euro).

### Statistical analysis

Categorical variables were expressed in absolute frequencies and percentages, while continuous variables were expressed in means, standard deviations, median, and interquartile ranges. The normality assumption was evaluated using the Kolmogorov-Smirnov criterion. Parametric and nonparametric criteria (Chi-squared test, Mann-Whitney U test) were used to correlate the groups of patients with and without limitation decisions and the differences in demographic and clinical characteristics. Wilcoxon signed-rank test was used to conduct a paired difference test of repeated measurements (costs before and after limitation decisions). In all cases, 5% or less (p-value<0.05) was statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (IBM SPSS) version 25.0.

## Results

Decisions to limit NBIs were made in 164 (36.12%) patients (Figure 1). The baseline characteristics of the patients were described in detail in Tables 1, 2.

The NBIs most often limited were vasoactive drugs (78,0%) and invasive mechanical ventilation (57,9%) (Table 3). The total cost of all patients for the study period was 3.835.933,83€. Variable, direct, and indirect fixed costs accounted for 36.7%, 50.4%, and 12.8% of the total ICU costs, respectively. The total cost (Figure 2) of patients without limitation of NBIs was 2,328,543€, while for the patients with limitation of NBIs, it was 1,507,391€, a difference of 821,000€. The cost per patient was, both as a whole and in its categories (variable, fixed), higher in the group of patients with a decision to limit NBIs (Table 1). All cost categories, including the average daily cost after the limitation of NBIs, were reduced to a statistically significant degree (p<0.001) (Table 4). The total cost of the patients with the limitation of NBI was 1,105,262.13€ before the decision, while after the decision, it was 402,129.22€.

