

1 **Prognostic factors for 30-days mortality in eighty years aged and older critically ill**
2 **patients: a single center retrospective cohort study**

3 **Abstract**

4 **Background/aim:** Nowadays, with the rise in average life expectancy, the rate of
5 hospitalization of the older population in intensive care unit (ICU) is gradually increasing.
6 Unfortunately, there are no ideal combination of prognostic factors predicting the
7 mortality in older patients admitted to the ICU. In the present study, we aim to determine
8 the prognostic factors and their impacts on short-time mortality in older critically ill
9 patients.

10 **Materials and methods:** This retrospective cohort study was performed between January
11 2019 and February 2020. We included 133 patients aged ≥ 80 years and hospitalized ≥ 24
12 hours in the ICU.

13 **Results:** A total of 133 critically ill patients enrolled in the present study. And, the median
14 age of the patients was 85 (80-106) years. 30-days and overall ICU mortality rates were
15 found 30.1% and 34.6% respectively. The patients were grouped as survivors (n=94) and
16 non-survivors (n=39). Hospital length of stay before the ICU admission was found
17 significantly longer in non-survivors (p=0.001). Sequential Organ Failure Assessment
18 (SOFA) score and Acute Physiology and Chronic Health Evaluation-II (APACHE-II)
19 score were significantly higher in non-survivors (p<0.001, p<0.001). Also, blood lactate
20 level and glucose level were respectively significantly higher in non-survivors (p<0.001,
21 p=0.006). We found that modified Nutrition Risk in Critically Ill (mNUTRIC) score and

1 prehospital Clinical Frailty Scale (CFS) were independent prognostic factors for the older
2 critically ill patients (HR=9.19, 95% CI=1.47-57.32, p=0.018, HR=20.16, 95% CI=2.63-
3 54.07 p=0.004).

4 **Conclusion:** mNUTRIC score and prehospital CFS score were the most important
5 prognostic factors in the admission of older patients to intensive care units.

6 **Key words:** Older, ICU, frailty, modified nutric score, prognostic factors, mortality

7 **1. Introduction**

8 As a result of decrease in mortality and childbirth rates in the worldwide, the world
9 population getting older. With the rising life expectancy, the number of older patients
10 admitted to medical services has been rising in countries with a growing population due
11 to the increased prevalence of chronic morbidity and functional impairment.
12 Consequently, the admission rates of the older patients to the intensive care unit (ICU)
13 have increased [1-5].

14 Currently, there are no ideal combination of prognostic factors predicting the mortality in
15 older patients admitted to the ICU. Although, it has been thought that mortality increases
16 in parallel with the age of patients who are admitted to the ICU, recent clinical studies
17 also shown that age is not a crucial prognostic factor for mortality in older patients [3,4,6].

18 In addition, traditional disease severity scoring systems may not be able to predict the
19 mortality in older patients admitted to the ICU. Because, these scoring systems may not
20 provide significant data about a patient's prehospital clinical status, such as cognitive
21 impairment, decreased functional capacity, and frailty. These prehospital data may be

1 important markers of mortality and morbidity, especially in the older patients admitted to
2 the ICU. For this reason, there is a need for specific scoring systems that can be used in
3 older patients instead of traditional scoring systems that improve better outcomes [6-8].
4 Considering the above, in the present study, we aimed to evaluate the clinical
5 characteristics and outcomes of the older critically ill patients, and also determine the
6 prognostic factors and their impacts on 30-days overall mortality.

7 **2. Materials and methods**

8 **2.1. Study design**

9 This single-center retrospective cohort study was performed in a 12-beds adult tertiary
10 ICU of Malatya Training and Research Hospital between January 2019 and February
11 2020. A total of 717 patients were admitted to the ICU during the study period. A total of
12 222 patients aged 80 years and older in the ICU were assessed for eligibility. Of these, 89
13 were excluded from the study due to various reasons. And a total of 133 patients were
14 enrolled in the study (Figure 1).

15 **2.2. Data collection and definitions**

16 The following data were recorded and analyzed: all patients' demographic and clinical
17 data, laboratory findings, types of respiratory support, the reason for admission,
18 admission source, treatment options, hospital length of stay (LOS) before ICU admission,
19 ICU length of stay (LOS), outcomes, scores on the Acute Physiology and Chronic Health
20 Evaluation-II (APACHE-II) and Sequential Organ Failure Assessment (SOFA), modified
21 Nutrition Risk in Critically Ill (mNUTRIC) and Clinical Frailty Scale (CFS). Patients'

1 data and scores reported in this study were collected within the first 24 hours following
2 the ICU admission.

3 The nutritional status of the patients was assessed according to the mNUTRIC score
4 within the first 24 h of the ICU admission. mNUTRIC score includes the following
5 variables: age, number of comorbidities, days from hospital to ICU admission, APACHE-
6 II score, and SOFA score. And the patients with mNUTRIC scores ≥ 5 were defined as
7 high nutritional risk [9].

8 The prehospital frailty status of the patients was assessed according to the CFS [10]. And
9 the patients who had CFS ≥ 5 were defined as frail. CFS was calculated based on patients'
10 medical records and the interview of the patients and/or their relatives.

11 APACHE-II and SOFA scores were used for the assessment of the severity of illness.
12 These scores were calculated based on the patients' worst clinical and laboratory findings
13 observed during the first 24 h following the admission of ICU [11,12]. And also, patients'
14 Glasgow coma scale (GCS) was calculated at the time to the admission of ICU.

15 **2.3. Measurement of outcome**

16 All of the patients were followed during their ICU stay or until death. All-cause of short
17 time mortality was defined as death within 30 days after the ICU admission. Patients'
18 mortality data were collected from the hospital medical record system.

