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Original study

Association between timing of medical intensive care unit admission and outcome of emergency department patients: a retrospective cohort study

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Abstract

Background: **Critically ill Emergency Department (ED) patients may benefit from timely triage to the Intensive Care Unit (ICU), as there is a "window of critical opportunity." Several authors have investigated the relationship between delayed ED-to-ICU transfer and poor outcome. However, covariates often obscured this relationship.**
Objectives: **To examine the impact of direct (DICU-P) versus indirect (IDICU-P) ED-to-ICU admission on patient outcomes and assess whether delay in critical care provision is a contributing factor. To compare survival for up to 12 months.**
Design and Setting: **Single-center retrospective cohort study.**
Methods: **Unplanned medical ED-to-ICU admissions between 2015 and 2019 were classified as DICU-P or IDICU-P (hospital ward stay < 48 hours). Groups were divided according to Length Of Stay (LOS) as ICU-LOS < 48h or ICU-LOS ≥ 48h. A timeline analysis was conducted. Propensity Score Matching (PSM) was used to account for bias (age, gender, SAPS II, APACHE IV admission diagnosis) and achieve pseudo-randomization.**
Main outcomes: **LOS and mortality, both for ICU and in-hospital, and 1 year mortality.**
Results: **IDICU-P patients had higher mortality rates (ICU, p = 0.006; post-ICU, p = 0.0005; hospital, p < 0.0001), longer LOS (hospital, p = 0.007), but were older (p <0.0001) and sicker (SAPS II, p = 0.0002). After PSM, a trend for higher mortality rates (hospital, p = 0.030; early in ICU (LOS-ICU < 48h), p = 0.034) and longer LOS (hospital, p = 0.030) persisted, with elderly patients being responsible for this disparity. ICU mortality was equal after 48 hours, while post-ICU and long-term mortality up to 30 days and 12 months were higher in IDICU-P (both p < 0.0001; after PSM, p = 0.018 and p = 0.009, respectively). COPD exacerbations, pneumonia, and congestive heart failure showed higher hospital mortality in IDICU-P.**
Conclusion: **Indirect ICU admission of ED patients in need of critical care was associated with higher mortality and longer LOS but also with higher age and severity of illness. Mortality was consistently higher for up to 12 months after ICU admission and showed no catch-up mortality. After correcting for biases with PSM, the significance often diminished; however, a general trend was confirmed. This finding highlights the importance of correct triage in the ED.**

Keywords: **Intensive Care Units, Critical care, Emergency Medicine, Patient Transfer, Treatment Outcome.**

Introduction

Admission to the Intensive Care Unit (ICU), a high-cost service with limited capacity, has become a major research topic due to the growing importance of cost-effectiveness in healthcare. Given the scarcity of ICU beds and the significant financial burden that ICU services can impose on hospitals' budgets, ICU admissions should not be considered lightly[1]. Conversely, patients should receive

Preliminary data from the survey were presented at ESICM LIVES 2022 Annual Congress, Paris, France.
The study was approved by the Committee for Medical Ethics of az Sint-Blasius (az Sint-Blasius, Kroonveldlaan 50, 9200 Dendermonde, chairperson Dr. Sabine Serry, approval number B0122021000008) on December 8, 2021. The EU-GDPR requirements were met.

appropriate medical care at all times and any delay can lead to poor outcomes.

In the Emergency Department (ED), it is crucial to determine the necessary level of care while considering the extent of functional impairment[2,3]. The widely accepted viewpoint is that besides clinical indications, only patients with a significant chance of experiencing meaningful recovery should be admitted to the ICU[2,4]. However, identification of the level of care required is insufficient. Previous research has suggested that critically ill patients have a "window of critical opportunity" to maximize the benefits of ICU treatment, similar to the initial "golden hour" of trauma or the "door-to-balloon time" in acute myocardial infarction. Once this window is passed, the advantage of ICU treatment diminishes[1,5,6].

Contrary to common beliefs, patients admitted from the ED to the ICU are not necessarily the sickest. As factors such as functional impairment must be taken into consideration, it has been reported that patients with delayed ICU admission are older, have higher clinical severity, and more comorbidities[1,4,5,7-12]. The unequal distribution of patient and disease characteristics, which often burden the delayed group, may contribute to the higher mortality rate and longer hospital stay observed in patients who are admitted to the ward but later require critical care. However, this imbalance in characteristics may also confound the association between delayed ICU admission and worse outcomes, obscuring its role as an independent factor for outcomes. While it is intuitive that missing the "window of critical opportunity" would negatively impact the outcome, numerous studies have advocated for this and suggested possible reasons and solutions. It has also been suggested that some diagnoses are more sensitive than others to this delay[4,7,12-16]. However, few have been able to identify delayed ICU admission as an independent factor influencing the outcome due to confounding variables[9-11,13-16].

The primary objective of this study was to assess triage in the ED, particularly focusing on whether there was a difference in outcomes between patients admitted directly to the ICU and those admitted indirectly. Additionally, we aimed to assess the impact of this delay in initiating critical care on patient outcomes, verifying it as an independent and significant factor on the outcomes of these patients. The primary outcomes of interest were the length of stay (LOS) in the ICU and hospital, as well as mortality rates observed in the ICU and hospital, at 30 days, and one year after admission.

Methods

Setting and study design

We conducted a retrospective single-center cohort study at Sint-Blasius General Hospital, Dendermonde, Belgium, a 438-bed general hospital with university affiliation and a 12-bed mixed medical-surgical ICU. The study was approved by the Committee for Medical Ethics of az Sint-Blasius (az Sint-Blasius, Kroonveldlaan 50, 9200 Dendermonde, chairperson Dr. Sabine Serry, approval number B0122021000008) on December 8, 2021, and met EU-GDPR requirements.

Data collection

Intensivists collected demographic data, hospital and ICU LOS data, Acute Physiology And Chronic Health Evaluation IV (APACHE IV) admission diagnoses, and Simplified Acute Physiology Score II (SAPS II) scores. All intensivists were trained to collect the data. Physiological data were collected from paper records. Demographic and laboratory data were collected electronically. All data were entered into a dedicated ICU database (Mediscore ICU; Itémedical, Tiel, the Netherlands). Mortality data, including ICU, in-hospital, and long-term mortality up to 12 months after admission, were extracted from the ICU database and electronic patient files linked to the Belgian National Registry, showing the actual vital status or date of death. The Standardized Mortality Ratio (SMR) was calculated by dividing the observed mortality by the expected mortality using data from the original SAPS II database[17].

