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Emergency Department to ICU Time Is Associated With Hospital Mortality: A Registry Analysis of 14,788 Patients From Six University Hospitals in The Netherlands*

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Objectives: Prolonged emergency department to ICU waiting time may delay intensive care treatment, which could negatively affect patient outcomes. The aim of this study was to investigate whether emergency department to ICU time is associated with hospital mortality.

Design, Setting, and Patients: We conducted a retrospective observational cohort study using data from the Dutch quality registry National Intensive Care Evaluation. Adult patients admitted to the ICU directly from the emergency department in six university hospitals, between 2009 and 2016, were included. Using a logistic regression model, we investigated the crude and adjusted (for disease severity; Acute Physiology and Chronic Health Evaluation IV probability) odds ratios of emergency department to ICU time on mortality. In addition, we assessed whether the Acute Physiology and Chronic Health Evaluation IV probability modified the effect of emergency department to ICU time on mortality. Secondary outcomes were ICU, 30-day, and 90-day mortality.

Interventions: None.

Measurements and Main Results: A total of 14,788 patients were included. The median emergency department to ICU time was 2.0 hours (interquartile range, 1.3–3.3 hr). Emergency department to ICU time was correlated to adjusted hospital mortality ($p < 0.002$), in particular in patients with the highest Acute Physiology and Chronic Health Evaluation IV probability and long emergency department to ICU time quintiles: odds ratio, 1.29; 95% CI, 1.02–1.64 (2.4–3.7 hr) and odds ratio, 1.54; 95% CI, 1.11–2.14 (> 3.7 hr), both compared with the reference category (< 1.2 hr). For 30-day and 90-day mortality, we found similar results. However, emergency department to ICU time was not correlated to adjusted ICU mortality ($p = 0.20$).

Conclusions: Prolonged emergency department to ICU time (> 2.4 hr) is associated with increased hospital mortality after ICU admission, mainly driven by patients who had a higher Acute Physiology and Chronic Health Evaluation IV probability. We hereby provide evidence that rapid admission of the most critically ill patients

to the ICU might reduce hospital mortality. (*Crit Care Med* 2019; 47:1564–1571)

Key Words: critically ill; emergency department; intensive care unit; length of stay; mortality

Ideally critically ill patients, except for those requiring palliative care or an acute intervention, should be admitted to the ICU as soon as possible to receive the best appropriate care. However, delays in admission are common, due to triage, diagnostics, and logistical reasons (1–4).

Patients can be admitted to the ICU from different departments; postoperative patients in need of intensive care, deteriorating patients coming from the ward or acute patients admitted from the emergency department (ED).

In patients admitted from hospital wards, it was shown that an increased hospital length of stay (LOS) before ICU admission was correlated with mortality (5). However, data on mortality of patients admitted directly to the ICU from the ED are conflicting. Saukkonen et al (6) reported that crude hospital mortality was lowest in the quartile of patients with the shortest LOS in the ED. Chalfin et al (7) found that a delayed transfer from ED to ICU increases hospital LOS and ICU mortality (adjusted for Acute Physiology and Chronic Health Evaluation [APACHE] II score). However, using Australian and New Zealand Intensive Care Society registry data, Carter et al (8) were unable to demonstrate an adjusted correlation between time in the ED and hospital mortality.

On top of these conflicting results, ED to ICU time may vary between hospitals and especially between countries. For example, reported median ED to ICU time in Australia and New Zealand was 3.9 hours, but 4.8 hours in Finland (6, 8). In The Netherlands, the median ED to ICU time may be shorter: 2.2 hours (9), and this may modify the effect on mortality.

Since data are conflicting and there is a lack of European nationwide data, we considered a large study on the correlation between ED to ICU time and hospital mortality would be necessary. In addition, we studied this association with secondary mortality endpoints (i.e., ICU, 30-d, and 90-d mortality).

MATERIALS AND METHODS

Study Population and Data Collection

We conducted a retrospective observational cohort study using data from the National Intensive Care Evaluation (NICE) registry. This registry was developed by The NICE foundation and contains the complete and continuous registration of all available data of the 84 cooperating ICUs in The Netherlands (10). For this study, we included all adult patients who were admitted to the ICU directly from the ED, between 2009 and 2016 in six academic medical centers (Amsterdam University Medical Center, Erasmus MC University Medical Center, Leiden University Medical Center, Radboud University Medical Center, University Medical Center Groningen, and University Medical Center Utrecht).

