Association between timing of intensive care unit admission and outcomes for emergency department patients with community-acquired pneumonia*

Bertrand Renaud, MD; Aline Santin, MD; Eva Coma, MD; Nicolas Camus, MD; Dave Van Pelt, MD, MSc; Jan Hayon, MD; Merce Gurgui, MD; Eric Roupie, MD; Jérôme Hervé, MD; Michael J. Fine, MD, MSc; Christian Brun-Buisson, MD; José Labarère, MD, PhD

Objective: **To compare the 28-day mortality and hospital length of stay of patients with community-acquired pneumonia who were transferred to an intensive care unit on the same day of emergency department presentation (direct-transfer patients) with those subsequently transferred within 3 days of presentation (delayed-transfer patients).**

Design: **Secondary analysis of the original data from two North American and two European prospective, multicenter, cohort studies of adult patients with community-acquired pneumonia.**

Patients: **In all, 453 non-institutionalized patients transferred within 3 days of emergency department presentation to an intensive care unit were included in the analysis. Supplementary analysis was restricted to patients without an obvious indication for immediate transfer to an intensive care unit.**

Interventions: **None.**

Measurements and Main Results: **The sample consisted of 138 delayed-transfer and 315 direct-transfer patients, among whom 150 (33.1%) were considered to have an obvious indication for immediate intensive care unit admission. After adjusting for the quintile of propensity score, delayed intensive care unit transfer was associated with an increased odds ratio for 28-day mortality (2.07; 95% confidence interval, 1.12–3.85) and a decreased odds ratio for discharge from hospital for survivors (0.53; 95% confidence interval, 0.39–0.71). In a propensity-matched analysis, delayed-transfer patients had a higher 28-day mortality rate (23.4% vs. 11.7%; $p = 0.02$) and a longer median hospital length of stay (13 days vs. 7 days; $p < .001$) than direct-transfer patients. Similar results were found after excluding the 150 patients with an obvious indication for immediate intensive care unit admission.**

Conclusions: **Our findings suggest that some patients without major criteria for severe community-acquired pneumonia, according to the recent Infectious Diseases Society of America/American Thoracic Society consensus guideline, may benefit from direct transfer to the intensive care unit. Further studies are needed to prospectively identify patients who may benefit from direct intensive care unit admission despite a lack of major severity criteria for community-acquired pneumonia based on the current guidelines. (Crit Care Med 2009; 37:2867–2874)**

KEY WORDS: pneumonia; community-acquired infection; emergency department; intensive care; severity of illness index; time to admission

Community-acquired pneumonia (CAP) is a leading cause of severe sepsis (1, 2) and can result in multiorgan failure, particularly respiratory distress and shock (3, 4). Accordingly, approximately 10% of emergency department (ED) patients with CAP are subsequently transferred to the intensive care unit (ICU), and CAP patients account for nearly 10% of medical ICU admissions (5). The estimated mortality rates of CAP patients admitted to an ICU range from 20% to 50% (6). Patients with overt hemodynamic or respiratory compromise that present to the ED and require life support, such as inotropic drug support or mechanical ventilation, are generally transferred to the ICU within the first few hours of admission. However, because rapidly progressive pneumonia is not always obvious