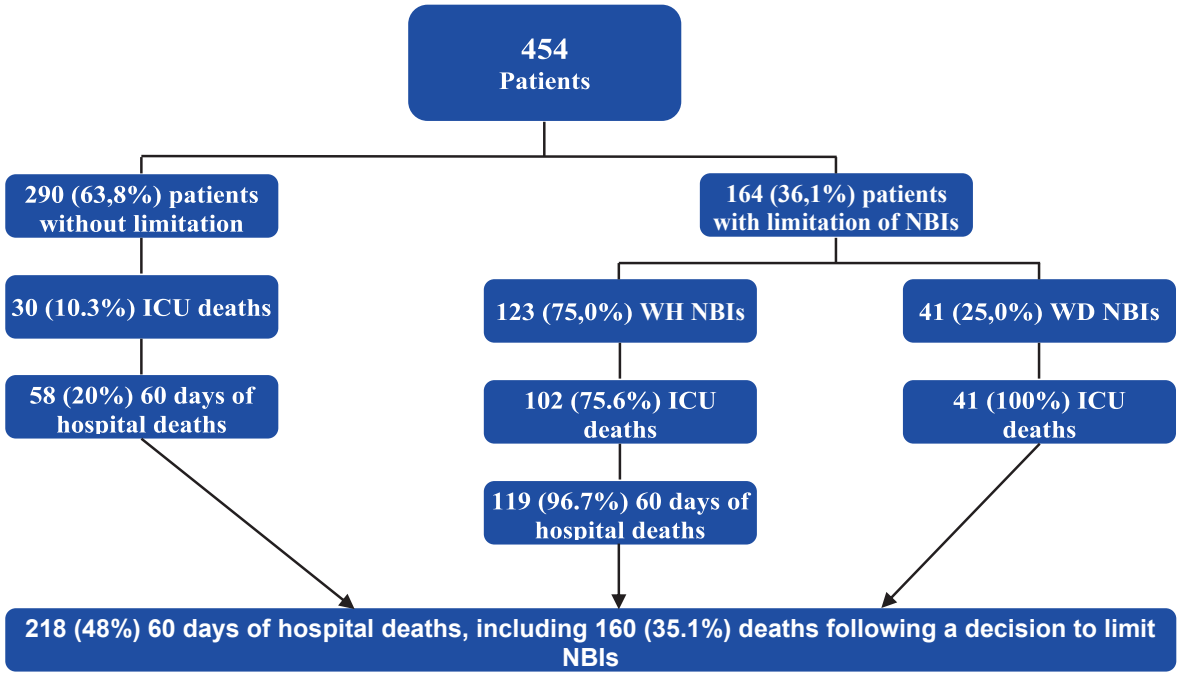



**Fig.1. Patient flow chart**

**Table 1. Patients' characteristics**

| Patients' characteristics | All patients (N=454) | Patients with no limitation of NBIs (N=290) | Patients with limited NBIs (N=164) | P-value |
|---|---|---|---|---|
| Gender – Male, n (%) | 304 (67,0) | 195 (67,2) | 109 (66,5) | 0,866 |
| Age, median (IQR) | 65 (21) | 62 (22) | 70 (14) | 0,000 |
| APACHE IV, median (IQR) | 58 (35) | 50 (31) | 71 (42) | 0,000 |
| APACHE IV PDR, median (IQR) | 28,4 (36,6) | 17,35 (27,2) | 48,9 (31,9) | 0,000 |
| LOS, median (IQR) | 5 (12) | 4,5 (11) | 7 (13) | 0,004 |
| **Reason for admission n (%)** | | | | |
| Surgery | 99 (21,81) | 92 (31,7) | 7 (4,3) | 0,001 |
| Acute respiratory failure (COVID-19) | 95 (20,93) | 41 (14,1) | 54 (32,9) | 0,001 |
| Acute Respiratory Failure | 59 (13) | 41 (14,1) | 18 (11,0) | 0,385 |
| Traumatic brain injury | 43 (9,47) | 22 (7,6) | 21(12,8) | 0,094 |
| Nontraumatic CNS injuries | 43 (9,47) | 25 (8,6) | 18 (11,0) | 0,409 |
| Cardiac arrest | 33 (7,27) | 11 (3,8) | 22 (13,4) | 0,001 |
| Sepsis | 25 (5,51) | 11 (3,8) | 14 (8,5) | 0,052 |
| Multiple trauma | 18 (3,96) | 17 (5,9) | 1 (0,6) | 0,005 |
| Multiple trauma (with TBI) | 14 (3,08) | 9 (3,1) | 5 (3,0) | 0,607 |
| Other | 25 (5,51) | 21 (7,2) | 4 (2,4) | 0,033 |
| **Comorbidities at ICU admission n (%)** | | | | |
| Chronic pulmonary disease | 72 (15,9) | 36 (12,4) | 36 (22,0) | 0,011 |
| Cardiovascular disease | 134(29,5) | 80 (29,5) | 54 (32,9) | 0,412 |
| Chronic kidney disease | 26 (5,7) | 8 (2,8) | 18 (11,0) | 0,001 |
| Hypertension | 170 (37,4) | 96 (33,1) | 74 (45,1) | 0,012 |
| Disorders of thyroid gland | 31 (6,8) | 20 (6,9) | 11 (6,7) | 0,553 |
| Diabetes mellitus | 88 (19,4) | 46 (15,9) | 42 (25,6) | 0,014 |
| Cancer | 39 (8,6) | 26 (9,0) | 13(7,9) | 0,862 |
| Obesity | 22 (4,8) | 11 (3,8) | 11 (6,7) | 0,177 |
| Other | 186 (41,0) | 128 (44,1) | 58 (35,4) | 0.074 |
| ICU mortality, n (%) | 173 (38,1) | 30 (10,3) | 143 (87,2) | 0,000 |
| 60 days hospital mortality, n (%) | 218 (48,0) | 58 (20,0) | 160 (97,6) | 0,000 |
| SMR, 95% Confidence Interval (CI) | 1,18 (0.88- 1.58) | 0,47 (0.28-0.78) | 1,74 (1.55-2.05) | |
| Variable costs per patient, mean (SD) | 3111,87 (4306,06) | 3047,71 (4661,21) | 3226,02 (3599,26) | 0,017 |
| Fixed direct costs per patient, mean (SD) | 4263,75 (5029,56) | 3969,38 (5010,92) | 4798,06 (5047,95) | 0.004 |
| Fixed indirect costs per patient, mean (SD) | 1087,44 (1282,75) | 1012,36 (1278,00) | 1223,72 (1287,44) | 0,004 |
| Total cost per patient, mean (SD) | 8467,85 (10179,37) | 8029,46 (10490,42) | 9247,79 (9582,97) | 0,004 |
| Average daily cost per patient, mean (SD) | 832,10 (163,82) | 832,59 (159,46) | 831,24 (171,80) | 0,716 |