All independent variables were available in the NICE registry, except the registration of ED to ICU time. The ED to ICU time was defined as the time of physical admission of the patient at the ED until the time of physical admission of the patient to the ICU. ED admission date and time were retrospectively collected from the participating centers and were merged with NICE data, in order to calculate ED to ICU time. The ED to ICU time was categorized into quintiles.

Primary and Secondary Outcomes: Mortality Outcomes

The primary outcome was hospital mortality, and the secondary outcomes were ICU mortality, 30-day mortality, and 90-day mortality. Based on deterministic linkage, we combined data from the NICE registry with the insurance claims database in The Netherlands (Vektis data) (11). As most of the Dutch inhabitants do have health insurance and their date of decease is included in the insurance claims database, we were able to assess 30-day mortality and 90-day mortality endpoints (12).

Statistical Analysis

For descriptive statistics, results are presented as medians (interquartile ranges [IQRs]) and *n* (%) where appropriate. Categorical variables are presented as frequencies (%). Baseline characteristics were analyzed and compared between quintiles of ED to ICU time, using conventional statistical tests. Continuous variables were compared between quintiles of ED to ICU time with analysis of variance or Kruskal-Wallis test when they were normally or nonnormally distributed, respectively. In order to test whether a continuous variable followed a normal distribution, we used the Kolmogorov-Smirnov test. Categorical variables were compared between quintiles of ED to ICU time with chi-square test or the Fisher exact test.

For the analysis of the primary outcome (hospital mortality), a logistic regression model was used. The ED to ICU time quintile with the shortest ED to ICU time was the reference group. We built our models in three steps, where all models were adjusted for the university hospital of admission using a dummy variable for each hospital. First, we estimated the odds ratios (ORs) for the association between ED to ICU time quintiles and hospital mortality. Second, we adjusted for disease severity, using the APACHE IV probability. Third, we assessed whether the APACHE IV probability modified the effect of ED to ICU time on hospital mortality. Therefore, terms for the interaction between the APACHE IV probability and ED to ICU time were included in the model. The APACHE IV model consists of the following components: the APACHE III score (consisting of the acute physiology score in the first 24 hr, comorbidities, and age), admission diagnosis (445 different diagnoses), and reason for ICU admission (medical, urgent, or elective) (13). The APACHE IV probability was divided into quintiles, the first and second quintile were merged into one group because we expected only a few events in these two quintiles.

Finally, after having fitted the logistic model, a Wald test was used to assess whether there were statistically significant differences in hospital mortality between the five quintiles for ED to ICU time, and this was also done separately for each APACHE IV probability category. The secondary outcome, ICU mortality, was analyzed in the same way.

For the other secondary mortality outcomes, 30-day and 90-day mortality, we built Cox proportional hazards models. Some patients (5.5% of our study population) were not registered in the insurance claims database, and 30-day and 90-day mortality could not be retrieved. As the observation time was shorter than 30 or 90 days for some patients, their survival duration was censored at the last observation in the NICE registry. Therefore, a Cox proportional hazards model was used as such a model properly takes into account this censoring in the estimation of the hazard ratios (HRs) for 30-day and 90-day mortality. Again, we adjusted all models for the university hospital using a dummy variable. First, the association between ED to ICU time and 30-day and 90-day mortality was estimated. Second, we adjusted for disease severity. Third, we assessed whether the disease severity modified the effect of ED to ICU time on mortality. Again, after having fitted the Cox proportional hazards model, the Wald test was used to assess whether there were statistically significant differences in 30-day and 90-day mortality between the five quintiles for ED to ICU time, and this was also done separately for each APACHE IV probability category. Statistical analyses were performed with R (version 3.5.0; R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org), and a *p* value of less than 0.05 was considered statistically significant. The medical ethical committee of the Erasmus MC reviewed the research proposal and concluded that the anonymized data were not subject to the Dutch Research on Humans Subjects Act (in Dutch "WMO") and waived the need for informed consent.

RESULTS

Population and Baseline Characteristics

Between January 1, 2009, and December 31, 2016, a total of 15,144 patients were admitted to the ICU directly from the ED in the participating hospitals. Patients were excluded when there