***See also p. 2979.**

From the Department of Emergency Medicine (BR, AS, NC, JH), AP-HP, Groupe Hospitalier Henri Mondor-Albert Chenevier, Créteil, France; Servei d'Atenció Continuada USAC (EC), Institut Català d'Oncologia, Hospital Duran i Reynals, L'Hospitalet de Llobregat, Barcelona, Spain; Université Paris 12 (NC, CBB), Faculté de Médecine, Créteil, France; Department of Critical Care and Pulmonary Consultants (DVP), The Medical Center of Aurora, Aurora, CO; Department of Critical Care Medicine (JH), Centre Hospitalier Intercommunal de Poissy Saint-Germain, Saint-Germain-en-Laye, France; Department of Emergency Medicine (MG), Hospital de la Santa Creu I Sant Pau, Barcelona, Spain; Department of Emergency Medicine (ER), Centre Hospitalier Universitaire de Caen, Hôpital Côte de Nacre, Caen, France; Université de Caen-Basse Normandie (ER), Faculté de médecine, Caen, France; Center for Health Equity Research and Promotion (MJF), VA Pittsburgh Healthcare System, Pittsburgh, PA; Division of General Internal Medicine (MJF), Department of Medicine, University of Pittsburgh, Pittsburgh, PA; Réanimation Médicale (CBB), AP-HP, Groupe hospitalier Henri Mondor-Albert Chenevier, Créteil, France; Quality of Care Unit (JL), Centre Hospitalier Universitaire de Grenoble, Grenoble, France.

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For information regarding this article, E-mail: bertrand.renaud@hmn.aphp.fr

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Table 1. Comparison of study design and patient eligibility criteria across study populations

Study Characteristics	Pneumonia PORT	EDCAP	Pneumocom-1	Pneumocom-2
Enrollment period	October 1991–March 1994	January 2001–December 2001	February 2002–July 2003	January 2003–December 2003
Number of study sites	5	32	16	14
Country	United States and Canada	United States	France	Spain
Inclusion criteria				
Age ≥18 yrs	X	X	X	X
Clinical diagnosis of pneumonia	X	X	X	X
New radiographic pulmonary infiltrate	X	X	X	X
Provision of informed consent	X	X	X	X
Exclusion criteria				
Discharge within 7–10 days of presentation[a]	X	X	X	X
Positive HIV antibody titer	X	X	X	X
Immunosuppression[b]	—	X	X	X
History of cystic fibrosis	—	X	X	—
Ventilated via a tracheotomy or chronic use of mechanical ventilation	—	X	X	—
Other[c]	—	X	—	—
Enrolled patients, n	2287	3201	925	853
Patients transferred to ICU within 3 days of ED presentation, n	127	220	79	27

HIV, human immunodeficiency virus; ICU, intensive care unit; ED, emergency department; PORT, Pneumonia Patient Outcome Research Team; EDCAP, Emergency Department Community-Acquired Pneumonia.

[a]Seven days for the Pneumocom-1 and Pneumocom-2 studies and 10 days for the Pneumonia PORT and EDCAP studies; [b]immunosuppression was defined as: (1) leukemia or lymphoma; (2) white blood cell count $<3000/mm^3$ or an absolute neutrophil count $<1000/mm^3$ on presentation; (3) asplenia, anatomical or functional; (4) hypogammaglobulinemia; (5) immunosuppressive or myelosuppressive drug therapy within the 30 days preceding presentation; (6) documentation of patient "on chemotherapy," or (7) radiation therapy; [c]other exclusion criteria were: (1) pulmonary tuberculosis; (2) confirmed diagnosis of pneumonia within 30 days of presentation; (3) transfer from an acute care hospital or on-site nursing care facility; (4) residence in a chronic care hospital immediately before presentation; (5) psychosocial problems incompatible with outpatient treatment, enrollment, or follow-up; (6) pregnancy; (7) illicit drug use within the past 30 days; (8) alcoholism with evidence of end-organ damage; (9) homelessness; (10) incarceration as a prisoner; (11) admission for palliative care; or (12) previous enrollment in a competing research protocol.

on admission, some patients who do not present with an overt life-threatening condition may require transfer to an ICU a few days after hospitalization (3, 7). Few studies have assessed clinical outcomes for this subset of patients who are initially admitted to a hospital ward and later transferred to an ICU (8).

The aim of this study was to compare the 28-day mortality and hospital length of stay for CAP patients who were admitted directly to an ICU on the same day of ED presentation (i.e., direct-transfer patients) with those transferred to an ICU bed within 3 days of admission to a non-ICU ward (i.e., delayed-transfer patients). In a supplementary analysis, we focused on the subset of patients without obvious indication for immediate ICU admission at ED presentation.