Inclusion and exclusion criteria

All ICU admissions from January 1, 2015, to December 31, 2019, were extracted from the ICU database. Planned medical patients, patients with medical complications after surgery, and those transferred from other hospitals were excluded. Patients who underwent surgery (both elective and emergency) or who experienced medical complications after surgery were excluded for several reasons. First, comparing mortality rates between emergency surgical and medical patients requiring critical care is difficult because of inherent biases. Second, it is essential to recognize the level of care provided by operating room teams, who bridge the gap between the ED and ICU and often already provide critical care. Third, the admission of emergency surgical patients could be considered both direct and indirect, which could introduce confusion. All the patients in our ICU database were assigned an APACHE IV diagnosis. Diagnoses or pathologies that originated

exclusively in the emergency department or ward were excluded. To avoid bias in patients who were repeatedly readmitted to the ICU, those readmitted during the same hospital stay were excluded. All patients admitted to the ICU from the ward whose initial hospital entry was not through the ED were excluded from the study. We did not encounter any missing data in any of the reviewed cases.

Plan of investigation

After inclusion, the patients were classified into two groups: those who were directly admitted to the ICU from the ED (DICU-P) and those who were initially admitted to a general ward from the ED and transferred to the ICU later (IDICU-P). As this study aimed to assess triage in the ED, IDICU-P with a hospital ward LOS ≥ 48h were excluded, in order to only select patients whose ICU admission was likely due to a deterioration of their initial presentation at the ED and thus were probably subject to wrongful triage in the ED. Consequently, it was possible to take a closer look at the aforementioned "critical window of opportunity." Therefore, IDICU-P represents only those hospitalized < 48h in a ward before ICU admission. For both groups, patients were divided into two categories: ICU-LOS < 48h or ICU-LOS ≥ 48h. Timelines were created to provide a more detailed examination of the various subgroups, while allowing for a chronological review of the series of events. As age, sex, severity of illness, and comorbidities are independent risk factors for mortality, a balanced sample of DICU-P and IDICU-P was created using Propensity Score Matching (PSM) to control for selection and confounding bias and achieve pseudo-randomization. The SAPS II score was used as a surrogate for illness severity and comorbidity18. PSM provided two matching cohorts, in which the delay in providing critical care was an independent and determining factor. Finally, a survival analysis up to 12 months after ICU admission was performed.

Statistical analysis

The zero hypothesis (H0) states that there is no disparity in outcomes between the DICU-P and IDICU-P, while the alternative hypothesis (H1) suggests that a difference exists.

Statistical analyses were performed using XL-Stat (Lumivero (2022). XLSTAT statistical and data analysis solution. New York, USA. https://www.xlstat.com), Statskingdom (https://www.statskingdom.com), VassarStats (http://www.vassarstats.net), and MedCalc (https://www.medcalc.org).

DICU-P and IDICU-P were compared using the Mann-Whitney test for continuous variables with non-Gaussian distribution, and data were reported as median and interquartile range (IQR). Effect size for continuous variables were automatically calculated. Categorical data were compared using the chi-square or Fisher's exact test, and by calculating the relative risk and 95% confidence interval (CI). SMR was used as measure for effect size in hospital mortality.

For Propensity Score Matching, the optimal matching algorithm was determined to be the Mahalanobis distance algorithm with one-to-one and caliper matching. The maximal allowable distance was set at 0.10 of the pooled standard deviation of the logit of the propensity score, and the confidence level was set at 95%. The maximum tolerance for the absolute difference in propensity scores was 0.001. The covariates included in the model were age, sex, APACHE IV admission diagnosis, and the SAPS II score. The detailed PSM results can be obtained from the corresponding author upon request. To determine whether the PSM cohorts were similar, we measured the effect size using Cohen's d for the logit of the propensity score. A (very) small effect size is being pursued as it indicates better matching and thus (very) similar cohorts.

Kaplan–Meier survival analysis with the log-rank test was performed to assess survival rates up to 30 days and 12 months after ICU admission. The relative risk of mortality was calculated using 95% confidence intervals (CIs). Statistical significance was set at $P < 0.05$.

Results

The study included 5685 ICU admissions between January 2015 and December 2019, as shown in Figure 1. A total of 3020 admissions were excluded from the study: 700 patients with planned medical admissions, 1662 (un)planned surgical admissions, 324 with pathologies that were not represented in either group, 219 admissions that were not transferred from the ED, and 115 readmissions during the same hospital stay.

Of the 2665 eligible patients, 2054 were directly transferred from the ED (DICU-P) and 611 passed a general ward before ICU admission. Of the 611 patients, 292 stayed for less than 48h in the ward before ICU admission (IDICU-P). 1163 DICU-P stayed for less than 48h in the ICU and 891 stayed for 48h or more. A total of 146 IDICU-P stayed for less than 48h in the ICU, and 146 stayed for 48h or more. After PSM, two groups of 288 patients who were comparable in all the selected covariates were obtained.

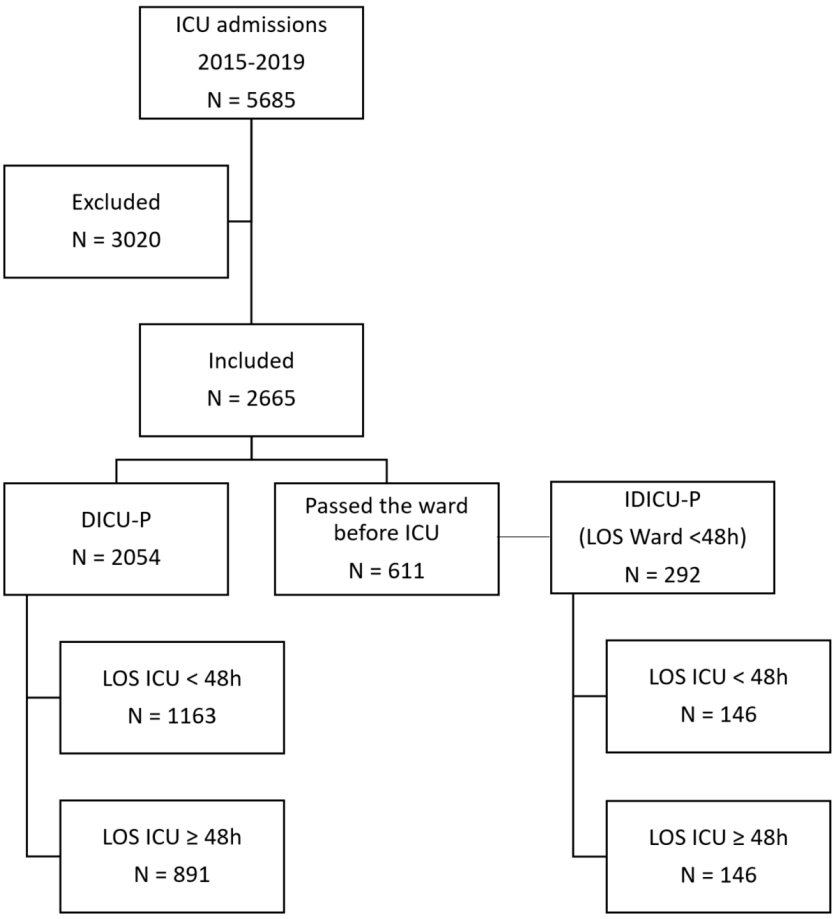

Fig. 1 — Flow diagram of the study.
DICU-P, direct ICU admission; IDICU-P, indirect ICU admission; LOS, length of stay.