TABLE 1. Baseline and In-Hospital Characteristics

Baseline Characteristics	All Patients (*n* = 14,788)	ED to ICU Time < 1.2 hr (*n* = 2,956)	ED to ICU Time 1.2–1.7 hr (*n* = 2,998)	ED to ICU Time 1.7–2.4 hr (*n* = 2,938)	ED to ICU Time 2.4–3.7 hr (*n* = 2,956)	ED to ICU Time 3.7–24.0 hr (*n* = 2,940)	*p*
Age, yr, median (IQR)	59 (45–71)	59 (43–71)	59 (43–71)	60 (45–71)	59 (45–71)	59 (46–70)	0.38
Male, gender, *n* (%)	9,151 (61.9)	1,854 (62.8)	1,884 (62.9)	1,842 (62.8)	1,840 (62.3)	1,731 (58.9)	0.006
APACHE IV score, median (IQR)	64 (42–92)	71 (45–99)	69 (45–99)	68 (44–100)	61 (40–88)	54 (36–76)	< 0.001
APACHE IV predicted mortality, median (IQR)	0.16 (0.05–0.50)	0.23 (0.07–0.62)	0.21 (0.06–0.62)	0.20 (0.06–0.60)	0.14 (0.04–0.41)	0.10 (0.03–0.26)	< 0.001
Most common admission diagnoses[a], *n* (%)							
Cardiac arrest	2,118 (14.3)	550 (18.6)	558 (18.6)	584 (19.9)	346 (11.7)	80 (2.7)	< 0.001
Trauma (nonoperative)	2,018 (13.6)	440 (14.9)	596 (19.9)	398 (13.5)	346 (11.7)	238 (8.1)	< 0.001
Intracranial/subdural/epidural hemorrhage	1,389 (9.4)	363 (12.3)	354 (11.8)	261 (8.9)	236 (8.0)	175 (5.9)	< 0.001
Respiratory failure	1,395 (9.4)	274 (9.3)	277 (9.2)	243 (8.3)	295 (10.0)	306 (10.4)	< 0.13
Overdose	895 (6.1)	245 (8.2)	180 (5.9)	174 (6.0)	167 (5.6)	129 (4.3)	< 0.001
Sepsis	683 (4.6)	65 (2.2)	97 (3.2)	109 (3.7)	177 (6.0)	235 (8.0)	< 0.001
Pneumonia	1,028 (7.0)	169 (3.1)	190 (3.2)	173 (3.5)	269 (4.9)	227 (3.9)	< 0.001
Trauma (operative)	450 (3.0)	21 (7.1)	38 (1.3)	55 (1.9)	125 (4.2)	211 (7.2)	0.245
Acute coronary syndrome	336 (2.3)	66 (2.2)	56 (1.9)	68 (2.3)	77 (2.6)	69 (2.3)	0.40
Aneurysm	286 (1.9)	22 (0.7)	33 (1.1)	19 (0.65)	57 (1.9)	155 (5.3)	< 0.001
In-hospital characteristics							
ED to ICU time, hr, median (IQR)	2.0 (1.3–3.3)	0.9 (0.7–1.1)	1.5 (1.3–1.6)	2.0 (1.9–2.2)	3.0 (2.7–3.3)	5.0 (4.2–6.3)	< 0.001
ICU LOS, d, median (IQR)	2.0 (1.0–4.0)	1.7 (0.7–4.2)	1.7 (0.7–4.4)	1.8 (0.8–4.5)	1.6 (0.7–4.2)	1.6 (0.7–3.9)	0.012
Hospital LOS, d, median (IQR)	5.8 (1.4–14.4)	4.1 (0.8–12.4)	5.2 (1.2–13.9)	5.8 (1.5–14.2)	6.1 (1.4–14.5)	7.6 (2.65–17)	< 0.001
ICU mortality, *n* (%)	2,683 (18.1)	616 (20.8)	619 (20.6)	608 (20.7)	511 (17.3)	329 (11.2)	< 0.001
Hospital mortality, *n* (%)	3,285 (22.2)	739 (25.0)	726 (24.2)	740 (25.2)	626 (21.2)	454 (15.4)	< 0.001

APACHE = Acute Physiology and Chronic Health Evaluation, ED to ICU time = emergency department to ICU time, IQR = interquartile range, LOS = length of stay.
[a]In total 445 different admission diagnoses were reported, the 10 most common admission diagnoses are shown.

was an invalid or nonretrievable ED to ICU time (n = 356). Therefore, a total of 14,788 patients were analyzed. In **Table 1**, the baseline and in-hospital characteristics are shown. Patients had a median age of 59 years (IQR, 45–71 yr) and 62% were male. The most common admission diagnoses were cardiac arrest (14.3%), trauma (nonoperative) (13.6%), intracranial/subdural/epidural hemorrhage (9.4%), and respiratory failure (9.4%). The median ED to ICU time was 2.0 hours (IQR, 1.3–3.3 hr) and the median LOS in the ICU and hospital were 2.0 days (IQR, 1.0–4.0 d) and 5.8 days (1.4–14.4 d), respectively. The overall ICU and hospital mortality were 18.1% and 22.2%, respectively.