MATERIALS AND METHODS

We performed a secondary analysis of the original data from four prospective, multicenter, cohort studies of adult patients presenting with CAP at the ED. Two studies were from North America: the Pneumonia Patient Outcomes Research Team study (9) and the EDCAP study (10). The other two studies were from Europe (Pneumocom-1 and Pneumocom-2) (5, 11). The protocol of each study was approved by the institutional review boards of the participating institutions.

Study Design and Patients

All four original studies prospectively enrolled consecutive consenting adults with a diagnosis of CAP (Table 1). The methods used for the Pneumonia Patient Outcomes Research Team, EDCAP, and Pneumocom studies have been reported previously (5, 9–11). Pneumonia Patient Outcomes Research Team, Pneumocom-1, and Pneumocom-2 were observational studies, whereas the EDCAP study was a cluster randomized controlled trial. Consistent with the scope of CAP (12), nursing home residents were excluded from the current analysis. For the specific purpose of the present study, only patients who were admitted to the ICU within 3 days of presentation were analyzed.

Baseline Data Collection

All studies used physicians' interviews and structured chart reviews to collect data regarding baseline demographic variables, comorbid conditions, physical examination findings, laboratory test results, and radiographic findings. For each patient, we calculated the Pneumonia Severity Index (PSI) using baseline characteristics. According to the original derivation and validation of the PSI, missing values were assumed to be normal (9).

Timing of ICU Transfer

We defined direct ICU transfer as direct admission from the ED to an ICU on the day of presentation. Conversely, we defined delayed ICU transfer as transfer to a medical ward on day 1 and transfer to an ICU on day 2 or 3. ICU admission was left at the discretion of the treating physician and there was no policy recommendation regarding the timing of ICU admission in the four original cohort studies.

Outcome Measures

The primary outcome measure was 28-day mortality. The secondary outcome was hospital length of stay measured among survivors discharged on or before 28 days. Follow-up data were collected by using structured chart reviews and telephone interviews with patients.

Statistical Analysis

Baseline characteristics were reported as mean and SD for continuous variables and as percentages for categorical variables. Baseline characteristics were compared between direct-transfer and delayed-transfer patients using

Table 2. Baseline characteristics of ED patients with community-acquired pneumonia who were transferred to the ICU within 3 days of ED presentation