19 **2.4. Statistical analysis**

20 Statistical Package for Social Sciences (SPSS) for Windows 22.0 software (SPSS Inc.,
21 Chicago, IL, USA) was used for the statistical analysis of the data obtained from the

1 hospital database. All results were analyzed with a confidence interval level of 95% and
2 a significance level of $p < 0.05$. The homogeneity and distribution of the variables were
3 assessed using the Skewness-Kurtosis. Frequencies and percentages were used for the
4 categorical data, continuous variables were presented as mean +/- standard deviation or
5 median (min-max) according to the distribution normality of data. We compared the
6 variables between survivors and non-survivors. Categorical variables were compared
7 using the Chi-squared Test. The Independent Samples T-Test was used for the analysis
8 of the two independent groups parametric data while Mann-Whitney-U Test was used for
9 the analysis of non-parametric data. We used the receiver operating characteristic (ROC)
10 curve to estimate the appropriate cut-off values of SOFA, APACHE-II, CFS, and
11 mNUTRIC score for determining the 30-days mortality. The Kaplan-Meier method was
12 used to determine the overall survival rates of the patients at day 30 and the Long-rank
13 Test was used to compare the differences in survival between the groups. After the
14 univariate survival analysis, Cox Regression analysis was used for the assessment of the
15 multivariate survival analysis.

16 **3. Results**

17 **3.1. Characteristics of the patients**

18 A total of 133 critically ill patients were included in the study. 75 (56.4%) of patients
19 were female and the median age of the patients was 85 (80-106) years. Hypertension
20 (68.4%), coronary artery disease (41.3%), dementia (35.3%), and chronic obstructive
21 pulmonary disease (24.4%) were the most common comorbidities. The emergency

1 department (55.6%) was the most frequent patient's source of admission to the ICU.
2 Sepsis (32.3%) was the most frequent cause of the admission to the ICU followed by
3 acute cardiogenic pulmonary edema (19.5%) and postoperative respiratory failure
4 (12.8%). Hospital LOS before the ICU admission was found 1.95 ± 4.40 days and ICU
5 LOS was found 11.40 ± 12.76 days.

6 The patients were grouped as survivors (n=94) and non-survivors (n=39). We found that
7 there were no statistical differences between the survivors' and the non-survivors' group
8 with respectively age, gender and diagnosis at ICU admission. However, hospital LOS
9 before the ICU admission was found significantly longer in non-survivors (p=0.001). And
10 also, ICU LOS was found significantly longer in survivors' group (p=0.015). We found
11 that SOFA, APACHE-II, CFS and mNUTRIC score were significantly higher in non-
12 survivors (p<0.001). Also, blood lactate level and glucose level were respectively
13 significantly higher in non-survivors (p<0.001, p=0.006). Comparison of the baseline
14 clinical characteristics and laboratory findings of the two groups are presented in Table 1
15 and Table 2.

16 We found that a total of 43 (32.4%) patients underwent invasive mechanical ventilation
17 and 33 (24.8%) patients underwent non-invasive mechanical ventilation. Non-survivors
18 had more invasive mechanical ventilation requirements (p<0.001). Also, the re-intubation
19 rate was found higher in non-survivors' group (5.3% vs 10.2%), but it was not statistically
20 significant (p=0.3). The use of vasoactive agents was found significantly higher in non-
21 survivors (p=0.004). Treatment options of the patients were presented in Table 3.

3.2. Short time survival analysis of the patients

We performed ROC curve analysis for finding the optimal cut-off value for determining the 30-days mortality in the older critically ill patients (Figure 2). The cut-off values of SOFA, APACHE-II, CFS, and mNUTRIC scores were presented in Table 4.

In the present study, we found that 30-days and overall ICU mortality rates were found at 30.1% and 34.6% respectively. Prognostic factors affecting the 30-days mortality in the older patients are presented in Table 5. The effects of the clinical characteristics and laboratory data on the 30-days survival showed that patients with hyperglycemia and hyperlactatemia during the ICU admission had significantly shorter survival times respectively ($p=0.001$, $p=0.023$). Also, we found significantly shorter survival time in patients with CFS ≥ 5 (Figure 3A), mNUTRIC score ≥ 5 (Figure 3B), SOFA score >5 (Figure 3C), and APACHE-II scores ≥ 23 (Figure 3D) ($p<0.001$).

After the univariate survival analysis, we used multivariate cox regression analysis for determining the independent risk factors of 30-days mortality. It was shown that prehospital CFS (HR=20.16, 95% CI=2.63-54.07 $p=0.004$) and mNUTRIC score (HR=9.19, 95% CI=1.47-57.32, $p=0.018$) were independent and significant prognostic factors for the 30-days mortality (Table 6).

4. Discussion

In the present study, we evaluated the clinical characteristics and the outcomes of the older critically ill patients. The main finding of our study showed that mNUTRIC score

1 and prehospital CFS score were the most important independent prognostic factors in the
2 admission of the older patients to intensive care units.

3 Nowadays, the rate of hospitalization of the older population in ICU is gradually
4 increasing with the increase in the average life expectancy [13]. Nielson et al. showed in
5 their study in 2014 that 12.6% of the patients who were admitted to the ICU consisted of
6 patients aged 80 and over, and that patients aged 80 and over who were admitted to
7 intensive care increased by 18% over the years [14]. In our study, 21.1% of the patients
8 who were admitted to the ICU during 13-months aged 80 years and over. The high
9 percentage of ≥ 80 -year-old patients in the present study can be explained by the
10 characteristic of the population in the city.

