

Effects of Delayed Initiation of End-of-life Care in Terminally Ill Intensive Care Unit Patients

Anirban H Choudhuri¹, Ankit Sharma², Rajeev Uppal³

ABSTRACT

Introduction: Early initiation of end-of-life (EOL) care in terminally ill patients can reduce the administration of unnecessary medications, minimize laboratory and radiological investigations, and avoid procedures that can provoke untoward complications without substantial benefits. This retrospective observational study was performed to compare early vs late initiation of EOL care in terminally ill ICU patients after the recognition of treatment futility.

Materials and methods: The medical records of all patients who were considered to be terminally ill any time after ICU admission between January 2014 and December 2018 were extracted from the ICU database. The patients who were recognized for treatment futility were eligible for inclusion. The patients who were already on EOL care prior to the ICU admission or whose diagnosis was unconfirmed were excluded from the study. The treatment futility was a subjective decision jointly undertaken by the primary physician and the intensivist based upon the disease stage and the available therapeutic options. The commencement of EOL care after recognition of treatment futility was divided into (a) early group (EG)—within 48 hours of decision of treatment futility and (b) late group (LG)—after 48 hours of recognition of treatment futility. Both the groups were compared for (a) ICU mortality, (b) length of ICU stay, (c) number of antibiotic-free days, (d) number of ventilator-free days, (e) number of medical and/or surgical interventions (insertion of central lines, drains, IABP, etc.), (f) number of blood and radiological investigations, and (g) satisfaction level of family members.

Results: Out of 107 terminally ill patients with diagnosis of treatment futility, 64 patients (59.8%) underwent early initiation of EOL against delayed initiation in 43 (40.2%) patients (1.3 ± 0.4 days vs 5.1 ± 1.6 days; $p = 0.01$). The patients in the late initiation group were younger in age (49 ± 3.6 years vs 66 ± 5.3 years; $p = 0.03$). The number of antibiotic-free days was higher in the early initiation group (12 ± 5.2 days vs 6 ± 7.5 ; $p = 0.02$). The number of medical and surgical interventions was lesser in the early initiation group (3.0 ± 0.7 episodes vs 12 ± 3.9 episodes; $p = 0.007$). The late initiation of EOL was caused by prognostic dilemma (30.2%), reluctance of the family members (44.1%), ambivalence of the primary physician (18.6%), and hesitancy of the intensivist (6.9%). The satisfaction level of the family members was similar in both the groups.

Conclusion: We conclude that delayed initiation of EOL care in terminally ill ICU patients after recognition of treatment futility can increase the antibiotic usage and medical and/or surgical interventions with no effect on the satisfaction level of the family members.

Keywords: Do not activate cardiopulmonary resuscitation, End-of-life care, Ethical issues.

Indian Journal of Critical Care Medicine (2020); 10.5005/jp-journals-10071-23454

INTRODUCTION

The demand for intensive care unit (ICU) beds exceeds supply in most parts of the world. This is true even in ICUs with high fatality rates.^{1,2} The early initiation of end-of-life (EOL) care in terminally ill ICU patients can reduce this gap. It also ensures many other benefits, viz., avoidance of unnecessary therapeutic interventions, reduced patient suffering, and less social and economic burden to the society. But the commencement of EOL care is often delayed due to various reasons, viz., lack of will or experience of the doctors, disagreement between the intensivist and primary physician toward initiation of EOL, benefit expectations from nonconventional therapies by the patients' relatives, and their nonacceptance in the hope for spontaneous miraculous recovery.³⁻⁵

This retrospective study of prospectively collected data was conducted to investigate the factors responsible for delay in the initiation of EOL care after recognition of treatment futility.

The aim of the study was to compare the early initiation of EOL against the late initiation of EOL in terms of following outcomes in the ICU mortality, length of stay, severity of disease at admission, antibiotic consumptions, medical and surgical interventions performed, laboratory and radiological investigations undertaken, and family satisfaction at discharge (or death) from ICU.

¹⁻³Department of Anesthesiology and Intensive Care, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research, New Delhi, India

Corresponding Author: Anirban H Choudhuri, Department of Anesthesiology and Intensive Care, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research, New Delhi, India, Phone: +91-11-43037408, e-mail: anirbanhc@rediffmail.com

How to cite this article: Choudhuri AH, Sharma A, Uppal R. Effects of Delayed Initiation of End-of-life Care in Terminally Ill Intensive Care Unit Patients. *Indian J Crit Care Med* 2020;24(6):404-408.