NBIs: Non Beneficial Interventions; APACHE: Simplified Acute Physiology Score; PDR: predicted death rate; LOS: length of stay; SMR: Standardised Mortality Ratio; IQR: Interquartile Range; SD: Standard Deviation; CNS: central nervous system; TBI: Traumatic brain injury.

**Table 2. Length of stay in ICU of patients with limitation of NBIs**

| | Withholding NBIs | | Withdrawing NBIs | |
|---|---|---|---|---|
| LOS (in ICU) | Before decision | After decision | Before decision | After decision |
| N | 123 | | 41 | |
| Mean | 8,93 | 3,94 | 4,12 | 2,49 |
| SD | 10,94 | 4,44 | 3,68 | 2,94 |
| Median | 6 | 2 | 3 | 2 |
| IQR | 12 | 4 | 4 | 3 |
| Min | 1 | 1 | 1 | 1 |
| Max | 64 | 27 | 15 | 17 |
| Sum | 1098 | 485 | 169 | 102 |

LOS: Length of stay; NBIs: Non-Beneficial Interventions

**Table 3. Type of Limited NBIs**

| Limited NBIs (n, %) | (N=164) |
|---|---|
| Vasoactive drugs | 128 (78,0) |
| Invasive mechanical ventilation | 95 (57,9) |
| Noninvasive mechanical ventilation | 27 (16,5) |
| Continuous renal replacement techniques | 17 (10,4) |

NBIs: Non-Beneficial Interventions

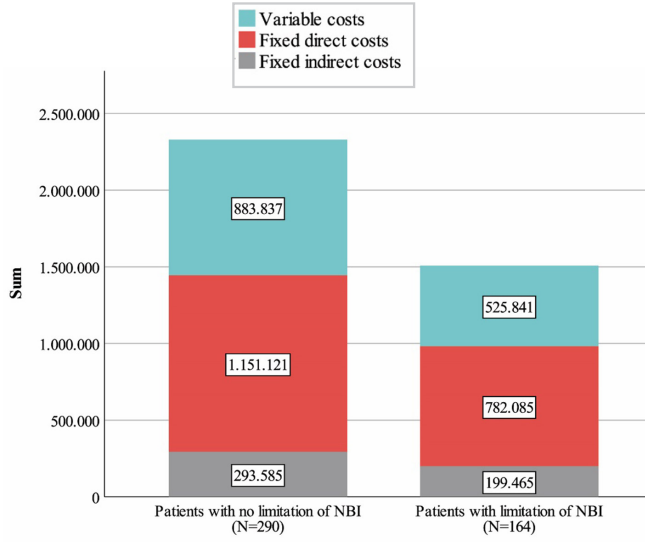



**Fig.2. Total patients cost per category.**

**Table 4. Cost category per patient before and after the limitation of NBIs**

| Cost category per patient | Mean (SD) | P value |
|---|---|---|
| Variable cost (before) | 2666,13 (3306,89) | 0,001 |
| Variable cost (after) | 556,6 (735,3) | |
| Fixed direct costs (before) | 3269,52 (4173,84) | 0,001 |
| Fixed direct costs (after) | 1514,76 (1759,64) | |
| Fixed indirect costs (before) | 833,86 (1064,5) | 0,001 |
| Fixed indirect costs (after) | 366,33 (448,78) | |
| Total cost (before) | 6769,53 (8331,59) | 0,001 |
| Total cost (after) | 2457,7 (2652,68) | |
| Daily cost (before) | 767,31 (405,52) | 0,001 |
| Daily cost (after) | 649,12 (243,14) | |

NBIs: Non-Beneficial Interventions; SD: Standard Deviation

## Discussion

Doctors and nurses in the ICU are constantly faced with the prospect of patient death and often the limitation of NBIs. The most common limitation of treatments in the study sample was withholding of NBIs, followed by withdrawal, which is consistent with the results of previous studies, particularly those from southern Europe, and probably consistent with the cultural background of these countries [17,18]. The positive association between increased age and limited NBIs argues that age was part of the clinical assessment and consideration of other factors that led to these decisions [19, 20, 21].