Primary Outcome: Hospital Mortality

For our primary outcome, we tested whether ED to ICU time was independently associated with hospital mortality. The results showed a significant negative correlation for the higher ED to ICU time quintiles (2.4–3.7 hr, > 3.7 hr) compared with the lowest ED to ICU time quintile (< 1.2 hr), with ORs of 0.82 (95% CI, 0.72–0.92) and 0.56 (95% CI, 0.49–0.64), respectively (**Fig. 1*A***). ED to ICU time as a whole was negatively associated with higher hospital mortality ($p < 0.001$). The actual ORs and 95% CIs are presented in **Table 2**, model A, under hospital mortality.

When we adjusted for the APACHE IV probability, the results showed a significant positive correlation for the higher ED to ICU time quintiles (2.4–3.7 hr, > 3.7 hr) compared with the lowest ED to ICU time quintile (< 1.2 hr), with ORs of 1.20 (95% CI, 1.03–1.39), and 1.27 (95% CI, 1.08–1.49), respectively (**Fig. 1*B***). ED to ICU time as a whole became positively associated with higher hospital mortality ($p < 0.002$). The actual ORs and CIs are presented in Table 2, model B, under hospital mortality.

We then tested whether the APACHE IV probability modified the association between ED to ICU time and hospital mortality. **Fig. 2*A*–*D*** presents the ORs of hospital mortality for the ED to ICU time quintiles for each APACHE IV probability group separately.

Patients with higher APACHE IV probabilities (> 25.7–60.9%; > 60.9%) and a longer ED to ICU time (> 3.7 hr) showed a positive correlation compared with the reference category (< 1.2 hr), with ORs of 1.32 (95% CI, 1.02–1.69) and 1.54 (95% CI, 1.11–2.14), respectively.

Only ED to ICU time as a whole was positively associated with higher hospital mortality in patients with the highest APACHE IV probability (Wald test $p = 0.019$). The results are presented in Table 2, model C, under hospital mortality.

Secondary Outcomes: ICU Mortality, 30-Day, and 90-Day Mortality

Regarding ICU mortality, we tested whether ED to ICU time was independently associated with ICU mortality. The results showed a significant negative association between ED to ICU time and ICU mortality ($p < 0.001$). However, after adjusting for the APACHE IV probability, the association turned positive but not significant ($p = 0.20$). When testing whether the APACHE IV probability modified the association between ED to ICU time and ICU mortality, we did not find any significant association in one of the APACHE IV probability groups. The actual ORs and 95% CIs are presented in Table 2, model A, B, C under ICU mortality.

Regarding crude hazards of death during the first 30 days after ICU admission, we found a significant negative association with higher ED to ICU time quintiles (2.4–3.7 hr, > 3.7 hr) compared with the reference category (< 1.2 hr), with HRs of 0.90 (95% CI, 0.81–0.99), and 0.61 (95% CI, 0.54–0.68). ED to ICU time as a whole was negatively associated with higher 30-day mortality ($p < 0.001$). When we adjusted for the APACHE IV probability, the results showed a significant positive association for the higher ED to ICU time quintiles (2.4–3.7 hr, > 3.7 hr) compared with the lowest ED to ICU time quintile (< 1.2 hr), with HRs of 1.21 (95% CI, 1.09–1.34) and 1.18 (95% CI, 1.05–1.33), respectively. ED to ICU time as a whole became positively associated with higher 30-day mortality ($p < 0.001$).

Table 3 model A and B under 30-day mortality present the complete HRs for the separate ED to ICU time quintiles and their association with 30-day mortality. Finally, we tested whether the APACHE IV probability modified the association between ED to ICU time and 30-day mortality. ED to ICU time in association with 30-day mortality for each APACHE IV probability group showed slightly higher p values compared with hospital mortality. The results are presented in Table 3 model C under 30-day mortality.

Regarding 90-day mortality, we found similar results with respect to the association with hospital mortality (Table 3, models A, B, and C under 90-day mortality).