Characteristics	Direct ICU Transfer[a] (n = 315)	Delayed ICU Transfer (n = 138)	OR for Delayed ICU Transfer (95% CI)	
			Unadjusted	Adjusted for Quintile of Propensity Score[b]
Male, n (%)	185 (58.7)	87 (63.0)	1.20 (0.79–1.81)	1.05 (0.66–1.67)
Age, mean (SD), yr	65.0 (16.2)	67.3 (15.8)	1.01 (0.99–1.02)	1.00 (0.99–1.02)
Comorbid conditions, n (%)				
Neoplastic disease	22 (7.0)	8 (5.8)	0.82 (0.36–1.89)	1.34 (0.52–3.49)
Liver disease	9 (2.9)	2 (1.4)	0.50 (0.11–2.34)	0.95 (0.18–5.05)
Congestive heart failure	69 (21.9)	34 (24.6)	1.17 (0.73–1.87)	0.96 (0.57–1.63)
Renal disease	38 (12.1)	19 (13.8)	1.16 (0.64–2.10)	0.90 (0.46–1.76)
Coronary artery disease	81 (25.7)	35 (25.4)	0.98 (0.62–1.55)	1.01 (0.61–1.68)
Chronic pulmonary disease	113 (35.9)	42 (30.4)	0.78 (0.51–1.20)	0.83 (0.51–1.37)
Cerebrovascular disease	20 (6.3)	17 (12.3)	2.07 (1.05–4.09)	1.29 (0.60–2.78)
Diabetes mellitus	61 (19.4)	40 (29.0)	1.70 (1.07–2.70)	1.07 (0.64–1.79)
Physical examination findings, n (%)				
Altered mental status	83 (26.3)	16 (11.6)	0.37 (0.21–0.65)	1.08 (0.54–2.13)
Respiratory rate ≥30 per min	130 (41.3)	37 (26.8)	0.52 (0.34–0.81)	0.98 (0.59–1.62)
Pulse rate ≥130 per min	67 (21.3)	13 (9.4)	0.38 (0.20–0.72)	0.86 (0.42–1.77)
Systolic BP <90 mm Hg	19 (6.0)	5 (3.6)	0.59 (0.21–1.60)	1.00 (0.34–2.98)
Temperature <36°C	19 (6.0)	9 (6.5)	1.09 (0.48–2.47)	1.39 (0.53–3.64)
Pulse oximetry <90%	149 (47.3)	55 (39.9)	0.74 (0.49–1.11)	1.01 (0.64–1.60)
Laboratory and radiograph findings, n (%)				
Arterial pH <7.40	124 (39.4)	11 (8.0)	0.13 (0.07–0.26)	0.79 (0.32–1.88)
BUN ≥11 mmol/L	120 (38.1)	44 (31.9)	0.76 (0.50–1.16)	0.94 (0.59–1.52)
PaO_2 <55 mm Hg	90 (28.6)	31 (22.5)	0.72 (0.45–1.16)	1.05 (0.61–1.79)
Sodium <130 mEq/L	41 (13.0)	14 (10.1)	0.75 (0.40–1.43)	0.99 (0.48–2.04)
Glucose ≥20 mmol/dL	19 (6.0)	7 (5.1)	0.83 (0.34–2.03)	0.99 (0.36–2.68)
Hematocrit <30 %	31 (9.8)	17 (12.3)	1.29 (0.69–2.41)	1.06 (0.53–2.16)
WBC count <4 Giga/L	13 (4.1)	6 (4.3)	1.06 (0.39–2.84)	1.02 (0.34–3.08)
Multilobar infiltrate	145 (46.0)	49 (35.5)	0.65 (0.43–0.98)	1.03 (0.64–1.66)
Pleural effusion	57 (18.1)	32 (23.2)	1.37 (0.84–2.23)	1.13 (0.65–1.95)
Pneumonia severity index, n (%)				
Class I	11 (3.5)	11 (8.0)	1.00	1.00
Class II	38 (12.1)	15 (10.9)	0.39 (0.14–1.10)	0.65 (0.22–1.93)
Class III	50 (15.9)	30 (21.7)	0.60 (0.23–1.55)	0.89 (0.33–2.46)
Class IV	120 (38.1)	63 (45.6)	0.52 (0.22–1.28)	1.01 (0.39–2.61)
Class V	96 (30.5)	19 (13.8)	0.20 (0.07–0.52)	0.89 (0.30–2.60)
Study cohorts, n (%)				
PORT	96 (30.5)	31 (22.5)	1.00	1.00
EDCAP	135 (42.9)	85 (61.6)	1.95 (1.20–3.17)	0.88 (0.50–1.56)
Pneumocom-1	64 (20.3)	15 (10.9)	0.73 (0.36–1.45)	0.87 (0.41–1.85)
Pneumocom-2	20 (6.3)	7 (5.1)	1.08 (0.42–2.81)	0.65 (0.22–1.88)

ICU, intensive care unit; ED, emergency department; CI, confidence interval; BP, blood pressure; BUN, blood urea nitrogen; PaO_2, partial pressure of oxygen in arterial blood gas analysis; WBC, white blood cell; IQR, interquartile range; OR, odds ratio.