Patients with limitations of NBIs had a higher disease severity score and a worse prognostic probability of death than patients without limitations of NBIs, and this has been documented by other researchers [5, 20, 21, 22, 23]. Although scoring systems such as APACHE are helpful, they may increase the likelihood of self-fulfilling prophecy by health professionals [24]. The relatively extended length of stay in the ICU before the decision is made, coupled with the increased rate of withholding of NBIs, partially invalidates the self-fulfilling prophecy theory.

In the present study, the length of stay in the ICU of patients with NBIs was longer than that of patients without NBIs [17, 22, 23].

The interpretation of this longer duration is probably due to the exhaustion of treatment options and may partly explain the delay in decisions, especially of WH of NBIs. In contrast, the length of stay and time to decision in patients with withdrawal were shorter. Physicians may have taken imminent death into account, resulting in early avoidance of aggressive interventions that were likely to prolong death and cause suffering. Physicians may perceive the length of stay in the ICU as a prognostic factor when considering making changes to therapeutic targets and indications for treatment [25]. It likely indicates a severe underlying disease, the failure of treatment or lack of treatment options in the context of the increased severity of the disease, or even the fact that these patients were admitted to the ICU for reasons beyond medical necessity. The sunk cost fallacy could also play an essential role in the admission decisions of patients with a low probability of survival. According to this logic, as long as ICU beds are available, they can be used regardless of the patient's survival prospects. This phenomenon has been referred to in the literature as the difficulty of parting with previously invested financial resources, even if these investments' outcomes do not meet expectations [26, 27].

Our study found that limitations of NBIs were applied most frequently in patients with medical rather than surgical conditions. The most significant proportion of patients with limitations of NBIs involved acute respiratory failure (COVID-19), cardiac arrest, and traumatic brain injury. The COVID-19 pandemic abruptly shifted the causes of admission for ICU pa-

tients by becoming the leading cause of admission for an extended period. The non-response of COVID-19 patients to treatment, combined with factors such as severity and age, may have contributed to the limitations of NBIs decisions. Similar results were found in the Flaatten study, where 37% of patients with COVID-19 had life support intervention limitations applied to them. Withholding was the most common limitation, and the 30-day mortality of patients with limitation of NBIs was 79% [28]. Other studies have reported medical causes of admissions as independent predictors of limitation or increased incidence rates [20, 21, 23]. In contrast to surgical patients in our study, limitation decision was low, probably mainly due to their conventional admission to the ICU for safety and controlled awakening [5, 11, 19, 22].

In the present study, as in previous ones, it is found that the limitations of NBIs are associated with a high rate of deaths in the ICU [17, 19, 29, 30]. The fact that 14% of patients survived ICU indicates that limitations of NBIs do not only occur at the end of life. Similarly, it has been reported in other studies that a proportion of patients survive in the ICU after NBIs limitation [17, 23, 31, 32]. These results demonstrate that the quality of remaining life will likely improve without aggressive interventions, as person-centered care persists and is best delivered in an ICU setting where patient/nurse ratios differ from those in a conventional hospital ward. Besides, caring for the "Other" (a term used for the suffering human being) is an ethical imperative for ICU doctors and nurses [33]. The high outcome death rate in patients with limitations indicates the need for early implementation of palliative care measures, especially for patients with extended stays or transfer to other structures capable of continuing it.