Source of support: Nil

Conflict of interest: None

MATERIALS AND METHODS

The study was conducted in the seven-bedded mixed medical surgical ICU of a university teaching hospital in India. After obtaining approval for waiver of informed consent from the institution ethics committee, the medical records of all consecutive patients who were admitted between January 2014 and December 2018 and were recognized as terminally ill at any time after ICU admission were

extracted from the ICU database. In order to determine terminal illness, all the files were independently reviewed by each of the three investigators subjectively and only those patients where at least two out of the three investigators were in agreement about the terminal nature of illness from the attached medical notes were considered as terminally ill.

The patients who were identified for treatment futility after ICU admission were only eligible for inclusion. The treatment futility was a subjective decision jointly between the primary physician and the intensivist after considering the disease stage, presence of comorbid illnesses, available therapeutic options, and the likelihood of response to treatment.

The patients already under EOL care prior to the ICU admission and those with unknown primary disease were excluded from the study.

The EOL care routinely consisted of either no initiation or escalation (if already initiated) of ventilatory support, no initiation or escalation (if already initiated) of inotropic or vasopressor drugs, no initiation or escalation (if already initiated) of antibiotic therapy, no major therapeutic interventions (CRRT, ECMO, etc.), no cardiopulmonary resuscitation (CPR), and continuation of all medications for supportive care and comfort. Minor interventions like insertion of chest drain, abdominal paracentesis, etc., performed for symptomatic relief were allowed.

Prognostic dilemma was considered when there was disagreement between the primary physician and the intensivist with regard to treatment futility.

The commencement of EOL care after recognition of treatment futility was divided into (a) early group (EG)—within 48 hours of decision of treatment futility and (b) late group (LG)—after 48 hours of recognition of treatment futility. The cutoff value of 48 hours was calculated on the basis of median time for the initiation of EOL among all patients.

Both the groups were compared for (a) ICU mortality, (b) length of ICU stay, (c) number of antibiotic-free days, (d) number of ventilator-free days, (e) number of medical and/or surgical interventions (insertion of central lines, drains, IABP etc.), (f) number of blood and radiological investigations, and (g) satisfaction level of family members.

In all patients on EOL, treatment was limited. In none of the patients, treatment was withdrawn. No patient left the hospital against medical advice (LAMA).

The number of patients' family satisfied with EOL care was derived from the retrieved medical records noted during family counseling at the time of discharge (or death) from the ICU. The patients' relatives who expressed satisfaction with the decision for EOL and the overall EOL care were categorized as "satisfied" and those who regretted the decision for EOL and/or were unhappy with EOL care were categorized as "dissatisfied." The satisfaction level of the legal guardian of the patient was only considered.

All statistical analysis was performed using the software SPSS 24.0 (SPSS, Inc., Chicago, IL, USA). Mean (SD), median (interquartile range), and percentage values were used to summarize baseline characteristics and outcome data. Results were expressed as the mean \pm SD and percentage when appropriate. $p < 0.05$ was considered significant. χ^2 tests were used to compare proportions. The paired t -test and the Fischer exact test were used to compare outcomes in the two groups.

RESULTS

A total of 107 terminally ill patients were recognized for treatment futility during this period of whom 64 patients (59.8%) underwent early initiation of EOL (EG) against delayed initiation (LG) in 43 (40.2%) patients (1.3 ± 0.4 days vs 5.1 ± 1.6 days; $p = 0.01$) (Table 1). The demography and baseline clinical features of patients in both the groups were similar except that the patients in the LG group were younger in age (49 ± 3.6 years vs 66 ± 5.3 years; $p = 0.03$) (Table 1).

There was no difference between the groups with regard to disease severity, duration of ICU stay, and ICU mortality (Table 1).

The number of antibiotic-free days was higher in the EG group (12 ± 5.2 days vs 6 ± 7.5 ; $p = 0.02$) (Table 2). The number of medical and surgical interventions performed was also less in the EG group (3.0 ± 0.7 episodes vs 12 ± 3.9 episodes; $p = 0.007$) (Table 2). The satisfaction level of the patients' family members was similar in both the groups (Table 2).