DICU-P versus IDICU-P

Table I shows the most frequent APACHE IV admission diagnoses with their respective hospital mortality rates in DICU-P and IDICU-P. Significantly higher hospital mortality in IDICU-P was observed in patients with pneumonia, congestive heart failure, and emphysema/bronchitis. Table II presents the characteristics and outcomes (LOS and mortality) of DICU-P and IDICU-P. Figure 2 displays the DICU-P and IDICU-P timelines, which provide a more detailed view of the different subgroups and permit the analysis of the sequence of events. Overall effect sizes for continuous variables were small.

Patient characteristics

When considering all patients, IDICU-P were significantly older than DICU-P; this was even more prominent in patients with LOS-ICU <48h. Beyond this threshold, the age difference became insignificant. Sex did not differ significantly between the groups. When comparing subgroups (e.g., patients who deceased within 48h, patients who were discharged within 48h but died in the hospital), older age in the IDICU-P remained notable when compared to the DICU-P, although the difference was not significant. In the subgroup of patients who died in the ICU after staying in the ICU for more than 48h, DICU-P were older than IDICU-P, although this difference was not statistically significant.

Length of stay (LOS)

There were no significant differences in LOS-ICU, regardless of the population. The hospital LOS was significantly longer in IDICU-P when considering all patients and in patients with LOS-ICU ≥48h. In contrast, DICU-P with LOS-ICU <48u had a longer LOS in the hospital, but this was not significant. The LOS-hospital after ICU discharge did not differ significantly between DICU-P and IDICU-P when considering the total population and those with LOS-ICU <48u. In the timelines, a distinction was made between those who died in the hospital after ICU discharge and those who did not. A similar LOS-post-ICU was observed in those who left the hospital alive after being discharged from ICU <48h, but a significantly shorter LOS-post-ICU was noticed in IDICU-P who died in the hospital after being discharged from the ICU <48h (1.5 days vs 4.5 days in DICU-P patients). The IDICU-P with LOS-ICU ≥48h had a longer

Table I. — Top 10 APACHE IV admission diagnoses & hospital mortality.

APACHE-IV Admission Diagnoses	Total N	DICU-Patients N (N died in hosp)	IDICU-Patients N (N died in hosp)	Statistics Fisher's exact p value
Bleeding GI, aggregated, all causes	219	186 (19)	33 (5)	p = 0.374
Pneumonia, aggregated, all causes	216	179 (37)	37 (14)	p = 0.033
Sepsis, aggregated, all causes	162	136 (29)	26 (9)	p = 0.204
Emphysema/bronchitis	154	133 (15)	21 (6)	p = 0.043
CVA, cerebrovascular accident/stroke	151	141 (10)	10 (1)	p = 0.452
CHF, congestive heart failure	149	132 (14)	17 (5)	p = 0.045
Renal failure, acute	120	109 (15)	11 (1)	p = 1.000
Rhythm disturbance (conduction defect)	76	63 (2)	13 (0)	p = 1.000
Seizures (primary-no structural brain disease)	60	48 (1)	12 (1)	p = 0.363
Infarction, acute myocardial, non-Q wave	49	38 (1)	11 (0)	p = 1.000
DICU: Direct Intensive Care Unit admission; IDICU: Indirect Intensive Care Unit admission.				

hospital LOS after ICU discharge than the DICU-P. This was consistent when considering subgroups with LOS-ICU ≥48h (Figure 2).

SAPS II, Mortality & SMR

The median SAPS II score was significantly higher in IDICU-P when considering the total population and those with LOS-ICU <48h. SAPS II scores were comparable in patients with LOS-ICU ≥48h. The timelines showed a difference in the SAPS II between the subgroups, which was in concordance with their features. When all patients were considered, the mortality (ICU, post-ICU, and total/hospital) was significantly higher in IDICU-P. In the population with LOS-ICU <48h, this difference in mortality was also present but only reached significance in ICU mortality and total/hospital mortality. Patients with LOS-ICU ≥48h had a slightly higher ICU mortality rate when they were directly admitted. Post-ICU and total/hospital mortality rates in these patients were higher in IDICU-P.

The SMR was significantly higher for both DICU-P and IDICU-P when considering the total population and those with LOS-ICU <48h. In the population with LOS-ICU ≥48h, neither reached statistical significance.

Propensity score matching

Propensity Score Matching yielded 288 patients in each group. Four IDICU-P had no match. The two groups had comparable means of the logit of the propensity score and standard deviations (0.654 ± 0.266 (IDICU-P) vs. 0.665 ± 0.266 (DICU-P), 95% CI [-0.044; 0.043]), resulting in Cohen's d = 0.004, which indicates a small effect size. The Hosmer-Lemeshow test was not statistically significant (P=0.181). These findings suggest that the model accurately fits the data. Table 3 shows a comparison between the DICU-P and IDICU-P after PSM. Figure 3 shows the timelines of DICU-P and IDICU-P after PSM. Again, effect sizes for continuous variables were, consistently, small.

Patient characteristics

As PSM accounted for the covariates of age and sex, there was no difference in the median age or sex. The timelines after PSM showed a similar pattern in terms of age variation between subgroups, as observed before PSM. IDICU-P who died in the ICU <48h after admission were notably older, although the difference was not significant.

Length of stay (LOS)

All statements made before PSM were confirmed. When significance was reached before matching, it was maintained after PSM (see Table III).

SAPS II, Mortality & SMR

As PSM accounted for SAPS-II, no difference was observed between the DICU-P and IDICU-P, and the timelines after PSM displayed a similar pattern in terms of SAPS-II variation between the subgroups, as seen before PSM. ICU and post-ICU mortality rates did not differ, but total hospital mortality was significantly higher in IDICU-P when considering all patients. In the PSM cohort, a significantly higher early mortality rate was also observed in IDICU-P. Furthermore, there was a similar trend in mortality as that before PSM, but the significance was lost. SMR was only significantly higher in IDICU-P when considering the total population and in those with LOS-ICU <48h. In the population with LOS-ICU ≥48h, again, neither reached significance.

Survival up to 12 months after ICU admission

Most deaths occurred within the first 30 days after ICU admission and the mortality rate was significantly higher in IDICU-P (Relative Risk (RR) 1.81; p < 0.0001; see Table IV). At 12 months, mortality was also significantly higher in IDICU-P

Table II. — Direct vs. Indirect ICU admission, total population.