The SMR was also higher in patients with limitations of NBIs, which other researchers have noted [22]. The higher SMR is likely due to factors such as the admission of patients to the ICU with increased severity, the negative progression of underlying severe disease, and the development of complications. Although expected, the positive association of mortality and SMR with life support limitations suggests problems with their use as measures of ICU quality, and caution is needed in interpreting their results [34]. In addition, the timing of the COVID-19 pandemic influenced the results to some extent. Mortality prediction tools in COVID-19 patients may have inaccuracies, as disease severity scale scores developed before the pandemic may underestimate severity in these specific patient groups and need to be revised [35, 36].

The cost per patient, both as a whole and in its categories (variable and fixed), was higher in patients with limitations of NBIs than in the group without limitations. This result indicates an increased use of resources by patients with limitations. These results are consistent with other studies regarding the ICU patients' group at the end of life [37, 38, 39, 40]. Costs were likely influenced by factors such as the reason for admission, disease severity, and inability to transfer to another setting of appropriate care. Reducing the use of ICU resources may be feasible in countries where intermediate units and hospital wards provide a high level of care. As a previous study mentioned, dedicated hospice inpatient units are potentially significant sources of bed days and cost savings [41]. The lack of specialized palliative care services in public hospitals in Greece and the lack of suitable alternative models of outpatient healthcare structures to transfer these patients place a heavy burden of end-of-life care on the ICU. Greece is among the countries facing a shortage of palliative care services, often home-based and insufficient to meet the population's needs [42]. The average daily cost per patient found was 832€±163.82€, and these amounts are consistent with previous analyses of ICU costs in European countries [43, 44]. Interestingly, this study's average daily cost per patient showed no differences between the groups. The fact that average daily cost per patient has no differences may be because, as other researchers have found, fixed costs burden the variation in average daily costs - largely dependent on the length of stay - and less by variable costs [ 45,46,47].

In the group of patients with limitations, the length of stay in the ICU after the decision decreased, as other researchers had mentioned [17].

The timing of the decision impacted cost variation, and the type of limitation (WH, WD) may also affect our result. Our results also support the findings in the literature that demonstrate the importance of time limitation. The study by Zhao et al. showed that half of the patients and their relatives made limitation of NBIs decision less than four days after admission to the ICU, resulting in an immediate reduction in length of stay and costs, revealing an overall reduction in ICU resource utilization and out-of-pocket costs for patients and their relatives [48]. Our study showed a reduction of 118€ in ICU daily costs. Buttrick et al. also found an average decrease in ICU charges of 68.929$ per patient

with limitations of NBIs [49]. Bouttell et al. retrospectively cost the limitation of NBIs and found a reduction in hospital costs [12]. However, cost comparisons are difficult because each study uses different calculation methods. Nevertheless, involving palliative care in critically ill patients has been shown to reduce resource overuse and length of stay in hospitals [50, 51, 52, 53].

Shifting care goals from aggressive treatment to comfort care reduced variable and fixed costs in the ICU. According to the results, the total cost of all patients after the limitation was 402,129€. If these patients had been transferred to other care structures after the decision had been taken, these costs would have been avoided. For example, this opportunity cost could have been used to pay the nursing staff in this ICU for one year. At the same time, 587 days of ICU care could have been freed up for other patients with a better survival prospect, as other researchers have also pointed out [41, 54].

These data reveal significant potential cost savings and overall better management of ICU resource utilization. Our study provides essential data on the limitations of NBIs' impact on ICU costs and the potential to avoid such costs. Additionally, our study highlights a lack of care structures for patients nearing the end of life. It underscores the need to create such structures or redefine the role of the ICU to incorporate timely specialized palliative care services. Future healthcare planning decisions should be based on these estimates.

### Limitations

The present study has several limitations. The study was conducted in a single ICU, which limits the findings' generalizability, as the specific unit's care patterns may influence these. The study period coincided with the pandemic outbreak, which may have influenced the results as a proportion of the sample involved patients with COVID-19. The hospitalization of these patients was new to the physicians and nurses in the ICU, and it may have affected the making and timing of containment decisions, costs, and the care of these patients. Also, the reasons that led to the decisions had not been recorded since it was not the main object of our study. We did not record criteria or details about care delivery after limitations. Although no specific palliative care protocol was implemented, care was based on the general principles of palliative care and the principles of humanitarian care that apply in the ICU.