The late initiation of EOL was caused by prognostic dilemma (30.2%), reluctance of the family members to accept EOL care (44.1%), ambivalence of the primary physician to start EOL care (18.6%), and hesitancy of the intensivist to start EOL care (6.9%) (Fig. 1).

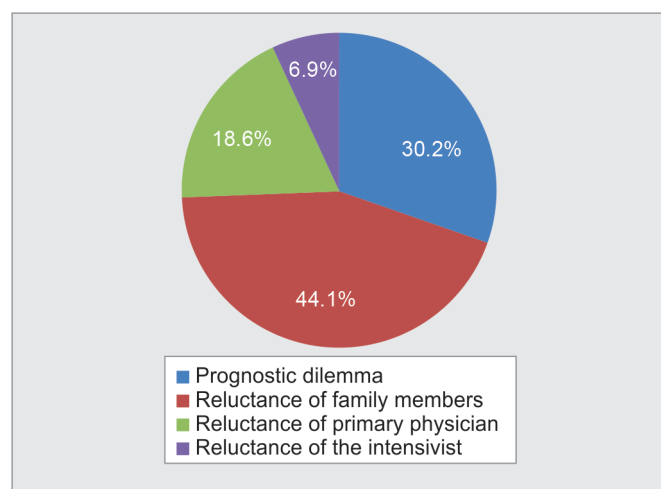
Table 1: Demography and clinical features of terminally ill patients

	EG (n = 64)	LG (n = 43)	p value
Age (mean \pm SD) (years)	66 \pm 5.3	49 \pm 3.6	0.03*
Sex (M/F)	45/19	26/17	0.12
Primary disease			
• Stoke	16	10	0.06
• TBI	5	4	0.09
• Heart failure	9	3	0.07
• Respiratory failure	13	12	0.26
• Liver failure	17	6	0.34
• Malignancy	18	11	0.15
• Sepsis	36	29	0.28
• Multiorgan failure	47	22	0.06
Comorbid diseases			
• CVS disease	22	12	0.18
• Hypertension	34	14	0.23
• Diabetes	19	16	0.14
• Renal disease	07	04	0.09
• Thyroid disease	05	02	0.07
• COPD, asthma	12	06	0.12
APACHE II score (mean \pm SD)	24 \pm 11.3	21 \pm 4.6	0.14
Onset of EOL care after diagnosis of treatment futility (mean \pm SD)	1.3 \pm 0.4	5.1 \pm 1.6	0.01*
Duration of ICU stay (mean \pm SD) (days)	19 \pm 9.5	24 \pm 6.4	0.08
ICU mortality (%)	58 (90.6%)	35 (81.3%)	0.10
Duration between initiation of EOL and death (mean \pm SD) (days)	6.1 \pm 2.4	4.9 \pm 1.8	0.20

*Significant

Table 2: Comparison between EG and LG groups in terms of outcome

	EG (n = 64)	LG (n = 43)	p value
Number of antibiotic-free days (mean ± SD)	12 ± 5.2	6 ± 7.5	0.02*
Number of ventilator-free days	11 ± 4.7	10 ± 8.3	0.07
Number of surgical and medical interventions (CVP lines, percutaneous drains, IABP)	3.0 ± 0.7	12 ± 3.9	0.007*
Number of laboratory and radiological investigations	30 ± 8.1	38 ± 4.2	0.09
Satisfaction level of patient family members (%)	45 (70.3%)	29 (67.4%)	0.18

**Fig. 1:** Causes of delayed initiation of end-of-life

DISCUSSION

Our study found a large proportion of patients with delayed commencement of EOL care in the ICU after the recognition of treatment futility. It is reported in the literature that the timely institution of EOL care in ICU is more dependent on the successful assessment of patients' clinical condition, adroit professionalism, proper communication, and is not essentially marred by legal hurdles or ethical compulsions.⁶ Although this is true that the practice of EOL in terminally ill patients is subject to be influenced by the prevailing legislations of the state, the fact remains that such legislations are unlikely to inhibit the EOL practice if adequate knowledge sharing is practiced between the primary physician and intensivist to arrive upon a consensus decision and a diligently drafted communication policy is adopted for securing consent from the patients' family members.^{7,8} The main impediment for early EOL care in our study was reluctance on part of the family members of the patient toward EOL acceptance. The communication techniques for facilitating family members' acceptance of EOL care are akin to any other ICU procedures that entail planning, practice, preparation, and skill.⁸ In our ICU, the communication for EOL care is routinely undertaken by the senior consultant. However, since patients' relatives were counseled by doctors with variable proficiency and experience in their persuasive skills, the higher rate of delayed initiation of EOL in our study might have occurred due to greater number of counseling sessions getting performed by doctors of