11 Problems are experienced in the follow-up of the older patients in ICU due to the
12 consideration that life expectancy will be short as well as due to the underlying
13 comorbidities [13,15]. It has been demonstrated in numerous clinical studies that
14 mortality increases in parallel with the age of patients who are admitted to the ICU, and
15 age is an independent risk factor for mortality [3,16]. However, recent studies have shown
16 that chronological age is not an independent risk factor for mortality. Besides, it has been
17 underscored that rather than chronological age, biological age is more important for
18 survival [6,15,17].

19 Many studies evaluating the survival in critically ill older patients are single-centered
20 retrospective cohort studies and include different age and disease groups. Therefore, 30-
21 days and ICU mortality rates vary in studies. In previous studies, the mortality rate soars

1 to 50% in critically ill older patients in ICU [1,4,6,15-17]. In the present study, we found
2 that 30-days and overall ICU mortality rates were found 30.1% and 34.6% respectively.
3 In the present study, the general ward was the primary admission source for the older
4 patients admitted to the ICU. Also, we found that hospital LOS before the ICU admission
5 was 1.95 ± 4.40 days and ICU LOS was 11.40 ± 12.76 days. Clinical studies that evaluate
6 the association between hospital LOS before the ICU admission and survival of the
7 patients transferred to ICU showed that patients with longer hospital LOS before the ICU
8 admission had worse outcomes and survival. Thus, to improve outcomes in critically ill
9 older patients who have been admitted to ICU, it may be beneficial to establish rapid
10 response teams to rapidly recognize the clinical deterioration of patients who are followed
11 up in general wards, and to make early interventions [18,19].

12 Sepsis, defined as life-threatening organ dysfunction resulting from the dysregulated
13 response of the host to infection, is one of the most important causes of admission to ICU
14 and mortality. Advanced age is a significant risk factor for the development of sepsis, and
15 a dramatic increase is seen in the incidence of sepsis, particularly in those aged 80 and
16 over [6,15]. In the present study, we found that sepsis (32.3%) was the most frequent
17 cause of admission to the ICU followed by acute cardiogenic pulmonary edema (19.5%)
18 and postoperative respiratory failure (12.8%).

19 There are no prognostic factors and combinations that can be used during the admission
20 of the older critically ill patients to intensive care units, that are accepted by all clinicians,
21 and whose validity and reliability have been proven in the literature. The fact that the

1 clinical characteristics, which are used in conventional disease severity scorings, such as
2 the APACHE-II score, may be inadequate to accurately predict the survival of critically
3 ill patients, is increasingly gaining acceptance [6,8,20]. We found out that SOFA and
4 APACHE-II scores were not an independent and significant prognostic factor for 30-days
5 survival, albeit we determined that patients with higher SOFA and APACHE-II scores in
6 our study had higher mortality and shorter survival rates. Also, we found that patients
7 with higher serum levels of glucose and lactate had a shorter survival time. However,
8 these two variables were not independent and significant prognostic factors for the 30-
9 days survival.

10 Traditional disease severity scoring systems may not be able to detect significant data
11 about a patient's pre-illness state, such as cognitive impairment, decreased functional
12 capacity, and frailty. However, these data may be important markers of mortality and
13 morbidity, especially in the older patients. Assessing the clinical frailty of patients before
14 admission to the ICU, especially in critically ill patients, could facilitate better clinical
15 decisions [4,6,8].

16 The concept of clinical frailty is defined as a multivariate syndrome characterized by loss
17 of physical, physiological, and cognitive reserves rather than an acute disease state that
18 increases with age but is not specific to advanced age. Frail elders experience difficulty
19 in adapting to various stressful situations such as acute illness and trauma. Frailty can be
20 assessed using the CFS developed by Rockwood et al. CFS is a 9-point scale and a patient
21 with a score \geq of 5 is defined as frail [4,8,10,21,22].

1 The prevalence of pre-hospital frailty varies in previous studies and it increases with age.
2 More importantly, it has been suggested that an increased CFS score (CFS score of ≥ 5)
3 is a significant factor in short-term and long-term mortality in the older patients who have
4 been admitted to ICU [3,4,8,21,22]. In the present study, a total of 82 (61.6%) critically
5 ill patients had a CFS score ≥ 5 . Also, we found that the CFS score was significantly higher
6 in non-survivors ($p < 0.001$) and independent prognostic factors of 30-days mortality in
7 the older patients admitted to the ICU included a high CFS score (CFS score ≥ 5).
8 The majority of the patients who apply to the ICUs and particularly those who receive
9 mechanical ventilation support are at nutritional risk. In particular, this risk increases even
10 more in fragile and critically ill older patients. Hence, the nutritional risk should be
11 assessed in all patients who have been admitted to the ICU without wasting time [1,6,21].
12 Based on the mNUTRIC score developed by Heyland et al., patients are divided into low
13 (0-4) and high (5-9) risk groups to evaluate the nutritional risk in critical patients, and
14 early nutritional support is recommended for patients in the high-risk group [9,23].
15 Moreover, various studies have revealed that a high mNUTRIC score (mNUTRIC score
16 ≥ 5) is also associated with increased mortality and unfavorable outcomes. For this reason,
17 critically ill patients with high nutritional risk should be identified without delay and early
18 nutritional support should be initiated [24,25]. In the present study, a total of 89 (66.9%)
19 critically ill patients had mNUTRIC score ≥ 5 . Also, we found that patients with
20 mNUTRIC score ≥ 5 had a shorter survival time.

1 In conclusion, prehospital CFS and mNUTRIC score were the independent and
2 significant prognostic factors for the older critically ill patients. In addition to traditional
3 scoring systems that assess organ failure during admission of the older patients to the
4 ICU, assessment of pre-hospital frailty and nutritional risk status could be more effective
5 in predicting short and long-term mortality. Therefore, we recommend that prehospital
6 frailty and the nutritional risk assessment of the older patient should be routinely
7 performed for the more rational use of intensive care unit beds and sufficient prognostic
8 evaluation in these patient groups.