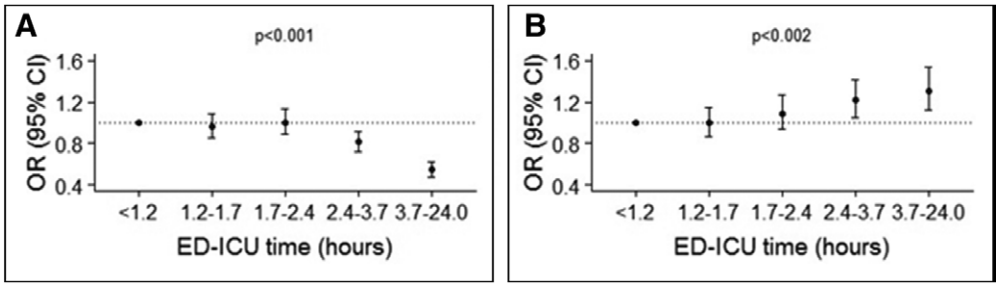

Figure 1. Odds ratios (ORs) for hospital mortality per length of stay in the emergency department. **A**, Emergency department to ICU time (ED to ICU time); adjusted for hospitals. **B**, ED to ICU time; adjusted for hospitals and Acute Physiology and Chronic Health Evaluation IV probability. The *p* values represent whether ED to ICU time as a whole is associated to hospital mortality. For the individual odds ratios and 95% CIs, we refer the reader to Table 2 model A and B under hospital mortality.

DISCUSSION

The present study was setup to examine the association between ED to ICU admission time and hospital mortality. For this purpose, we used data from six university hospitals in The Netherlands. This study showed that a longer ED to ICU time (> 2.4 hr) is associated with increased hospital mortality in patients with the highest APACHE IV probabilities. We found similar

TABLE 2. Odds Ratios for Hospital and ICU Mortality

Model	Hospital Mortality	*p*	ICU Mortality	*p*
"A" ED to ICU time; adjusted for hospitals				
ED to ICU time < 1.2 hr	Reference	$p < 0.001$	Reference	$p < 0.001$
ED to ICU time 1.2–1.7 hr	0.95 (0.85–1.07)		0.99 (0.88–1.13)	
ED to ICU time 1.7–2.4 hr	1.01 (0.89–1.14)		1.00 (0.88–1.13)	
ED to ICU time 2.4–3.7 hr	0.82 (0.72–0.92)[a]		0.81 (0.71–0.92)[a]	
ED to ICU time > 3.7 hr	0.56 (0.49–0.64)[a]		0.49 (0.42–0.57)[a]	
"B" ED to ICU time; adjusted for hospitals and APACHE IV probability				
ED to ICU time < 1.2 hr	Reference	$p < 0.002$	Reference	$p = 0.20$
ED to ICU time 1.2–1.7 hr	0.97 (0.84–1.12)		1.03 (0.88–1.19)	
ED to ICU time 1.7–2.4 hr	1.07 (0.92–1.24)		1.05 (0.90–1.22)	
ED to ICU time 2.4–3.7 hr	1.20 (1.03–1.39)[a]		1.18 (1.01–1.39)[a]	
ED to ICU time > 3.7 hr	1.27 (1.08–1.49)[a]		1.14 (0.96–1.37)	
"C" ED to ICU time × APACHE IV probability < 10.5%				
ED to ICU time < 1.2 hr	Reference	$p = 0.93$	Reference	$p = 0.94$
ED to ICU time 1.2–1.7 hr	0.79 (0.43–1.45)		0.81 (0.37–1.79)	
ED to ICU time 1.7–2.4 hr	1.02 (0.57–1.83)		0.79 (0.35–1.77)	
ED to ICU time 2.4–3.7 hr	1.01 (0.58–1.76)		0.71 (0.34–1.54)	
ED to ICU time > 3.7 hr	0.99 (0.58–1.70)		0.83 (0.41–1.71)	
ED to ICU time × APACHE IV probability 10.5–25.6%				
ED to ICU time < 1.2 hr	Reference	$p = 0.07$	Reference	$p = 0.27$
ED to ICU time 1.2–1.7 hr	0.87 (0.59–1.30)		0.95 (0.59–1.53)	
ED to ICU time 1.7–2.4 hr	1.32 (0.90–1.93)		1.01 (0.62–1.63)	
ED to ICU time 2.4–3.7 hr	1.41 (0.97–2.03)		1.40 (0.90–2.18)	
ED to ICU time > 3.7 hr	1.12 (0.76–1.63)		0.93 (0.58–1.48)	
ED to ICU time × APACHE IV probability 25.7–60.9%				
ED to ICU time < 1.2 hr	Reference	$p = 0.09$	Reference	$p = 0.89$
ED to ICU time 1.2–1.7 hr	0.97 (0.76–1.24)		1.01 (0.77–1.32)	
ED to ICU time 1.7–2.2 hr	1.08 (0.84–1.38)		1.07 (0.82–1.39)	
ED to ICU time 2.4–3.7 hr	1.04 (0.81–1.24)		1.00 (0.76–1.31)	
ED to ICU time > 3.7 hr	1.32 (1.02–1.69)[a]		1.13 (0.86–1.49)	
ED to ICU time × APACHE IV probability > 60.9%				
ED to ICU time < 1.2 hr	Reference	$p = 0.019$	Reference	$p = 0.09$
ED to ICU time 1.2–1.7 hr	1.03 (0.83–1.27)		1.07 (0.87–1.31)	
ED to ICU time 1.7–2.4 hr	0.99 (0.81–1.24)		1.06 (0.86–1.31)	
ED to ICU time 2.4–3.7 hr	1.29 (1.02–1.64)[a]		1.33 (1.05–1.67)[a]	
ED to ICU time > 3.7 hr	1.54 (1.11–2.14)[a]		1.33 (0.98–1.81)	