less persuasive skill. However, this is only speculation as the data for the same are not available.

The second cause for late initiation of EOL care in our study was the existence of diagnostic dilemma. Even after extensive literature search, we were unable to find sufficient evidence to correlate diagnostic dilemma with late initiation of EOL care. But it is established that the diagnostic strategy most commonly adopted for ICU patients is of hypothetical-deductive model where case-based discussions led by senior physicians are analyzed and distilled down to one or two possible diagnoses and then differentiated by a key test or maneuver.⁹ This hypothetical-deductive method incorporates a dynamic and probabilistic view of potential diagnoses and seeks information to adjust for the relative probabilities of competing hypotheses. In the ICU, this falters when too many physicians are involved in the acquisition of information without using it for the meaningful course of action. The situation is common when multiple referrals from different departments are sought for a patient triggering a lot of unfocused activity. This may be partly true for our ICU, although data for conclusive support are lacking in our study.^{10,11}

The third cause of delayed initiation of EOL care was reluctance of the primary physician to commence EOL despite recognizing treatment futility. It is reported that physicians vary a great deal in their assessment of the available nonpalliative treatments for the patients and many are reluctant to discuss EOL till the exhaustion of all possible options. It is also reported that physicians vary in their capacity and consistency to appreciate the patients or their relatives' willingness for EOL care and are hesitant to discuss EOL with family members until they are sure about maximum receptivity. They rely on their instincts for the same.¹²⁻¹⁴ Since our primary physicians are from diverse specialties with variable attitude toward EOL, the delay in initiation of EOL care can be explained on this variation in discriminatory capacity.

The last cause for delayed initiation of EOL care in our study was inhibition on the part of intensivists to initiate the same. The factors applicable for the primary physician are equally relevant for the intensivists though to a less degree, depending upon their understanding and experience. It is observed that many intensivists overestimate survival and some are skeptical about the benefits of EOL care.^{15,16}

Our study found a delayed initiation of EOL care in the younger patients and this may be explained by the greater uncertainty and slower acceptance of EOL in this group. Since the experiences and preferences for EOL are consistent with the developmental age, certain cognitive and psychological changes in the young are likely to generate much more negative emotions, viz., grief, despair, anger, etc., in their relatives, which impede early initiation of EOL.^{17,18}

Our study has found a greater number of antibiotic-free days and lesser number of medical and/or surgical interventions in the early EOL group. While this is a logical expectation without much need for broader explanation, it is important to note that antibiotics lead to symptomatic relief in only 33% of patients with advanced cancer during the last several weeks of life and in an even meager proportion of patients (9.2%) in the last week of life.¹⁹ Despite this, about 64% of terminally ill ICU patients receive antibiotics till they die and some get even after consenting for "do not resuscitation" orders.²⁰ It is important to realize the perils of antibiotic administration in terminal illness and carefully weigh the potential risks against the possible benefits. The occurrence of adverse effects and risk for drug interactions are more common

during terminal illness and increasing cost is a serious constraint. Moreover, antimicrobial use increases the risk of multidrug-resistant organism (MDRO) colonization and causes psychological burden to the patient during implementation of infection-control measures, viz., patient isolation. This is in perpetual conflict with the goals of EOL care where infection is often seen as a "natural" cause of "dying" process not always requiring treatment.