9 **Acknowledgement and/or disclaimers**

10 None declared.

11 **Financial disclosure**

12 This manuscript did not receive any specific grant from funding agencies in the public,
13 commercial, or not-for-profit sectors.

14 **Conflict of interest**

15 The authors have stated explicitly that there are no conflicts of interest in connection with
16 this article.

17 **Informed consent**

18 The study protocol was approved by the Clinical Ethics Committee of Inonu University
19 School of Medicine and fulfilled the Declaration of Helsinki (protocol no:2020/126). The
20 written informed consent form was not obtained due to the retrospective nature of the
21 study.

1 **References**

- 2 **1.** Sim YS, Jung H, Shin TR, Kim DG, Park SM. Mortality and outcomes in very
3 elderly patients 90 years of age or older admitted to the ICU. *Respiratory Care*. 2015; 60
4 (3): 347-355. doi: 10.4187/respcare.03155
- 5 **2.** Robert R, Skrifvars MB, Ranzani OT. Is this critically ill patient elderly or too
6 old? *Intensive Care Medicine*. 2017; 43 (12): 1884-1886. doi: 10.1007/s00134-017-4965-
7 z
- 8 **3.** Bagshaw SM, Webb SA, Delaney A, George C, Pilcher D et al. Very old patients
9 admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis.
10 *Critical Care*. 2009; 13 (2): R45. doi: 10.1186/cc7768
- 11 **4.** Flaatten H, De Lange DW, Morandi A, Andersen FH, Artigas A et al. The impact
12 of frailty on ICU and 30-day mortality and the level of care in very elderly patients (\geq 80
13 years). *Intensive Care Medicine*. 2017; 43 (12): 1820-1828. doi: 10.1007/s00134-017-
14 4940-8
- 15 **5.** Heyland D, Cook D, Bagshaw SM, Garland A, Stelfox HT et al. The very elderly
16 admitted to ICU: A quality finish? *Critical Care Medicine*. 2015; 43 (7): 1352-1360. doi:
17 10.1097/CCM.0000000000001024
- 18 **6.** Flaatten H, de Lange DW, Artigas A, Bin D, Moreno R et al. The status of
19 intensive care medicine research and a future agenda for very old patients in the ICU.
20 *Intensive Care Medicine*. 2017; 43 (9): 1319-1328. doi: 10.1007/s00134-017-4718-z

- 1 7. Nates JL, Nunnally M, Kleinpell R, Blosser S, Goldner J et al. ICU admission,
2 discharge, and triage guidelines: a framework to enhance clinical operations,
3 development of institutional policies, and further research. *Critical Care Medicine*. 2016;
4 44 (8): 1553-1602. doi: 10.1097/CCM.0000000000001856.
- 5 8. Fronczek J, Polok KJ, Nowak-Kozka I, Wludarczyk A, Gorka J et al. Frailty is
6 associated with an increased mortality among patients ≥ 80 years old treated in Polish
7 ICUs. *Anaesthesiology Intensive Therapy*. 2018; 50 (4): 245-251. doi:
8 10.5603/ait.a2018.0032
- 9 9. Rahman A, Hasan RM, Agarwala R, Martin C, Day AG et al. Identifying
10 critically-ill patients who will benefit most from nutritional therapy: further validation of
11 the "modified NUTRIC" nutritional risk assessment tool. *Clinical Nutrition*. 2016; 35 (1):
12 158-162. doi: 10.1016/j.clnu.2015.01.015
- 13 10. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB et al. A global
14 clinical measure of fitness and frailty in elderly people. *Canadian Medical Association*
15 *Journal*. 2005; 173 (5): 489-495. doi: 10.1503/cmaj.050051
- 16 11. Campbell NN, Tooley MA, Willatts SM. APACHE II scoring system on a general
17 intensive care unit: audit of daily APACHE II scores and 6-month survival of 691 patients
18 admitted to a general intensive care unit between May 1990 and December 1991. *Journal*
19 *of the Royal Society of Medicine*. 1994; 87 (2): 73-77.
- 20 12. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A et al. The SOFA
21 (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure.

1 On behalf of the working group on sepsis-related problems of the european society of
2 intensive care medicine. *Intensive Care Medicine*. 1996; 22 (7): 707-710. doi:
3 10.1007/BF01709751

4 **13.** Angus DC. Admitting Elderly Patients to the Intensive Care Unit-Is it the Right
5 Decision? *Journal of the American Medical Association*. 2017; 318 (15): 1443-1444. doi:
6 10.1001/jama.2017.14535

7 **14.** Nielsson MS, Christiansen CF, Johansen MB, Rasmussen BS, Tonnesen E et al.
8 Mortality in elderly ICU patients: a cohort study. *Acta Anaesthesiologica Scandinavica*.
9 2014; 58 (1): 19-26. doi: 10.1111/aas.12211

10 **15.** Martin-Loeches I, Guia MC, Vallecocchia MS, Suarez D, Ibarz M, et al. Risk
11 factors for mortality in elderly and very elderly critically ill patients with sepsis: a
12 prospective, observational, multicenter cohort study. *Annals of Intensive Care*. 2019; 9
13 (1): 26. doi: 10.1186/s13613-019-0495-x

14 **16.** Giannasi SE, Venuti MS, Midley AD, Roux N, Kecskes C et al. Mortality risk
15 factors in elderly patients in intensive care without limitation of therapeutic effort.
16 *Medicina Intensiva*. 2018; 42 (8): 482-489. doi: 10.1016/j.medine.2018.08.001