APACHE = Acute Physiology and Chronic Health Evaluation, ED to ICU time = emergency department to ICU time.

[a]$p < 0.05$.

Values represent the odds ratios and 95% CIs.

The *p* is analyzing whether ED to ICU time as a total factor is associated with the hospital and ICU mortality, we used a Wald test for the ED to ICU variables. Model diagnostics can be found in **Table A** (Supplemental Digital Content 1, http://links.lww.com/CCM/E859).

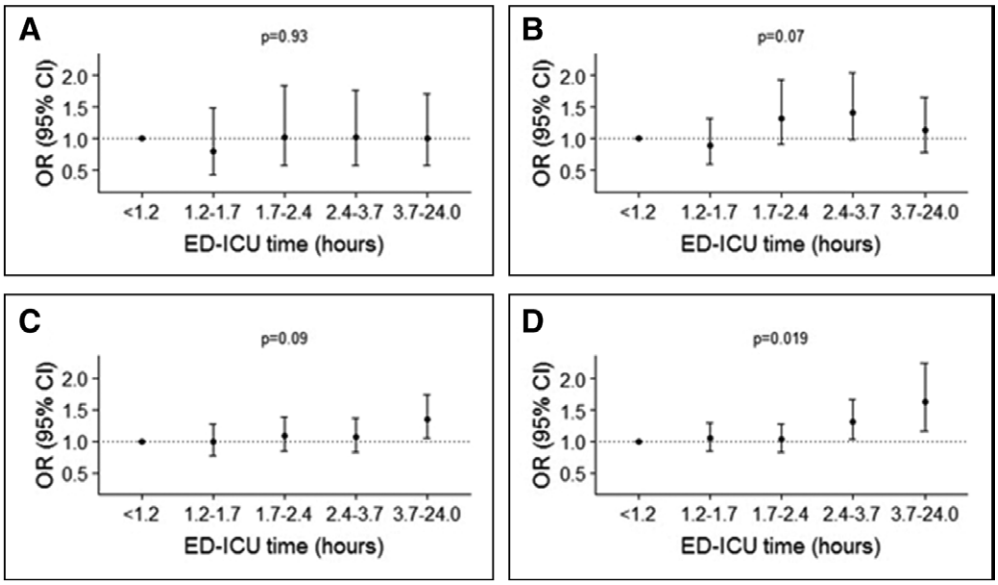

Figure 2. Odds ratios (ORs) for hospital mortality per length of stay in the emergency department plotted for each Acute Physiology and Chronic Health Evaluation (APACHE) IV probability quantile. **A**, Association between emergency department to ICU time (ED to ICU time) and APACHE IV probability less than 10.5%. **B**, Association between ED to ICU time and APACHE IV probability 10.5–25.6%. **C**, Association between ED to ICU time and APACHE IV probability 25.7–60.9%. **D**, Association between ED to ICU time and APACHE IV probability greater than 60.9%. The *p* values represent whether ED to ICU time as a whole is associated to hospital mortality. For the individual odds ratios and 95% CIs, we refer the reader to Table 2 model C under hospital mortality.

patterns for 30-day and 90-day mortality. However, the association was less obvious for ICU mortality in comparison with hospital mortality. Our results are in line with some previous studies showing that indeed there is some evidence that ED to ICU time is associated with hospital mortality (7, 14–16), but our study showed that this effect could particularly be attributed to the most severely ill patients that have a long stay at the ED.

Other investigators have studied the correlation of admission day and time with hospital mortality (17). Our study connects to this line of research, by identifying ED to ICU time as a factor of potential influence on patient outcome before the patient arrives at the ICU.