The less number of medical and/or surgical interventions in the early group also do not require elaborate explanation as they conform to the standard practices and guidelines of EOL care.²¹

Our study found no difference between the early and late groups in the satisfaction level of the family members during discharge (or death) from ICU. It is reported in studies that the level of satisfaction after EOL is dependent on accessibility and coordination, effective symptom management, comfort level with the dying process, education and communication, emotional support, care on the individual level, and support of patients' decision-making.²²⁻²⁴ Therefore, the apprehension that the prospect of EOL care can lead to discontentment or displeasure among the family members is grossly unfounded. Although many studies have tried to identify the areas for improving the level of satisfaction of the family members, they are unable to find any single reasonable method that can be representative of all patient population. Hence, what we can infer from our finding and what is also in concordance with the results of other studies is that EOL care may be improved by targeting a select number of high-impact aspects of care, such as doctor availability, caring for patients in the absence of family members, the healthcare team working together as a cohesive team, and attentively listening to the needs of patients and their families.^{25,26} However, it is true that nearly 30% of our patients were overall dissatisfied with EOL care. This may be because of the subjective nature of assessment of the satisfaction level performed in our study based on counseling notes.

Our study had a few limitations. One, this study was conducted without calculation of sample size. The sample size calculation requires several statistically accurate inputs that are not available in the literature. Alternately, a pilot study could have been conducted to derive these inputs and measure the sample size. However, due to logistic problems of conducting a pilot study on these patients and also for the reason that sample size calculation is not mandatory in observational studies, we opted for a sample of convenience, which according to our belief is sufficiently large. Two, the patient satisfaction level in our study was derived from the available medical records that were noted during counseling during their ICU stay. We chose the notes obtained at the time of discharge (or death) to identify the patients' relatives who were satisfied or dissatisfied with EOL care. While this can represent a snapshot view, more objective measurement based on a valid questionnaire would have provided more accurate results. Third, all the inherent drawbacks of a retrospective observational study can be existent in our study. Despite these, this is one of the very few studies undertaken and certainly the first from India to find a correlation between treatment futility and EOL care in a mixed medical-surgical ICU.

To conclude, our study suggests that delayed initiation of EOL care in terminally ill ICU patients reduces the number of antibiotic-free days and increases the medical and/or surgical interventions without affecting the satisfaction level of the family members. However, more prospective studies are required to validate these findings in homogeneous group of patients.