	DICU-P	IDICU-P	Statistics
	ALL PATIENTS		
N patients	2054	292	
Age (y)	70 (IQR 18)	72.5 (IQR 19)	Z = -3.431; p < 0.0001
Gender (Male / Female, N)	1136 / 918	156 / 136	X^2 = 0.29; p = 0.590
LOS – ICU (days)	1.82 (IQR 2.17)	2.02 (IQR 2.87)	Z = 1.725; p = 0.084
LOS – Hosp post ICU (days)	5.95 (IQR 8.27)	6.95 (IQR 11.52)	Z = -1.910; p = 0.056
LOS – Hosp (days)	8.06 (IQR 9.98)	9.82 (IQR 13.16)	Z = -2.682; p = 0.007
Mortality – ICU (N)	137 (6.67%)	33 (11.3%)	X^2 = 7.48; p = 0.006
Mortality – Hosp (post-ICU) (N)	131 (6.38%)	34 (11.64%)	X^2 = 12.02; p = 0.0005
Mortality – Hosp (Total) (N)	268 (13.05%)	67 (22.95%)	X^2 = 20.46; p < 0.0001
SAPS II score Expected hosp mortality	30 (IQR 19) 10.6%	33 (IQR 21) 14%	Z = -3.717; p = 0.0002
SMR (SAPS II associated)	1,23 (1.08-1.38)	1,63 (1.24-2.02)	
	POPULATION LOS-ICU <48h		
N patients	1163	146	
Age (y)	69 (IQR 25)	72 (IQR 20)	Z = -2.656; p = 0.008
Gender (Male / Female, N)	641 / 522	73 / 73	X^2 = 1.17; p = 0.2794
LOS – ICU (days)	1.03 (IQR 0.89)	0.97 (IQR 0.85)	Z = 1.757; p = 0.079
LOS – Hosp post ICU (days)	4.88 (IQR 6.98)	3.60 (IQR 8.02)	Z = 0.959; p = 0.337
LOS – Hosp (days)	5.62 (IQR 7.64)	4.08 (IQR 8.15)	Z =1.1093; p = 0.275
Mortality – ICU (N)	73 (3.6%)	25 (8.6%)	X^2 = 20.49; p < 0.0001
Mortality – Hosp (post-ICU) (N)	50 (4.6%)	10 (8.3%)	X^2 = 2.4; p = 0.121
Mortality – Hosp (Total) (N)	123 (10.5%)	35 (23.9%)	X^2 = 21.93; p < 0.0001
SAPS II score Expected hosp mortality	27 (IQR 18) 7.9%	32 (IQR 24) 12.8%	Z = -3.095; p = 0.002
SMR (SAPS II associated)	1,34 (1.1-1.58)	1,87 (1.25-2.49)	
	POPULATION LOS-ICU ≥48h		
N patients	891	146	
Age (y)	71 (IQR 18)	73 (IQR 18)	Z = -1.408; p = 0.159
Gender (Male / Female, N)	495 / 396	83 / 63	X^2 = 0.04; p = 0.842
LOS – ICU (days)	3.61 (IQR 2.90)	3.83 (IQR 3.15)	Z = -1.907; p = 0.057
LOS – Hosp post ICU (days)	7.13 (IQR 9.95)	10.06 (IQR 11.91)	Z = -2.652; p = 0.008
LOS – Hosp (days)	11.29 (IQR 11.17)	15.64 (IQR 14.13)	Z = -4,286; p < 0.0001
Mortality – ICU (N)	64 (7.2%)	8 (5.5%)	X^2 = 0.330; p = 0.566
Mortality – Hosp (post-ICU) (N)	81 (9.8%)	24 (17.4%)	X^2 = 6.280; p = 0.012
Mortality – Hosp (Total) (N)	145 (16.3%)	32 (21.9%)	X^2 = 2.820; p = 0.093
SAPS II score Expected hosp mortality	35 (IQR 18) 16.7%	36 (IQR 18) 18.1%	Z = -1.310; p = 0.190
SMR (SAPS II associated)	0.98 (0.82-1.14)	1.21 (0.79-1.63)	

DICU-P: patients directly admitted in ICU; IDICU-P: patients indirectly admitted in ICU; LOS: length of stay; ICU: intensive care unit; Hosp: hospital; SAPS: Simplified Acute Physiology Score; SMR: Standardized Mortality Rate.

(RR 1.55; p < 0.0001). The Kaplan-Meier survival distribution is presented in Figures 4 (30 days) and 5 (12 months), with log-rank observed values of 26.544 (P < 0.0001) and 24.920 (P < 0.0001), respectively. There was no significant difference in mortality between the groups, suggesting similar survival and the absence of catch-up mortality (74 of 106 vs. 287 of 481; X2 = 3.775; P = 0.052) between 30 days and 1 year.

A survival analysis was also performed in the PSM cohort. On day 30, mortality was higher in IDICU-P (RR 1.50, p = 0.018). At 12 months, a