17 **17.** Le Borgne P, Maestraggi Q, Couraud S, Lefebvre F, Herbrecht JE et al. Critically
18 ill elderly patients (≥ 90 years): Clinical characteristics, outcome and financial
19 implications. *PLoS One*. 2018; 13 (6): e0198360. doi: 10.1371/journal.pone.0198360

- 1 **18.** Nahra R, Schorr C, Gerber D. Pre-intensive care unit length of stay and outcome
2 in critically ill patients. *CHEST Journal*. 2005; 128 (4_MeetingAbstracts): 298S. doi:
3 10.1378/chest.128.4_MeetingAbstracts.298S
- 4 **19.** Simpson K, Williams G, Quasim T. Length of hospital stay prior to ICU admission
5 and outcome. *Critical Care*. 2011; 15 (Suppl 1): P465. doi: 10.1186/cc9885
- 6 **20.** Langlais E, Nesseler N, Le Pabic E, Frasca D, Launey Y et al. Does the clinical
7 frailty score improve the accuracy of the SOFA score in predicting hospital mortality in
8 elderly critically ill patients? A prospective observational study. *Journal of Critical Care*.
9 2018; 46: 67-72. doi: 10.1016/j.jcrc.2018.04.012
- 10 **21.** Muscedere J, Waters B, Varambally A, Bagshaw SM, Boyd JG et al. The impact
11 of frailty on intensive care unit outcomes: a systematic review and meta-analysis.
12 *Intensive Care Medicine*. 2017; 43 (8): 1105-1122. doi: 10.1007/s00134-017-4867-0
- 13 **22.** Silva-Obregon JA, Quintana-Diaz M, Saboya-Sanchez S, Marian-Crespo C,
14 Romera-Ortega MA et al. Frailty as a predictor of short- and long-term mortality in
15 critically ill older medical patients. *Journal of Critical Care*. 2020; 55: 79-85. doi:
16 10.1016/j.jcrc.2019.10.018
- 17 **23.** Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who
18 benefit the most from nutrition therapy: the development and initial validation of a novel
19 risk assessment tool. *Critical Care*. 2011; 15 (6): R268. doi: 10.1186/cc10546
- 20 **24.** Zhang P, Bian Y, Tang Z, Wang F. Use of nutrition risk in critically ill (NUTRIC)
21 scoring system for nutrition risk assessment and prognosis prediction in critically ill

1 neurological patients: a prospective observational study. *Journal of Parenteral and Enteral*
2 *Nutrition*. 2020; 45 (5): 1032-1041. doi: 10.1002/jpen.1977

3 **25.** Zhang P, He Z, Yu G, Peng D, Feng Y et al. The modified NUTRIC score can be
4 used for nutritional risk assessment as well as prognosis prediction in critically ill
5 COVID-19 patients. *Clinical Nutrition*. 2021; 40 (2): 534-541. doi:
6 10.1016/j.clnu.2020.05.051

7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

Table 1. Baseline characteristics of the patients					
		All patients (n=133)	Survivors (n=94)	Non-survivors (n=39)	P value
Median age, years (min-max)		85 (80-106)	84.50 (80-106)	86 (80-97)	0.481
Gender, n (%)	Male	58 (43.6%)	36 (38.2%)	22 (56.4%)	0.055
	Female	75 (56.4%)	58 (61.8%)	17 (43.6%)	
Comorbid disease, n (%)	Hypertension	91 (68.4%)	59 (62.7%)	32 (82.0%)	0.836
	Dementia	47 (35.3%)	35 (37.2%)	12 (30.7%)	0.105
	COPD	37 (27.8%)	21 (22.3%)	16 (41.0%)	0.271
	DM	35 (26.3%)	19 (20.2%)	16 (41.0%)	0.107
	CHF	31 (23.3%)	23 (24.4%)	8 (20.5%)	0.241
	CKD	5 (3.7%)	2 (2.1%)	3 (7.6%)	0.223
	Arrhythmia	23 (17.2%)	17 (18.0%)	6 (15.3%)	0.346
	CVD	20 (15.0%)	14 (14.8%)	6 (15.3%)	0.640
	Malignancy	6 (4.5%)	3 (3.1%)	3 (7.6%)	0.417
CAD	55 (41.3%)	35 (37.2%)	20 (51.2%)	0.717	
Hospital LOS before ICU admission, days (Me±SD)		1.95 ± 4.40	1.36 ± 3.51	3.36 ± 5.84	0.001
ICU LOS, days (Me±SD)		11.40 ± 12.76	12.36 ± 14.41	9.08 ± 7.05	0.015
Diagnosis, n (%)	Sepsis	43 (32.3%)	26 (27.7%)	17 (43.6%)	0.073
	PRF	17 (12.8%)	17 (18.1%)	0	
	ACPE	26 (19.5%)	22 (23.4%)	4 (10.3%)	0.081
	Exacerbation of COPD	9 (6.8%)	8 (8.5%)	1 (2.6%)	0.213
	PTE	3 (2.3%)	1 (1.1%)	2 (5.1%)	0.877
	Cardiac arrest	7 (5.3%)	4 (4.2%)	3 (7.6%)	0.145
	Stroke	15 (11.3%)	7 (7.4%)	8 (20.5%)	0.061
	Miscellaneous	13 (9.7%)	9 (9.6%)	4 (10.3%)	0.040
Admission source, n (%)	General ward	36 (27%)	19 (20.3%)	17 (43.5%)	0.005
	Emergency department	74 (55.6%)	53 (56.3%)	21 (53.8%)	0.788
	Operating room	23 (17.4%)	22 (23.4%)	1 (2.7%)	0.003
Glasgow Coma Scale, (Me±SD)		11.54±3.56	12.66±2.89	8.95±3.64	<0.001
APACHE-II scores, (Me±SD)		22.77±5.78	20.86±5.18	27.38±4.40	<0.001
Predicted mortality, % (Me±SD)		45.64±18.76	39.41±16.55	60.65±14.97	<0.001
SOFA score, (Me±SD)		5.83±3.10	5.03±2.78	7.74±3.03	<0.001