[a]Direct transfer to ICU refers to patients who were transferred to ICU on the same day of ED presentation; [b]the propensity score was derived using a random intercept logistic regression model that included all the variables displayed in this table (with the exception of Pneumonia Severity Index risk class) and corresponded to the conditional probability of delayed ICU transfer for a patient given his/her characteristics. The fact that the adjusted odds ratios of delayed ICU transfer were not significantly different from 1 reflected the absence of residual imbalances in baseline characteristics after adjusting for quintile of propensity score (see Materials and Methods).

two-tailed Student's *t* tests or Wilcoxon's rank sum tests when appropriate for continuous variables, and chi-square tests or Fisher's exact tests for categorical variables. Length of stay was reported as median and interquartile range, and was compared between the study groups using discrete time logistic hazard models.

Because timing of ICU transfer was not randomly assigned in this observational study, unadjusted comparisons of outcomes between direct-transfer and delayed-transfer patients might be confounded by imbalances in baseline characteristics. For this purpose, we performed multivariable logistic regression to estimate the odds ratios of 28-day mortality and hospital discharge associated with delayed ICU transfer after adjusting for the study cohort and the baseline characteristics listed in Table 2. To perform rigorous adjustment, odds ratios were adjusted for the original variables that made up the PSI instead of the PSI risk class. Random intercept logistic regression was used to account for patient clustering within the ED.

To assess the robustness of our findings, we performed propensity score analysis that compensated for differences in measured baseline characteristics between delayed and direct ICU transfer patients (13). Conceptually, the propensity score corresponds to the conditional probability of exposure to a treatment given the observed characteristics. Stratifying or matching treated and untreated patients on the propensity score tends to balance all observed characteristics that were used to construct the score, and in this way approximates the conditions of random treatment assignment (13). Practically, we derived a propensity score for delayed ICU transfer using a full non-parsimonious random intercept logistic regression model that included the patient characteristics listed in Table 2 (with the exception of PSI risk class) as covariates. This model yielded a c-statistic of 0.78, indicating a

satisfactory ability to differentiate between delayed-transfer and direct-transfer patients. Each patient was assigned a propensity score, which ranged from 0.01 to 0.90 and reflected the conditional probability of delayed ICU transfer given the baseline characteristics. Patients were stratified by quintiles of increasing propensity score. To validate our propensity score adjustment, we checked for the absence of significant residual imbalances in baseline characteristics after adjusting for the quintile of propensity score. We then estimated the odds ratios of 28-day mortality and hospital discharge associated with delayed ICU transfer after adjusting for the quintile of propensity score.

To compare outcomes among patients with a similar conditional probability of delayed ICU admission, we also defined a cohort of 111 direct-transfer and 111 delayed-transfer patients matched by propensity score. For this purpose, we used an algorithm to match each delayed-transfer patient to a single direct-transfer patient who had the nearest propensity score within one digit. If this could not be performed, that delayed-transfer patient was excluded from the propensity-matched analysis. We evaluated the propensity-matched cohort for significant residual imbalances in baseline characteristics. We then used logistic regression to estimate the odds ratios of 28-day mortality and discharge from hospital associated with delayed ICU transfer among propensity score-matched patients. This is the same strategy as reported previously (14, 15).

In a supplementary analysis, we repeated the multivariable and propensity score analyses using a subset of patients who did not have an obvious indication for immediate ICU transfer at ED presentation. In accordance with current guidelines (16), overt cardiovascular (i.e., hypotension requiring vasopressors) or respiratory (i.e., mechanical ventilation) failure in the ED was considered obvious indications for immediate ICU transfer.

Two-sided $p < .05$ was considered to be statistically significant. Analyses were performed using Stata version 10.0 (Stata Corporation, College Station, TX) and MLWiN version 2.0 (Center for Multilevel Modeling, Institute of Education, London, UK).

RESULTS

Of the 7,266 patients enrolled in the four cohort studies, 453 (6.2%) were noninstitutionalized patients who were admitted to the ICU within 3 days of ED presentation (Fig. 1). Our analytical sample consisted of 315 direct-transfer patients and 138 delayed-transfer patients. Of the 315 direct-transfer patients, 150 (33.1%) had an obvious indication for immediate ICU transfer.