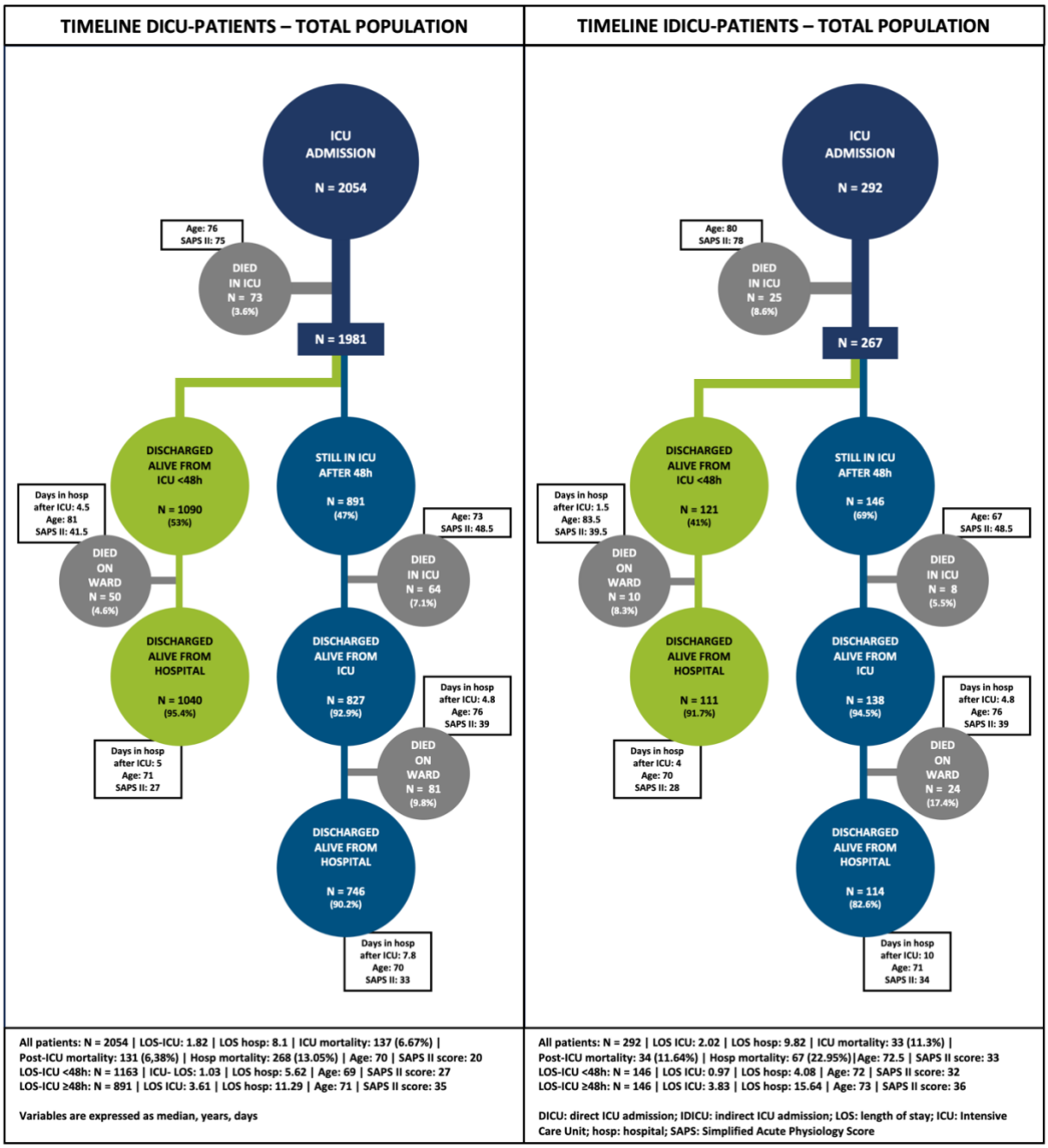

Fig. 2 — Timelines Direct & Indirect ICU admission – Total population.

higher mortality rate was observed in the IDICU-P (RR 1.39, p = 0.009). The Kaplan-Meier survival distribution is presented in Figures 6 (30 days) and 7 (12 months), showing log-rank observed values of 5.570 (P = 0.018) and 7.188 (P = 0.007), respectively. Again, there was no catch-up mortality (n = 69 of 103 vs. 46 of 74; X2 = 0.441; P = 0.507).

Discussion

This study provides a comprehensive understanding of the discrepancies in outcomes between medical patients admitted to the ICU either directly from the ED or indirectly after being transferred from a ward.

Our study confirms previous findings that a delay in ICU admission is associated with increased mortality rates both in the ICU and post-ICU stay, as well as a longer overall hospital stay. It is important to recognize that there was an imbalance between the delayed and direct admission groups, with the delayed group having a higher age and SAPS II scores. After adjusting for confounding factors through PSM, the hospital stay remained significantly longer, and the mortality trend was preserved, although it only reached statistical significance for overall hospital and early ICU mortality. The good news here is that 75% of ED patients who ended up in the ICU were admitted directly without delay. We can also support the observation that patients with

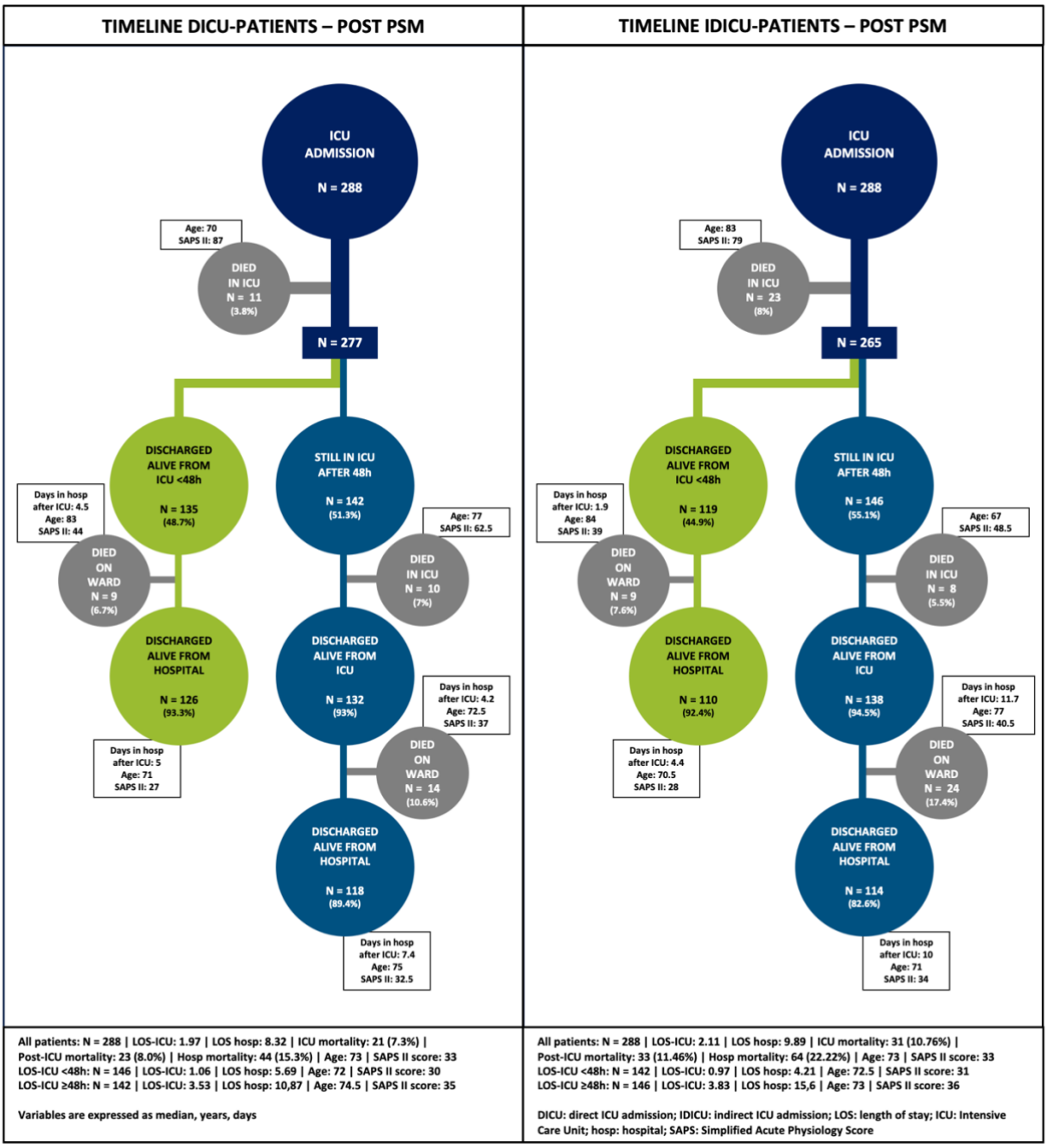

Fig. 3 — Timelines Direct & Indirect ICU admission – After Propensity Score Matching (PSM).

pneumonia, COPD exacerbation, and congestive heart failure who have delayed access to critical care demonstrate excess mortality compared to those directly admitted, whereas those with Acute Myocardial Infarction (AMI), sepsis, or stroke do not[7,13]. We share the point of view of Liu et al. that disparities in diagnosis-specific excess mortality can be attributed to growing adherence to standardized clinical guidelines for specific high-risk conditions[13].