CFS score, (Me±SD)	5.45±1.70	4.88±1.54	6.82±1.25	<0.001
mNUTRIC score, (Me±SD)	5.51±1.69	4.95±1.59	6.87±1.03	<0.001
ICU: intensive care unit; LOS: length of stay; CHF: chronic heart failure; CKD: chronic kidney disease; CVD: cerebrovascular disease; PRF: postoperative respiratory failure; DM: diabetes mellitus; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; ACPE: acute cardiogenic pulmonary edema; PTE: pulmonary thromboembolism; APACHE-II: acute physiology and chronic health evaluation II; SOFA: sequential organ failure assessment; CFS: clinical frailty scale; mNUTRIC: modified the nutrition risk in critically ill; Me: mean; SD: standard derivation				

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33

1
2
3
4
5
6

Table 2. Baseline laboratory findings of the patients				
	All patients (n=133)	Survivors (n=94)	Non-survivors (n=39)	P value
Hb (g/dL)	11.55±2.80	11.44±2.74	11.81±2.97	0.495
Ht (%)	35.96±8.15	35.53±8.33	37.32±7.55	0.384
Wbc (10³/μL)	12.08 (2.20-303.61)	11.68 (3.04-303.61)	12.85 (2.20-84.80)	0.127
Lymph (10³/μL)	0.95 (0.14-6.64)	0.96 (0.10-4.33)	0.92 (0.14-6.64)	0.533
Plt (10³/μL)	230±105	219±89	258±135	0.050
Urea (mg/dL)	75 (24-419)	75 (24-419)	76 (36-230)	0.820
Crea (mg/dL)	1.32 (0.34-8.20)	1.31 (0.34-8.20)	1.38 (0.74-4.31)	0.328
AST (U/L)	29 (6-4384)	29 (6-4384)	27 (14-2142)	0.980
ALT (U/L)	18 (4-3062)	19 (4-3062)	15 (5-663)	0.725
Tot bil (mg/dL)	0.76 (0.10-3.92)	0.76 (0.10-3.92)	0.72 (0.23-2.62)	0.892
Glucose (mg/dL)	150 (69-773)	140 (69-773)	198 (102-510)	0.006
Albumin (g/dL)	3.17±0.59	3.22±0.54	3.05±0.68	0.130
CRP (mg/dL)	7.19 (0.04-48.00)	7.00 (0.04-48.00)	7.89 (0.09-46.70)	0.127
pH	7.34±0.09	7.35±0.09	7.32±0.10	0.183
Lactate (mmol/L)	2.10 (0.20-13.80)	1.95 (0.20-9.90)	3.30 (1.20-13.80)	<0.001
CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; Wbc: white blood cell; Lymph: Lymphocytes; Plt: platelets; Hb: hemoglobin; Ht: Hematocrit; Tot bil: total bilirubin; Crea: creatinin				

7
8
9
10
11
12
13
14
15
16
17
18
19

1
2
3
4
5
6
7
8
9
10
11
12
13
14

Table 3. Treatment options of the patients in the ICU					
	All patients (n=133)	Survivors (n=94)	Non-survivors (n=39)	<i>P</i> value	
Vasopressor therapy, n (%)	50 (37.5%)	28 (29.7%)	22 (56.4%)	0.004	
Renal replacement therapy, n (%)	7 (5.2%)	5 (5.3%)	2 (5.1%)	0.964	
Blood transfusion, n (%)	72 (54.1%)	55 (58.5%)	17 (43.5%)	0.116	
Respiratory support, n (%)	COT	57 (42.8%)	53 (56.3%)	4 (10.2%)	<0.001
	NIMV	33 (24.8%)	24 (24.4%)	9 (23%)	0.765
	IMV	43 (32.4%)	17 (19.3%)	26 (66.8%)	<0.001
Re-intubation, n (%)	9 (6.7%)	5 (5.3%)	4 (10.2%)	0.302	
Tracheostomy, n (%)	4 (3%)	3 (3.2%)	1 (2.5%)	0.847	
ICU: intensive care unit; COT: conventional oxygen therapy; NIMV: non-invasive mechanical ventilation; IMV: invasive mechanical ventilation					

15
16
17
18
19
20
21
22
23
24
25
26
27
28

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20

Table 4. The optimal cut-off value of Clinical Frailty scale, mNUTRIC score, SOFA score, APACHE-II scores for the prediction of mortality						
	AUC	95% CI	Sensitivity	Specificity	Cut-off value	P value
SOFA score	0.759	0.674-0.845	73.8%	62.8%	5	< 0.001
APACHE-II scores	0.835	0.768-0.902	84.6%	64.9%	23	< 0.001
CFS score	0.822	0.752-0.892	82.1%	69.1%	5	< 0.001
mNUTRIC score	0.841	0.774-0.908	95.9%	64.9%	5	< 0.001

APACHE-II: acute physiology and chronic health evaluation II; SOFA: sequential organ failure assessment, CFS: clinical frailty scale, mNUTRIC: modified the nutrition risk in critically ill, AUC: Area under curve, CI: Confidence interval

21
22
23
24
25
26
27
28
29
30

1
2
3
4
5

Table 5. Comparison of mean survival time according to demographic characteristics and ICU parameters