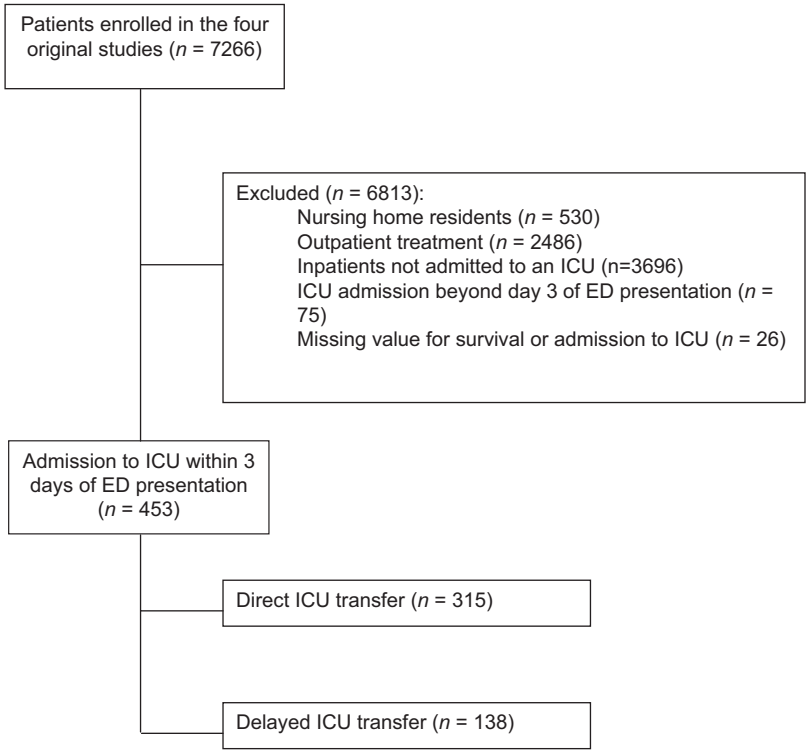

Figure 1. Patient enrollment. Direct intensive care unit (*ICU*) transfer was defined as direct transfer to an ICU on the day of emergency department (*ED*) presentation, while delayed ICU transfer was defined as subsequent admission to an ICU on the second or third day of ED presentation.

Overall, patients were 66 yrs old on average (SD, 16), 272 (60%) were male, 347 (77%) were enrolled in the North American cohort studies, and the 28-day mortality rate was 15.4%. Direct-transfer patients were more likely to have abnormal clinical findings (altered mental status, tachypnea, and tachycardia), acidosis, and multilobar infiltrates at ED presentation and therefore were more likely to be in PSI risk class V (Table 2). Conversely, delayed-transfer patients were more likely to have comorbid conditions (cerebrovascular disease and diabetes mellitus). No significant associations persisted between baseline characteristics and the odds of delayed ICU admission after adjusting for the quintile of propensity score (Table 2).

Unadjusted 28-day mortality rates were 13.6% and 19.6% for direct-transfer and delayed-transfer patients ($p = .11$; Table 3). Among the 383 patients who were alive at discharge, the median hospital length of stay was 10 and 13 days for direct-transfer and delayed-transfer patients, respectively ($p = .22$). After adjusting for baseline characteristics or quintile of propensity score, delayed ICU transfer was associated with increased odds of 28-day mortality and decreased odds of hospital discharge (Table 3). No significant interaction was found between delayed ICU transfer and the study cohort for 28-day mortality ($p = .37$) and discharge from the hospital ($p = .61$), after adjusting for the quintile of propensity score. Whereas no residual imbalances persisted in baseline characteristics among propensity-matched patients, delayed ICU transfer was associated with a higher 28-day mortality rate (23.4% vs. 11.7%; $p = .02$) and longer median hospital length of stay (13 days vs. 7 days; $p < .001$; Table 4).