Triage may be a possible underlying factor that could influence ED to ICU time and mortality of patients admitted to the ICU. A proper triage system is necessary to recognize and diagnose the most severely ill patients. The accuracy and differences between triage systems has previously been investigated (18–20). More importantly, Bilben et al (21) added the National Early Warning Score (NEWS) as triage system next to the Manchester Triage Scale; the most commonly used triage system in Europe (22). The NEWS, comparable to the Modified Early Warning Score (23), which is currently used in hospital wards to detect patients with increased risk of death or unplanned ICU admission, showed comparable predictive effects in ED patients as in ward patients. Implementing additional triage scoring systems could lead to better identification of the most severely ill patients and prevent a possible delayed admission to the ICU, which could result in lower mortality. Furthermore, prediction models, who can identify patients at high risk of death in the ED, and benchmarking tools, who enable hospitals to identify factors causing delays in emergency transfers, can be promising to help the most severely ill patients in time and improve the adequacy of rapid response teams in the hospital (24, 25).

Another important factor which may influence mortality of patients admitted to the ICU is the care provided in the ED. In some cases, the ED staff may not have enough time to provide the required attention and medical care for those requiring intensive care (18). Then the strain of clinical needs outweighs the clinical resources, and this may worsen patient outcomes.

Besides triage and the care provided in the ED, the capacity strain on ICU beds is also a factor which can influence ED to ICU time and worsen patient outcomes (26). Harris et al (27) showed that prompt admissions to the ICU showed lower 90-day mortality compared with the controls (median delay of 11 hr; IQR, 6–26) in hospital ward patients. Prompt admissions were possible more often when two or more ICU beds were available compared with one or less ($p < 0.001$). Therefore, a continuous and proper reassessment of the bed occupancy could result in a lower capacity strain and more prompt admissions when urgently needed, also for patients coming from the ED.

Last, the study of Kuijsten et al (17) was able to show that time of admission (night vs day) could be of influence on patient outcomes. We assessed whether admission time in the ED (night vs day) could be of influence on the association between ED to ICU time and hospital mortality. However, in our study, ED admission time did not have an effect on the association between ED to ICU time and hospital mortality and was therefore not included in the models.

A question that arose during the analyses of the data (despite the adjusting for APACHE IV probability that included diagnosis) was whether the admission diagnosis on its own could modify the association between ED to ICU time and hospital mortality. Besides cardiac arrest (14.3%), the most common admission diagnoses were trauma (nonoperative) (13.6%), intracranial/subdural/epidural hemorrhage (9.4%), and respiratory failure (9.4%). We preformed sub-analyses with these admission diagnoses. We found that only in patients with cardiac arrest in both crude and adjusted analysis, ED to ICU time was significantly associated with higher hospital mortality. These results indicate that admission diagnosis may be a possible explanation for the obtained findings and may represent a venue for future research. In **Tables B** and **C** (Supplemental Digital Content 1, http://links.lww.com/CCM/E859), the results of these analyses are presented for reference only. **Table D** (Supplemental Digital Content 1, http://links.lww.com/CCM/E859) demonstrates the most common admission diagnoses per APACHE IV probability group.