Through timeline analysis, distinguishing ICU LOS and highlighting different subgroups, other findings and nuances were identified. Among the directly admitted patients, 3.6% died within 48h after ICU admission. Given their relatively young median age and high SAPS-II, it can be inferred that a considerable proportion of them were "too sick to benefit" (TSTB) from intensive care, but received maximum efforts to survive. Conversely, one of the most noteworthy findings of this study was that ICU mortality in the first 48h after ICU admission was more than twice as high in patients with delayed admission. It is plausible that some patients who were initially denied admission to the ICU due to their age and/or comorbidities were actually considered TSTB at the ED but were subsequently admitted to the ICU due to rapid deterioration, in which the earlier decision not to admit the patient to ICU was overruled. This raises the issue of Do Not Resuscitate (DNR) orders, which is beyond the scope of this study. However, the main reason for the higher mortality rate is more likely to be due to missing the "critical window of opportunity";

Table III. — Direct vs. Indirect ICU admission, after Propensity Score Matching.

	DICU-P	IDICU-P	Statistics
	ALL PATIENTS		
N patients	288	288	
Age (y)	73 (IQR 19)	73 (IQR 18.3)	Z = 0.285; p = 0.775
Gender (Male / Female, N)	143 / 145	155 / 133	X^2 = 1.000; p = 0.317
LOS – ICU (days)	1.97 (IQR 2.43)	2.11 (IQR 2.89)	Z = -0.575; p = 0.565
LOS – Hosp post ICU (days)	6.01 (IQR 8.69)	6.99 (IQR 10.89)	Z = -1.622; p = 0.105
LOS – Hosp (days)	8.32 (IQR 9.14)	9.89 (IQR 13.03)	Z = -2.174; p = 0.030
Mortality – ICU (N)	21 (7.3%)	31 (10.8%)	X^2 = 1.712; p = 0.191
Mortality – Hosp (post-ICU) (N)	23 (8.0%)	33 (11.5%)	X^2 = 2.450; p = 0.117
Mortality – Hosp (Total) (N)	44 (15.3%)	64 (22.2%)	X^2 = 4.558; p = 0.033
SAPS II score Expected hosp mortality	33 (IQR19) 14%	33 (IQR 21) 14%	Z = -0.748; p = 0.454
SMR (SAPS II associated)	1.09 (0.77-1.41)	1.59 (1.2-1.98)	
	POPULATION LOS – ICU <48h		
N patients	146	142	
Age (y)	72 (IQR 19.75)	72.5 (IQR 19)	Z = -0.480; p = 0.631
Gender (Male / Female, N)	74 / 72	72/ 70	X^2 = 0; p = 0.997
LOS – ICU (days)	1.06 (IQR 0.85)	0.97 (IQR 0.85)	Z = 1.137; p = 0.255
LOS – Hosp post ICU (days)	5.01 (IQR 7.50)	3.71 (IQR 8.39)	Z = 0.398; p = 0.691
LOS – Hosp (days)	5.69 (IQR 7.92)	4.21 (IQR 8.11)	Z = 0.309; p = 0.758
Mortality – ICU (N)	11 (3.8%)	23 (8.0%)	X^2 = 4.501; p = 0.034
Mortality – Hosp (post-ICU) (N)	9 (6.7%)	9 (7.6%)	X^2 = 0.077; p = 0.781
Mortality – Hosp (Total) (N)	20 (13.7%)	32 (22.5%)	X^2 = 3.044; p =0.081
SAPS II score Expected hosp mortality	30 (IQR 21) 10.6%	31 (IQR 23) 11.7%	Z = -0.359; p = 0.720
SMR (SAPS II associated)	1.29 (0.72-1.86)	1.92 (1.25-2.59)	
	POPULATION LOS – ICU ≥48h		
N patients	142	146	
Age (y)	74.5 (IQR 18)	73 (IQR 17.5)	Z = 0.975; p = 0.330
Gender (Male / Female, N)	69 / 73	83 / 63	X^2 = 1.97; p = 0.160
LOS – ICU (days)	3.53 (IQR 2.28)	3.83 (IQR 3.12)	Z = -1.949; p = 0.051
LOS – Hosp post ICU (days)	7.05 (IQR 8.96)	10.06 (IQR 11.91)	Z = -2.582; p = 0.010
LOS – Hosp (days)	10.87 (IQR 9.65)	15.64 (IQR 14.11)	Z = -4.050; p < 0.0001
Mortality – ICU (N)	10 (7%)	8 (5.5%)	X^2 = 0.300; p = 0.584
Mortality – Hosp (post-ICU) (N)	14 (10.6%)	24 (17.4%)	X^2 = 2.567; p = 0.109
Mortality – Hosp (Total) (N)	24 (16.9%)	32 (21.9%)	X^2 = 1.157; p = 0.282
SAPS II score Expected hosp mortality	35 (IQR 16.75) 16.7%	36 (IQR 17.75) 18.1%	Z = -0.671; p = 0.502
SMR (SAPS II associated)	1.01 (0.6-1.42)	1.21 (0.79-1.63)	

PSM: Propensity Score Matching; DICU-P: patients directly admitted in ICU; IDICU-P: patients indirectly admitted in ICU; LOS: length of stay; ICU: intensive care unit; Hosp: hospital; SAPS: Simplified Acute Physiology Score; SMR: Standardized Mortality Rate.

patients who were initially not TSTB at the ED but became TSTB at ICU admission because of the delay. Despite PSM corrected for age and SAPS II scores, the TSTB characteristics in the population who died in the ICU within 48h became even more apparent, namely (relatively) young patients with a high severity of illness.