## Conclusion

Our study showed that limiting NBIs in the ICU reduces healthcare costs. The emphasis on identifying cost-effective ways to deliver quality end-of-life care must remain at the forefront of economic and social consciousness. Decisions to limit NBIs in ICU and their impact on ICU resources merit further research as they affect ICU health professionals, the health economy, and society. Education, redesigning clinical protocols, reallocating resources, and establishing national policies are essential to improve the quality of care and maintain dignity at the end of life.

## Conflict of interest

None to declare.

## References

1. Cruz VM, Camalionte L, Caruso P. Factors associated with futile end-of-life intensive care in a cancer hospital. Am J HospPalliat Med 2015;32:329-34.
2. Huynh TN, et al. The opportunity cost of futile treatment in the ICU. Crit Care Med 2014;42:1977-82.
3. Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. N Engl J Med. 2007;356(5):469-478.
4. Sprung CL, Truog RD, Curtis JR, et al. Seeking worldwide professional consensus on the principles of end-of-life care for the critically ill: the consensus for worldwide end-of-life practice for patients in intensive care units (WELPICUS) study. Am J RespirCrit Care Med. 2014;190:855-66.
5. Azoulay E, Metnitz B, Sprung CL, Timsit JF, Lemaire F, Bauer P, et al. End-of-life practices in 282 intensive care units: data from the SAPS 3 database. Intensive care medicine. 2009;35(4):623-30.
6. Lightbody CJ, Campbell JN, Herbison GP, Osborne HK, Radley A, Taylor DR. Impact of a treatment escalation/limitation plan on non-beneficial interventions and harms in patients during their last admission before in-hospital death, using the Structured Judgment Review Method. BMJ open. 2018;8(10):e024264.
7. Ouyang DJ, Lief L, Russell D, Xu J, Berlin DA, Gentzler E, et al. Timing is everything: Early do-not-resuscitate orders in the intensive care unit and patient outcomes. PloS one. 2020;15(2):e0227971.
8. Angus D. Admitting elderly patients to the intensive care unit-is it the right decision? JAMA. 2017;318:1443-1444.
9. Robert R, Skrifvars MB, Ranzani OT. Is this critically ill patient elderly or too old? Intensive care medicine. 2017;43(12):1884-6.