TABLE 3. Hazard Ratios for 30-Day and 90-Day Mortality

Model	30-d Mortality	*p*	90-d Mortality	*p*
"A" ED to ICU time; adjusted for hospitals				
ED to ICU time < 1.20 hr	Reference	$p < 0.001$	Reference	$p < 0.001$
ED to ICU time 1.2–1.7 hr	1.00 (0.91–1.11)		1.00 (0.91–1.09)	
ED to ICU time 1.7–2.4 hr	1.04 (0.94–1.15)		1.03 (0.94–1.14)	
ED to ICU time 2.4–3.7 hr	0.90 (0.81–0.997)[a]		0.91 (0.83–1.00)	
ED to ICU time > 3.7 hr	0.61 (0.54–0.68)[a]		0.67 (0.60–0.74)[a]	
"B" ED to ICU time; adjusted for hospitals and APACHE IV probability				
ED to ICU time < 1.2 hr	Reference	$p < 0.001$	Reference	$p < 0.001$
ED to ICU time 1.2–1.7 hr	1.04 (0.94–1.14)		1.03 (0.94–1.14)	
ED to ICU time 1.7–2.4 hr	1.05 (0.95–1.17)		1.06 (0.96–1.16)	
ED to ICU time 2.4–3.7 hr	1.21 (1.09–1.34)[a]		1.21 (1.09–1.33)[a]	
ED to ICU time > 3.7 hr	1.18 (1.05–1.33)[a]		1.23 (1.11–1.37)[a]	
"C" ED to ICU time × APACHE IV probability < 10.5%				
ED to ICU time < 1.2 hr	Reference	$p = 0.31$	Reference	$p = 0.40$
ED to ICU time 1.2–1.7 hr	0.99 (0.58–1.68)		1.09 (0.72–1.69)	
ED to ICU time 1.7–2.4 hr	1.17 (0.70–1.96)		1.26 (0.82–1.92)	
ED to ICU time 2.4–3.7 hr	1.51 (0.95–2.42)		1.43 (0.97–2.12)	
ED to ICU time > 3.7 hr	1.24 (0.77–1.99)		1.28 (0.87–1.89)	
ED to ICU time × APACHE IV probability 10.5–25.6%				
ED to ICU time < 1.2 hr	Reference	$p = 0.07$	Reference	$p = 0.09$
ED to ICU time 1.2–1.7 hr	0.92 (0.66–1.29)		0.92 (0.69–1.23)	
ED to ICU time 1.7–2.4 hr	1.25 (0.91–1.74)		1.16 (0.87–1.54)	
ED to ICU time 2.4–3.7 hr	1.38 (1.01–1.88)		1.29 (0.98–1.69)	
ED to ICU time > 3.7 hr	1.11 (0.81–1.54)		1.17 (0.89–1.54)	
ED to ICU time × APACHE IV probability 25.7–60.9%				
ED to ICU time < 1.2 hr	Reference	$p = 0.22$	Reference	$p = 0.039$
ED to ICU time 1.2–1.7 hr	1.05 (0.86–1.27)		1.05 (0.87–1.26)	
ED to ICU time 1.7–2.4 hr	1.14 (0.94–1.39)		1.15 (0.96–1.39)	
ED to ICU time 2.4–3.7 hr	1.15 (0.95–1.40)		1.17 (0.98–1.41)	
ED to ICU time > 3.7 hr	1.24 (1.02–1.52)[a]		1.31 (1.09–1.58)[a]	
ED to ICU time × APACHE IV probability > 60.9%				
ED to ICU time < 1.2 hr	Reference	$p = 0.031$	Reference	$p = 0.014$
ED to ICU time 1.2–1.7 hr	1.05 (0.93–1.19)		1.05 (0.92–1.18)	
ED to ICU time 1.7–2.4 hr	0.98 (0.87–1.12)		0.97 (0.86–1.11)	
ED to ICU time 2.4–3.7 hr	1.18 (1.03–1.36)[a]		1.17 (1.02–1.35)[a]	
ED to ICU time > 3.7 hr	1.19 (0.99–1.42)[a]		1.22 (1.03–1.46)[a]	

APACHE = Acute Physiology and Chronic Health Evaluation, ED to ICU time = emergency department to ICU time.

[a]$p < 0.05$.

Values represent the hazard ratios and 95% CIs.

The *p* is analyzing whether ED to ICU time as a total factor is associated with 30-d and 90-d mortality, we used a Wald test for the ED to ICU variables. Model diagnostics can be found in Table A (Supplemental Digital Content 1, http://links.lww.com/CCM/E859).

The present sample, however, is too small to draw reliable conclusions about admission diagnosis as the only factor in explaining the higher mortality. For future research, it is therefore important to increase the sample size to draw more robust conclusions.

This study has some limitations. First, six university hospitals were included, and although these centers are representative for the eight university hospitals in The Netherlands (in terms of case-mix), we were not able to include referring hospitals due to the needed additional data on ED admission date and time that is not included in the NICE registry. This may limit the generalizability of our study. A next study should also include data from nonacademic ICUs. Second, the APACHE III score was calculated by using the worst values recorded in the first 24 hours of ICU admission. Patients could have been admitted to the ICU after one hour in the ED but also after 23 hours of ED time, which could have affected the APACHE IV probability.

Finally, since ED admission date and time were collected retrospectively, less than 3% of the patients ($n = 356$) had to be excluded due to a nonretrievable ED admission date. Again, this may influence the results but as this loss of patients is so low, we think this loss is negligible.

The results of the present study contribute to the discussion whether ED to ICU time influences mortality and provide venues for future research. Especially studies about ED to ICU time as an influencing factor in specific admission diagnoses are needed. Furthermore, future research may also extent to other outcomes, such as consistent pain score measurement, quality of life, and neurologic outcomes after ICU discharge. Nowadays, a coherent view on patient care and outcomes becomes increasingly significant in ICU research (28, 29).

CONCLUSIONS

This study shows that a longer ED to ICU time (> 2.4 hr) is associated with increased hospital mortality in the most severely ill patients. For the sickest patients, we provide evidence that rapid identification and transfer to the ICU might reduce hospital mortality.

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