After removing the 150 patients with an obvious indication for immediate ICU transfer from the analysis, the 28-day mortality rate was 10.9% and the median hospital length of stay was 10 days for direct-ICU-transfer patients (Table 3). In the subset of patients without obvious indication for immediate ICU admission, delayed ICU transfer was associated with increased odds of 28-day mortality and decreased odds of hospital discharge after adjusting for baseline characteristics or quintile of propensity score (Table 3). The differences remained significant in the propensity-matched cohort (Table 4).

Table 3. Odds ratios of 28-day mortality and discharge from hospital associated with delayed ICU transfer for emergency department patients with community-acquired pneumonia

	All Patients				Patients Without Obvious Indication for Immediate ICU Admission			
	Direct ICU Transfer (n = 315)	Delayed ICU Transfer (n = 138)	OR (95% CI)		Direct ICU Transfer (n = 165)	Delayed ICU Transfer (n = 138)	OR (95% CI)	
28-day mortality, n (%)	43 (13.6)	27 (19.6)	1.54 (0.91–2.61)	0.11	18 (10.9)	27 (19.6)	1.99 (1.04–3.79)	0.04
Adjusted for baseline characteristics	—	—	2.48 (1.21–5.08)	0.01	—	—	3.90 (1.60–9.49)	0.003
Adjusted for quintile of propensity score	—	—	2.07 (1.12–3.85)	0.02	—	—	3.08 (1.41–6.73)	0.005
Hospital length of stay,[a] median (IQR), days	10 (6–19)	13 (7–17)	0.86 (0.67–1.09)	0.22	10 (6–18)	13 (7–17)	0.77 (0.58–1.01)	0.06
Adjusted for baseline characteristics	—	—	0.52 (0.38–0.70)	<0.001	—	—	0.40 (0.28–0.58)	<0.001
Adjusted for quintile of propensity score	—	—	0.53 (0.39–0.71)	<0.001	—	—	0.51 (0.37–0.71)	<0.001

ICU, intensive care unit; IQR, interquartile range; OR, odds ratio; CI, confidence interval.

[a]The ORs of discharge from hospital were estimated using discrete time logistic hazard models for 382 patients (including 257 patients without obvious indication for immediate ICU transfer) who were alive at discharge. Length of stay was censored at 28 days. One patient was excluded because of missing data for hospital length of stay.

Table 4. Odds ratios of 28-day mortality and discharge associated with delayed ICU transfer for propensity-matched patients with community-acquired pneumonia

	All Propensity-Matched Patients				Propensity-Matched Patients Without Obvious Indication for Immediate ICU Transfer			
Outcome Measures	Direct ICU Transfer (n = 111)	Delayed ICU Transfer (n = 111)	OR (95% CI)		Direct ICU Transfer (n = 88)	Delayed ICU Transfer (n = 88)	OR (95% CI)	
28-day mortality, n (%)	13 (11.7)	26 (23.4)	2.31 (1.11–4.77)	0.02	5 (5.7)	20 (22.7)	4.88 (1.74–13.69)	0.003
Length of stay, median[a] (IQR), days	7 (4–13)	13 (7–17)	0.55 (0.40–0.76)	<0.001	9 (4–16)	14 (9–19)	0.54 (0.39–0.76)	<0.001

ICU, intensive care unit; IQR, interquartile range; OR, odds ratio; CI, confidence interval.

[a]The ORs of discharge from hospital were estimated using discrete time logistic hazard models for 182 patients (including 150 patients without obvious indication for immediate ICU transfer) who were alive at discharge. One patient was excluded because of missing data for hospital length of stay. Length of stay was censored at 28 days.

DISCUSSION

This pooled analysis of four prospective cohort studies suggests that direct transfer to an ICU is associated with better medical outcomes for ED patients with severe CAP. CAP patients who were transferred to an ICU on the same day of ED presentation had a lower odds ratio of 28-day mortality and shorter length of stay than delayed ICU admission patients in multivariable and propensity score analyses. Interestingly, this finding remained significant when restricting the analysis to patients who did not have an obvious indication for immediate ICU transfer.