10. Wilcox ME, Vaughan K, Chong CAKY, Neumann PJ, Bell CM. Cost-Effectiveness Studies in the ICU: A Systematic Review. Crit Care Med. 2019;47(8):1011-1017.
11. Wunsch H, Gershengorn H, Scales DC. Economics of ICU organization and management. Critical care clinics. 2012;28(1):25-37.
12. Bouttell J, Gonzalez N, Geue C, Lightbody CJ, Taylor DR. Cost impact of introducing a treatment escalation/ limitation plan during patients' last hospital admission before death. International journal for quality in health care. 2020;32(10):694-700.
13. Chin-Yee N, D'Egidio G, Thavorn K, Heyland D, Kyeremanteng K. Cost analysis of the very elderly admitted to intensive care units. Crit Care. 2017;21(1):109.
14. Brownlee S, Chalkidou K, Doust J, Elshaug AG, Glasziou P, Heath I, et al. Evidence for overuse of medical services around the world. Lancet. 2017;390(10090):156-68.
15. Jegers M, Edbrooke DL, Hibbert CL, Chalfin DB, Burchardi H. Definitions and methods of cost assessment: an intensivist's guide. ESICM section on health research and outcome working group on cost-effectiveness. Intensive care medicine. 2002;28(6):680-5.
16. Tan SS, Bouwmans CA, Rutten FF, et al. Update of the Dutch manual for costing in economic evaluations. Int J Technol Assess Health Care 2012; 28: 152-8.
17. Avidan A, Sprung CL, Schefold JC, Ricou B, Hartog CS, Nates JL, et al. Variations in end-of-life practices in intensive care units worldwide (Ethicus-2): a prospective observational study. The Lancet Respiratory Medicine. 2021;9(10):1101-10.
18. Monteiro NF, Simões I, Gaspar I, Carmo E. Do-not-resuscitate, and treatment limitation decisions - Six years of experience from a Portuguese General Intensive Care Unit. Rev Assoc Med Bras. 2019;65(9):1168-1173.
19. Wilkinson D, Savulescu J. A costly separation between withdrawing and withholding treatment in intensive care. Bioethics. 2014;28(3):127-37.
20. Blazquez V, Rodríguez A, Sandiumenge A, Oliver E, Cancio B, Ibañez M, et al. Factors related to limitation of life support within 48h of intensive care unit admission: A multicenter study. Med Intensiva (Engl Ed). 2019;43(6):352-61.
21. Adamski J, Weigl W, Musialowicz T, Lahtinen P, Reinikainen M. Predictors of treatment limitations in Finnish intensive care units. Acta Anaesthesiologica Scandinavica. 2022;66(4):526-38.
22. Rubio O, Arnau A, Cano S, Subirà C, Balerdi B, Perea ME, et al. Limitation of life support techniques at admission to the intensive care unit: a multicenter prospective cohort study. Journal of intensive care. 2018;6:24.
23. Bertolini G, Boffelli S, Malacarne P, Peta M, Marchesi M, Barbisan C, et al. End-of-life decision-making and quality of ICU performance: an observational study in 84 Italian units. Intensive care medicine. 2010;36(9):1495-504.
24. Lesieur O, Leloup M, Gonzalez F, Mamzer MF. Withholding or withdrawal of treatment under French rules: a study performed in 43 intensive care units. Annals of intensive care. 2015;5(1):56.
25. Wilkinson DJ, Savulescu J. Knowing when to stop: futility in the ICU. Current opinion in anaesthesiology. 2011;24(2):160-5.
26. Siewiera J, Tomaszewski D, Piechocki J, Kübler A. Withholding and withdrawing life-sustaining treatment: Experiences in limiting futile therapy from three Polish intensive care departments. Advances in clinical and experimental medicine. 2019;28(4):541-6.
27. Braverman JA, Blumenthal-Barby JS. Assessment of the sunk-cost effect in clinical decision-making. SocSci Med. 2012;75(1):186-192.
28. Arkes HR, Blumer C. The psychology of sunk cost. Organizational Behavior and Human Decision Processes. 1985;35(1):124-40.
29. Flaatten H, Guidet B, de Lange DW, et al. The importance of revealing data on limitation of life sustaining therapy in critical ill elderly Covid-19 patients. J Crit Care. 2022;67:147-148.
30. 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;322(17):1692-704.
31. Orban JC, Walrave Y, Mongardon N, Allaouchiche B, Argaud L, Aubrun F, et al. Causes and Characteristics of Death in Intensive Care Units: A Prospective Multicenter Study. Anesthesiology. 2017;126(5):882-9.
32. Christensen L, Jensen H, Kristensen S, Goldinger M, Gjedsted J, Christensen S, et al. Treatment limitations in intensive care units. Danish medical journal. 2021;68(8).
33. Ramazzotti D, Clardy P, Celi LA, Stone DJ, Rudin RS. Withholding or withdrawing invasive interventions may not accelerate time to death among dying ICU patients. PLoS One. 2019;14(2):e0212439.
34. Fernandez-Trujillo A, Vallverdu-Cartie H, Roman-Maestre B. Care ethics. A new bioethical approach to humanize the ICU. Medicina intensiva. 2016; 40(8):511-3.
35. Quill CM, Ratcliffe SJ, Harhay MO, Halpern SD. Variation in decisions to forgo life-sustaining therapies in US ICUs. Chest. 2014;146(3):573-82.
36. Kurtz P, Bastos LSL, Salluh JIF, Bozza FA, Soares M. SAPS-3 performance for hospital mortality prediction in 30,571 patients with COVID-19 admitted to ICUs in Brazil. Intensive Care Med.2021;47(9):1047-1049.
37. Stephens JR, Stümpfle R, Patel P, et al. Analysis of Critical Care Severity of Illness Scoring Systems in Patients With Coronavirus Disease 2019: A Retrospective Analysis of Three UK ICUs. Crit Care Med. 2021;49(1):e105-e107.
38. Chaudhuri D, Tanuseputro P, Herritt B, D'Egidio G, Chalifoux M, Kyeremanteng K. Critical care at the end of life: a population-level cohort study of cost and outcomes. Critical Care. 2017;21(1):124.