Additionally, IDICU-P who died within 48h in the ICU were found to be even older after PSM. This finding aligns with previous research indicating that elderly individuals often appear stable in the ward and are more likely to deteriorate acutely rather than gradually, making it challenging to identify those in need of critical care in a timely manner[19,20]. These

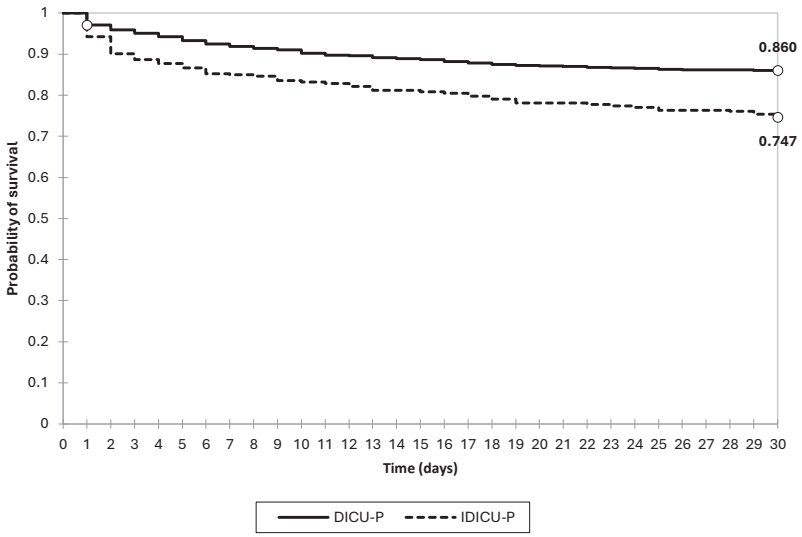

Fig. 4 — Kaplan-Meier Survival distribution – 30 days – total population – Direct vs. Indirect ICU admission.
DICU-P: Direct Intensive Care Unit admission (N = 2054); IDICU-P: Indirect Intensive Care Unit admission (N = 292) - Log-rank test: 26.554; P < 0.0001

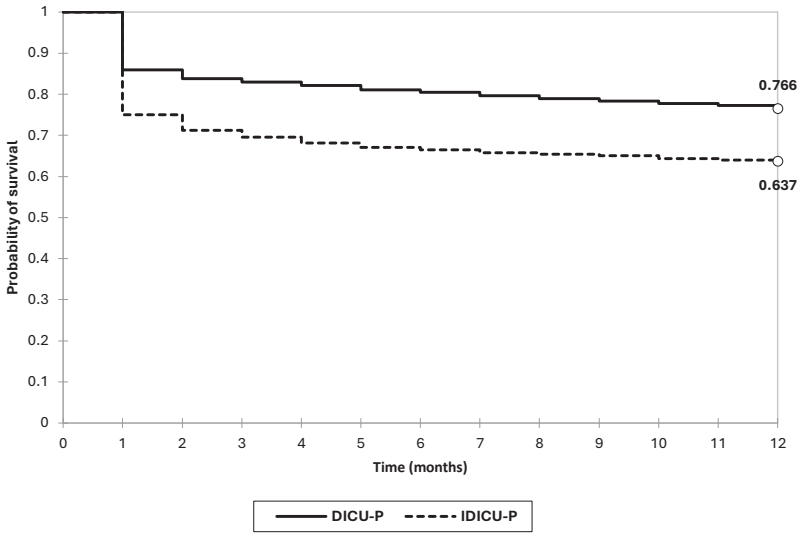

Fig. 5 — Kaplan-Meier Survival distribution – 1 year – total population – Direct vs. Indirect ICU admission.
DICU-P: Direct Intensive Care Unit admission (N = 2054); IDICU-P: Indirect Intensive Care Unit admission (N = 292) - Log-rank test: 24.920; P < 0.0001

patients may have benefited from close monitoring in the ICU as a "narrower window" could be assumed. These findings suggest that delayed ICU admission of elderly patients is correlated with an increased likelihood of early mortality. This is further supported by the fact that at 48h in the ICU, there was no significant difference in age between the two groups.

We observed a DICU-P-to-IDICU-P ratio higher than that in previous studies[1,4,8], which suggests that the high ED-to-ICU patient triage rate may be hospital related. As the ICU is not consistently fully occupied and there is no intermediate care unit, there might be overtriage of patients into the ICU. More than half of the directly admitted patients left the ICU alive within 48h, with a small percentage of post-ICU in-hospital mortality. Given their young median age and relatively favorable SAPS II, this suggests a significant number of "too well to benefit" (TWTB) patients. In the delayed admission group, fewer patients survived to leave the ICU within 48h, while a larger proportion of these patients died within the hospital after ICU discharge. The fact that these patients were older and had significantly shorter post-ICU LOS suggests that they had entered palliative care more frequently. This mortality can be attributed to missing "the window" and can be included in the previously mentioned higher early mortality in this group. After PSM, the TWTB population thinned out, but this did not alter previous statements.

The SMR was significant for both directly and indirectly admitted patients in the total population and in patients with an LOS-ICU <48h, indicating a

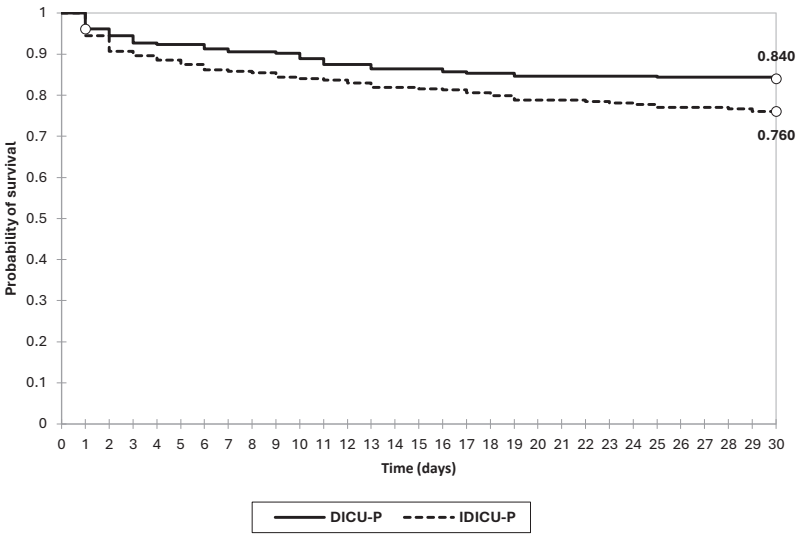

Fig. 6 — Kaplan-Meier Survival distribution – 30 days – after Propensity Score Matching – Direct vs. Indirect ICU admission.
DICU-P: Direct Intensive Care Unit admission (N = 288); IDICU-P: Indirect Intensive Care Unit admission (N = 288) - Log-rank test: 5.570; P = 0.018