REFERENCES

1. Iwashyna TJ, Kramer AA, Kahn JM. Intensive care unit occupancy and patient outcomes. *Crit Care Med* 2009;37(5):1545-1557. DOI: 10.1097/CCM.0b013e31819fe8f8.
2. Tanaka Gutiez M, Ramaiah R. Demand versus supply in intensive care: an ever-growing problem. *Crit Care* 2014;18(Suppl 1):P9. DOI: 10.1186/cc13199.
3. Woo JA, Maytal G, Stern TA. Clinical challenges to the delivery of end-of-life care. *Prim Care Companion J Clin Psychiatry* 2006;8(6):367-372. DOI: 10.4088/pcc.v08n0608.
4. Jensen HI, Ammentorp J, Johannessen H, Ørding H. Challenges in end-of-life decisions in the intensive care unit: an ethical perspective. *J Bioeth Inq* 2013;10(1):93-101. DOI: 10.1007/s11673-012-9416-5.
5. Coombs MA, Addington-Hall J, Long-Suthehall T. Challenges in transition from intervention to end of life care in intensive care: a qualitative study. *Int J Nurs Stud* 2012;49(5):519-527. DOI: 10.1016/j.ijnurstu.2011.10.019.
6. van der Werf TS, Zijlstra JG, Ligtenberg JJ, Tulleken JE. Decisions around the end of life on intensive care: making the transition from curative to palliative treatment. *Ned Tijdschr Geneesk* 2005;149(14):742-746.
7. Clements JM. Patient perceptions on the use of advance directives and life prolonging technology. *Am J Hosp Palliat Care* 2009;26(4):270-276. DOI: 10.1177/1049909109331886.
8. Bernal EW, Marco CA, Parkins S, Buderer N, Thum SD. End-of-life decisions: family views on advance directives. *Am J Hosp Palliat Care* 2007;24(4):300-307. DOI: 10.1177/1049909107302296.
9. Lighthall GK, Vazquez-Guillamet C. Understanding decision making in critical care. *Clin Med Res* 2015;13(3-4):156-168. DOI: 10.3121/cmr.2015.1289.
10. Kushniruk A, Patel V, Fleiszer D. Analysis of medical decision making: a cognitive perspective on medical informatics. *Proc Annu Symp Comput Appl Med Care* 1995. 193-197.
11. Patten VL, Zhang J, Yoskowitz NA, Green R, Sayan OR. Translational cognition for decision support in critical care environments: a review. *J Biomed Inform* 2008;41(3):413-431. DOI: 10.1016/j.jbi.2008.01.013.
12. Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. *N Engl J Med* 2002;346(14):1061-1066. DOI: 10.1056/NEJMs012528.
13. Teno JM, Fisher ES, Hamel MB, Coppola K, Dawson NV. Medical care inconsistent with patients' treatment goals: association with 1-year medicare resource use and survival. *J Am Geriatr Soc* 2002;50(3):496-500. DOI: 10.1046/j.1532-5415.2002.50116.x.
14. Wright AA, Katz IT. Letting go of the rope—aggressive treatment, hospice care, and open access. *N Engl J Med* 2007;357(4):324-327. DOI: 10.1056/NEJMp078074.
15. Choudhry NK, Fletcher RH, Soumerai SB. Systematic review: the relationship between clinical experience and quality of health care. *Ann Intern Med* 2005;142(4):260-273. DOI: 10.7326/0003-4819-142-4-200502150-00008.
16. Covinsky KE, Fuller JD, Yaffe K, Johnston CB, Hamel MB, Lynn J, et al. Communication and decision-making in seriously ill patients: findings of the SUPPORT project. the study to understand Prognoses and preferences for outcomes and risks of treatments. *J Am Geriatr Soc* 2000;48(S1):S187-S193. DOI: 10.1111/j.1532-5415.2000.tb03131.x.
17. Cataudella DA, Zelcer S. Psychological experiences of children with brain tumours at end of life: parental perspectives. *J Palliat Med* 2012;15(11):1191-1197. DOI: 10.1089/jpm.2011.0479.
18. Barling JA, Stevens JA, Davies KM. The reality of hospitalisation: stories from family members of their hospital experience for adolescents and young adults living with and dying from cancer. *Contemp Nurse* 2014;46(2):150-160. DOI: 10.5172/conu.2014.46.2.150.
19. Nakagawa S, Taya Y, Okamoto Y, Tsuneto S, Goya S, Tanimukai H, et al. Can anti-infective drugs improve the infection-related symptoms of patients with cancer during the terminal stages of their lives? *J Palliat Med* 2010;13(5):535-540. DOI: 10.1089/jpm.2009.0336.

20. Oh DY, Kim JH, Kim DW, Im SA, Kim TY, Heo DS, et al. Antibiotic use during the last days of life in cancer patients. *Eur J Cancer Care* 2006;15(1):74–79. DOI: 10.1111/j.1365-2354.2005.00603.x.
21. Silverberg LI. Survey of medical ethics in US medical schools: a descriptive study. *J Am Osteopath Assoc* 2000;100(6):373–378.
22. Dy SM, Shugarman LR, Lorenz KA, Mularski RA, Lynn J. RAND-southern California evidence-based practice center. A systematic review of satisfaction with care at the end of life. *Am Geriatr Soc* 2008;56(1):124–129. DOI: 10.1111/j.1532-5415.2007.01507.x.
23. Heyland DK, Cook DJ, Rocker GM, Dodek PM, Kutsogiannis DJ, Skrobik Y, et al. Canadian researchers at the end of life network (CARENET). Defining priorities for improving end-of-life care in Canada. *CMAJ* 182(16):E747–E752. DOI: 10.1503/cmaj.100131.
24. Dodek PM, Heyland DK, Rocker GM, Cook DJ. Translating family satisfaction data into quality improvement. *Crit Care Med* 2004;32(9):1922–1927. DOI: 10.1097/01.ccm.0000139920.53790.61.
25. Diffin J, Spence M, Spencer R, Mellor P, Grande G. Involving healthcare professionals and family carers in setting research priorities for end-of-life care. *Int J Palliat Nurs* 2017;23(2):56–59. DOI: 10.12968/ijpn.2017.23.2.56.
26. Chan RJ, Webster J. End-of-life care pathways for improving outcomes in caring for the dying. *Cochrane Database Syst Rev* 2013(11):CD008006. DOI: 10.1002/14651858.CD008006.pub3.