39. Aung YN, Nur AM, Ismail A, Aljunid SM. Characteristics and outcome of high-cost ICU patients. ClinicoEconomics and outcomes research: CEOR. 2019;11:505-13.

40. Marik PE. The Cost of Inappropriate Care at the end of life: Implications for an Aging Population. The American Journal of hospice & palliative care. 2015;32(7):703-8.

41. Chen B, Fan VY, Chou YJ, Kuo CC. Costs of care at the end of life among elderly patients with chronic kidney disease: patterns and predictors in a nationwide cohort study. BMC nephrology. 2017;18(1):36.

42. Binney ZO, Quest TE, Feingold PL, Buchman T, Majesko AA. Feasibility and economic impact of dedicated hospice inpatient units for terminally ill ICU patients. Critical care medicine. 2014;42(5):1074-80.

43. Lynch T, Connor S, Clark D. Mapping levels of palliative care development: a global update. Journal of Pain and Symptom Management.2013; 45(6):1094-1106.

44. Kosmidis D, Koutsouki S, Lampiri K, NagyEO, Anastassopoulos G, Papaioannou V, Pneumatikos I. Cost evaluation in adult ICU: α two-year study in a Greek state hospital. Health and Research Journal.2021;7(1),39-54.

45. Moerer O, Plock E, Mgbor U, et al. A German national prevalence study on the cost of intensive care: an evaluation from 51 intensive care units. Crit Care 2007;11:R69.

46. Luce JM, Rubenfeld GD. Can health care costs be reduced by limiting intensive care at the end of life? American Journal of respiratory and critical care medicine. 2002;165(6):750-4.

47. Khandelwal N, Benkeser D, Coe NB, Engelberg RA, Teno JM, Curtis JR. Patterns of Cost for Patients Dying in the Intensive Care Unit and Implications for Cost Savings of Palliative Care Interventions. Journal of palliative medicine. 2016;19(11):1171-8.

48. Hicks P, Huckson S, Fenney E, Leggett I, Pilcher D, Litton E. The financial cost of intensive care in Australia: a multicentre registry study. The Medical Journal of Australia. 2019;211(7):324-5.

49. Zhao Q, Zhang X, Fang Y, Gong J, Gu B, Ma G. Current situation and associated factors of withdrawing or withholding life support to patients in an intensive care unit of cancer center in China. PloS one. 2014;9(5):e98545.

50. Buttrick SS, Cajigas I, Achua JK, O'Phelan K, Goodman KW, Benveniste RJ. Prospective Study of Non-beneficial Care in Neurocritical Care Unit. World neurosurgery. 2018;119:e60-e3.

51. Siddiqui ST, Xiao E, Patel S, et al. Impact of Palliative Care on Interhospital Transfers to the Intensive Care Unit. J Crit Care Med (TarguMures). 2022;8(2):100-106.

52. Khandelwal N, Kross EK, Engelberg RA, Coe NB, Long AC, Curtis JR. Estimating the effect of palliative care interventions and advance care planning on ICU utilization: a systematic review. Critical care medicine. 2015;43(5):1102-11.

53. Hua M, Lu Y, Ma X, Morrison RS, Li G, Wunsch H. Association Between the Implementation of Hospital-Based Palliative Care and Use of Intensive Care During Terminal Hospitalizations. JAMA network open. 2020;3(1):e1918675.

54. Ma J, Chi S, Buettner B, Pollard K, Muir M, Kolekar C, et al. Early palliative care consultation in the medical ICU: a cluster randomized crossover trial. Crit Care Med. 2019;47:1707-15.

55. Heydari H. Home-based Palliative Care: A Strategy for Keeping Intensive Care Unit Beds Vacant. International Journal of community based nursing and midwifery. 2016;4(2):186-7.