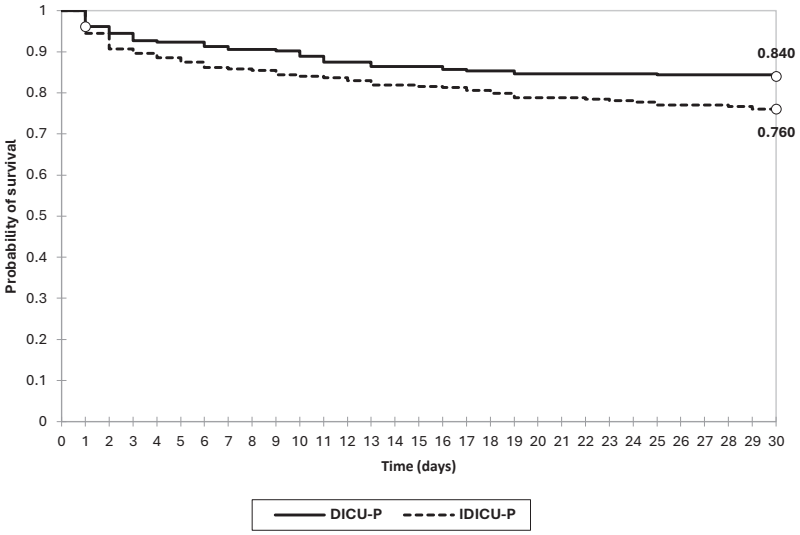

Fig. 7 — Kaplan-Meier Survival distribution – 1 year – after Propensity Score Matching – Direct vs. Indirect ICU admission.
DICU-P: Direct Intensive Care Unit admission (N = 288); IDICU-P: Indirect Intensive Care Unit admission (N = 288) - Log-rank test: 7.188; P = 0.007

much higher observed mortality than that expected based on SAPS II. After PSM, this significance was only observed in indirectly admitted patients. This finding can be attributed to the abundance of TWTB patients before PSM who had low SAPS II scores and low mortality rates, which distorted the true observed-to-expected (O/E) ratio. However, it resulted in a much higher SMR in the delayed admission group when the two groups had similar ages and severity of illness, indicating that delays in critical care were the culprit and thus an independent determinant of hospital mortality. This is consistent with previous research that emphasized the importance of customizing the SAPS II score by incorporating information on "patient location prior to ICU" and "length of hospital stay prior to ICU admission"[18]. Once patients survived the first 48h in the ICU, the benefit of early critical care became increasingly apparent, as evidenced by hospital mortality and SMR. Although ICU mortality after 48h was even slightly higher in directly admitted patients, probably because the proportion of those affected by the delay did not make it this far, it had a significant effect on post-ICU mortality and LOS. After PSM, this trend was preserved, but statistical significance was lost.

Analysis of the long-term mortality rates revealed that the initial mortality gap was preserved in both the general and PSM cohorts. No indications of catch-up mortality were found, underscoring the importance of correct initial triage of patients who may benefit from critical care, directly into the ICU.

Table IV. — Survival data up to 12 months after ICU admission.

	DICU-P	IDICU-P	Statistics
	ALL PATIENTS		
N patients	2054	292	
Mortality at 30 days	287 (13.97%)	74 (25.34%)	RR 1.81; 95% CI [1.45-2.27]; Z = 5.205; P < 0.0001
Mortality at 12 months	481 (23.42%)	106 (36.30%)	RR 1.55; 95% CI [1.31-1.84]; Z = 5.028; P < 0.0001
	AFTER PROPENSITY SCORE MATCHING		
N patients	288	288	
Mortality at 30 days	46 (15.97%)	69 (23.96%)	RR 1.50; 95% CI [1.07-2.10]; Z = 2.369; P = 0.018
Mortality at 12 months	74 (25.69%)	103 (35.76%)	RR 1.39; 95% CI [1.08-1.79]; Z = 2.592; P = 0.009

DICU-P: patients directly admitted in ICU; IDICU-P: patients indirectly admitted in ICU; RR: Relative Risk; CI: confidence interval.

Finally, although it is crucial to seize the "critical window of opportunity", it is equally important to avoid inappropriate use of ICU resources in TWTB patients, as well as disproportionate care in TSTB patients, as this can result in ethical violations, patient suffering, compassion fatigue, and moral distress in healthcare providers[21].

Strenghts and limitations

The present study has several strengths, including the meticulous efforts made to minimize biases and confounding factors as well as stratification and subgroup analysis by means of timelines. However, the consequence of our endeavors to minimize bias was a relatively small sample size after stratification, resulting in smaller subgroups and a loss of statistical power and significance. This was reflected in the consistency of the small effect size. Since no sensitivity analysis was performed and we only accounted for certain confounders based on prior work and clinical experience, residual bias and confounding factors might have persisted. It should be noted that this study was conducted at a single center, a regional general hospital, without an intermediate care unit. This limitation has both strengths and weaknesses. The fact that all patients were treated by the same team and data collection was performed by a select group of intensivists enhances internal validity; however, external validity is limited because of the absence of a step-up/step-down unit.

The retrospective nature of this study had several limitations. First, disease patterns are often dynamic (evolving). We can only speculate on why patients might have been initially triaged to the ICU or a normal ward. It is possible that patients presented with only mild symptoms in the ED, not justifying ICU admission, subsequently deteriorated in the ward, and were admitted to the ICU at the earliest possible time. In this case, there was neither any fault in the judgement nor any lack of acknowledgement of the severity of the illness. Rather, it is simply the unforeseeable nature of certain diseases that poses a challenge. However, it should be noted that not all deaths in the delayed admission group may have been prevented through direct admission. Second, it was impossible to determine the specific train of thought for each case at that time. It is possible that some 'delayed' patients had limited life expectancy and quality of life and that their physicians were reluctant to consider critical care support at an early stage. We also cannot determine if some ICU stays were shorter or longer due to logistic rather than medical reasons. Third, we could not determine the cases in which critical care was provided in the ED. Although critical care can already be started by emergency physicians, providing critical care is more than starting antibiotics, oxygen therapy, or noninvasive ventilation (NIV). Critical care also includes close-up monitoring and a higher nurse-to-patient ratio. It is the ability, clinical expertise, and availability of resources to escalate care quickly when a patient deteriorates. These features are more difficult to provide in the ED.

The use of SAPS II as a proxy for the severity of illness and comorbidities is a widely accepted practice, despite its limitations in accurately capturing the full scope of comorbidities. However, the Charlson Comorbidity Index and SAPS 3 scores are more widely accepted and comprehensive measures of comorbidities.

The purpose of this study was not to determine which patients could be saved through timely care but rather to identify the factors that influence the decision-making process regarding patient transfers. This limited our ability to draw meaningful conclusions regarding the effectiveness of interventions aimed at improving patient outcomes through early recognition and management.

Conclusions

Our study confirmed the differences in outcomes as well as the disparity in patient and disease characteristics between patients admitted directly or indirectly from the Emergency Department in the ICU. Delayed ICU admission was associated with longer hospital stays and higher mortality rates up to 12 months after admission, but also with advanced age and higher severity of illness, both confounding this association. After Propensity Score Matching, accounting for confounding factors, significance was often lost, but the general trend remained.

In addition, this study provides two suggestions to keep in mind when considering ICU admission. First, according to the rule of thumb, increasing age decreases the possibility of ICU admission. However, the excess early mortality in the elderly population when indirectly admitted, their narrower window of opportunity and the potential benefits of close-up monitoring in this population suggest that a lower admission threshold should be considered. Second, we confirmed previous findings that certain diagnoses (pneumonia, COPD exacerbation, and congestive heart failure) have increased time sensitivity in addition to not having well-defined practice guidelines (unlike AMI, stroke, and sepsis). In such cases, a lower threshold for ICU admission should be considered.

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