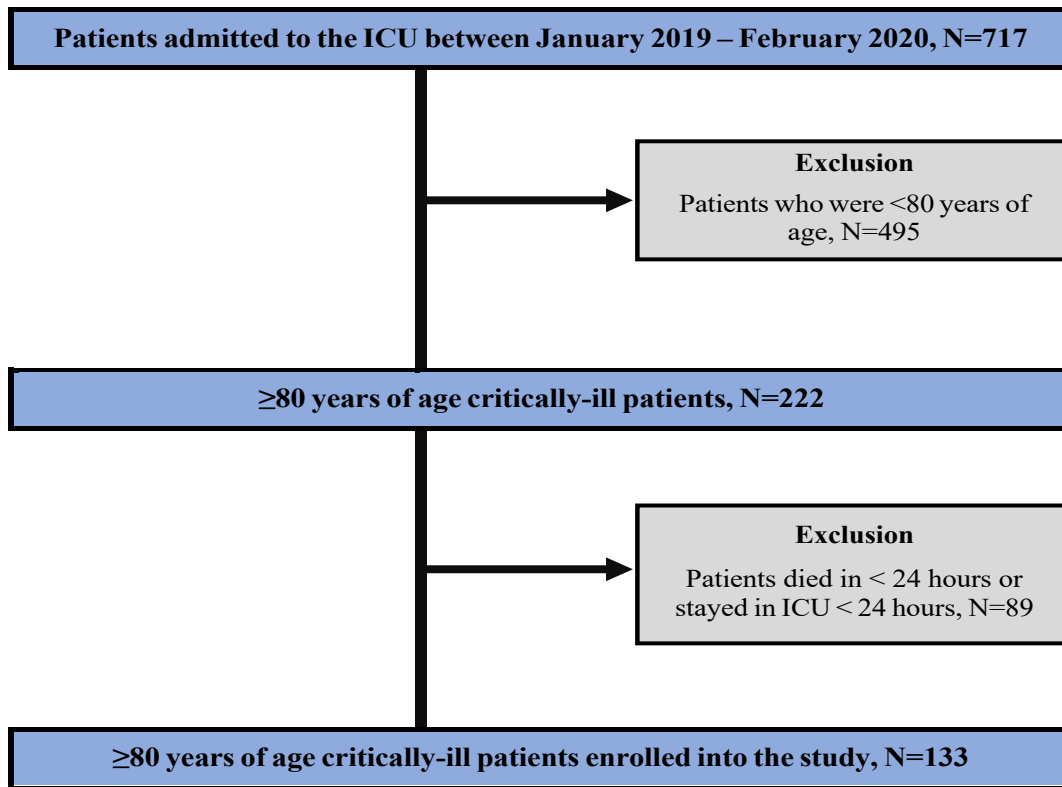
		Mean survival time (days±SE)	95% CI		P value
			Lower bound	Upper bound	
Gender	Male	22.00±1.44	19.17	24.83	0.074
	Female	25.26±1.08	23.14	27.38	
Admission source	General ward	19.88±1.90	16.15	23.61	0.002
	Emergency department	24.15±1.17	21.84	26.46	
	Operating room	29.04±1.17	27.21	30.61	
Vasoactive agent requirement	Yes	20.10±1.71	16.74	23.45	0.001
	No	26.10±0.89	24.35	27.84	
Type of respiratory support	COT	28.47±0.76	26.97	29.97	<0.001
	NIMV	23.84±1.86	20.19	27.48	
	IMV	17.72±1.71	14.36	21.07	
Clinical frailty scale	< 5	29.49±0.50	28.50	30.48	<0.001
	≥ 5	20.31±1.25	17.86	22.79	
SOFA score	< 5	26.81±0.92	24.99	28.62	<0.001
	≥ 5	20.55±1.45	17.70	23.41	
APACHE-II scores	< 23	28.07±0.78	26.53	29.60	<0.001
	≥ 23	19.56±1.42	16.77	22.34	
mNUTRIC score	< 5	29.44±0.39	28.67	30.21	<0.001
	≥ 5	18.81±1.39	16.07	21.55	
Hyperglycemia	Yes	20.03±2.25	15.61	24.46	0.001
	No	26.73±0.91	24.94	28.52	
Hyperlactatemia	Yes	21.89±1.32	19.29	24.48	0.023
	No	26.30±1.03	24.27	28.32	
Hypoalbuminaemia	Yes	22.12±1.58	19.02	25.22	0.077
	No	24.81±1.04	22.76	26.87	

CI: Confidence interval, SE: Standard error; SOFA: Sequential organ failure assessment, APACHE-II: Acute physiology assessment and chronic health evaluation II, mNUTRIC: Modified the nutrition risk in critically ill, CFS: Clinical frailty scale, COT: Conventional oxygen therapy; NIMV: Non-invasive mechanical ventilation; IMV: Invasive mechanical ventilation

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

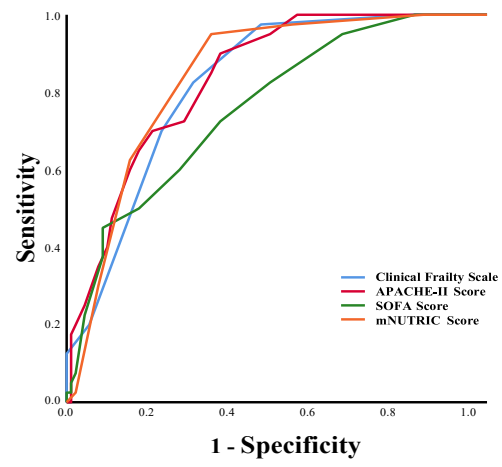
Table 6. Multivariate Cox regression analysis of 30 days mortality				
	Hazard ratio	95% CI		P value
		Lower bound	Upper bound	
SOFA score	0.30	0.07	1.28	0.106
APACHE-II scores	3.05	0.78	11.88	0.106
CFS score	20.16	2.63	54.07	0.004
mNUTRIC score	9.19	1.47	57.32	0.018
Vasoactive agent requirement	1.62	0.60	4.39	0.336
Hyperglycemia	0.79	0.30	2.07	0.644
Hyperlactatemia	0.34	0.10	1.10	0.074
CI: Confidence interval, SOFA: Sequential organ failure assessment, APACHE-II: Acute physiology assessment and chronic health evaluation II, mNUTRIC: modified the nutrition risk in critically ill, CFS: clinical frailty scale				

17
18
19



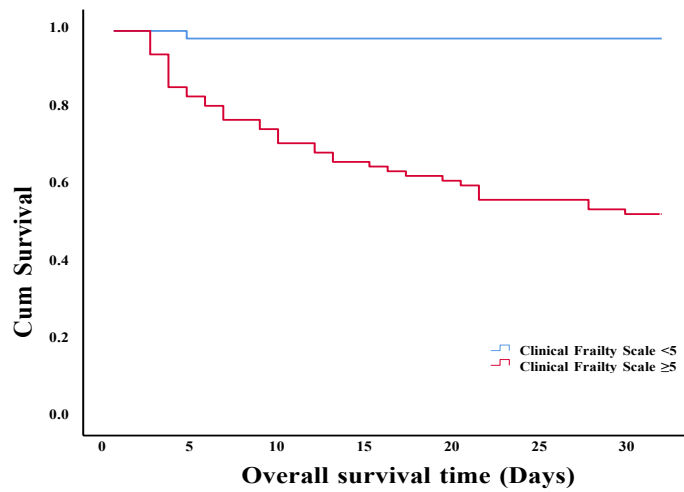
1

2 **Figure 1.** Flow-chart of the study



1

2 **Figure 2.** Receiver operating characteristic curves of different scores predicting short
3 time mortality



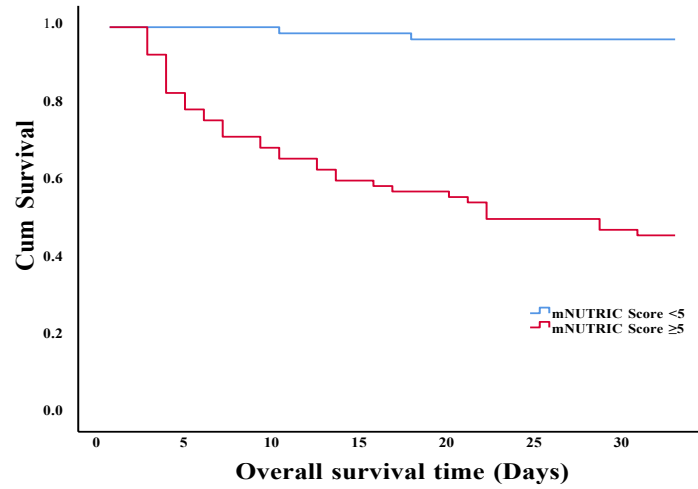
1

2 **Figure 3A.** Kaplan-Meier curves of 30-days survival analysis shows the impact of Clinical

3 Frailty Scale in the older critically ill patients.

4

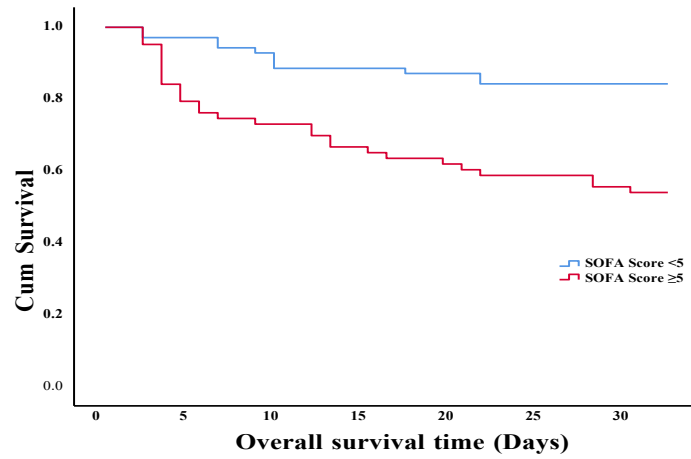
1



2

3 **Figure 3B.** Kaplan-Meier curves of 30-days survival analysis shows the impact of
4 modified Nutrition Risk in Critically Ill score in the older critically ill patients.

1

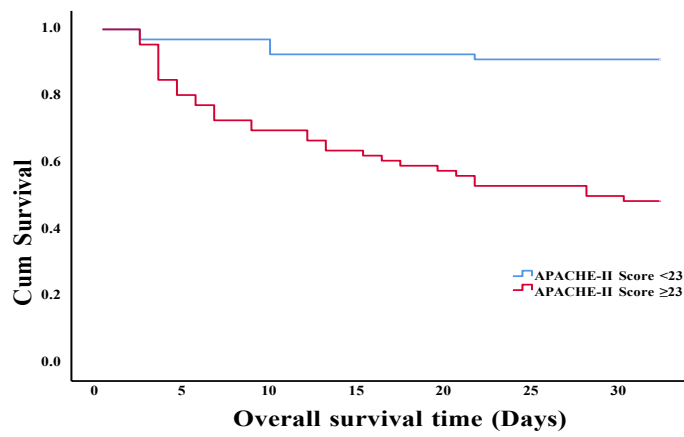


2

3 **Figure 3C.** Kaplan-Meier curves of 30-days survival analysis shows the impact of
4 Sequential Organ Failure Assessment score in the older critically ill patients.

5

1



2

3 **Figure 3D.** Kaplan-Meier curves of 30-days survival analysis shows the impact of Acute
4 Physiology and Chronic Health Evaluation-II score in the older critically ill patients.