This study supports the 2007 Infectious Diseases Society of America/American Thoracic Society guideline recommendations advocating direct transfer to the ICU from the ED for adult patients with CAP and at least one major criterion for severe CAP (16). However, a substantial proportion of other patients with rapidly progressive pneumonia will have organ failure develop within a few days of ED presentation (3). As many as 45% of patients with CAP who ultimately require ICU admission have been reported to be initially admitted to a non-ICU setting (7).

Other studies have reported delayed ICU transfer as an important problem (17–19). Therefore, a major challenge in the management of CAP is to identify which ED patients are at risk for rapidly developing adverse medical outcomes despite a lack of major severity criteria (20). Despite several important insights regarding pneumonia management, the main clinical features suggesting which patients warrant direct transfer to the ICU remain poorly defined (20–23). Our findings support the need for broader criteria for pneumonia patients requiring direct ICU admission.

Medical outcomes can be improved by expanding the scope of intensive care to patients at high risk for severe sepsis. In this context, it has been demonstrated that rapid therapeutic intervention and referral to the ICU was an effective strategy (24–27). In a related approach, Alberti et al (2) developed the Risk of Infection to Severe Sepsis and Shock Score to help identify which patients were at risk

for progressing to a more severe stage and would benefit from early therapeutic interventions. The findings of our study are consistent with this approach in the specific scope of severe CAP (28).

Developing better prediction models of incipient severe sepsis is important because there is circumstantial evidence to suggest that mortality is increased for critically ill patients who are cared for in a non-ICU setting and for those not directly transferred from the ED to an ICU (29). Among patients with diverse diagnostic categories, Simpson et al (19) showed that delayed transfer was associated with higher rates of adverse outcomes. Similarly, Saukkonen et al (18) reported a 13% estimated overall crude difference in mortality between patients who were directly admitted to the ICU and those who were not (mortality rates: 20% vs. 33%, respectively). In a similarly diverse population transferred from the ED to an ICU, delayed transfer was independently associated with lower hospital survival (odds ratio, 0.7, 95% confidence interval, 0.56–0.89) (17). Unlike these earlier studies, our findings focused on disease-specific sepsis and were adjusted for confounding variables.

Our findings are of clinical relevance as the need for intensive care exceeds the availability of beds and staff (17, 30). In the absence of a validated predictive tool to qualify the need for ICU admission among critically ill patients presenting to the ED, the ICU admission decision is often restricted by patient age, co-morbidities, and preadmission functional dependency (31, 32), and remains a matter of individual clinical judgment (16, 19). Therefore, our findings may help to rationalize the decision to admit patients to the ICU and the utilization of ICU beds. Of note, early ICU admission survivors had a shorter length of stay than their delayed admission counterparts, which may also help decrease the shortage of ICU beds. Furthermore, earlier identification of patients who are candidates for ICU admission allows time to discuss treatment options with the patient, their care providers, and the medical team (33).

Our study took advantage of data available from four large, prospective, cohort studies (including 453 ICU admissions) of patients from North America and Europe (5, 9–11). There were substantial differences across the four cohort studies inpatient characteristics, ICU admission rates, and outcomes (Table 2). However, the absence of significant first-order interaction between delayed ICU transfer and the study cohort suggests that our results are consistent across studies. In fact, we believe that pooling original data from four cohort studies involving 44 hospitals in North America and Europe enhances the external validity of our findings. Despite these differences, similar trends were observed toward the improvement of medical outcomes (decreased mortality and length of stay) across the four original study populations, strengthening the robustness of this study's findings.

The selection of patients for inclusion in the present study has several distinctive features from previous studies on severe CAP. First, the study population was restricted to patients transferred to the ICU within 3 days of presentation. Pneumonia is the most common cause of severe sepsis (1, 34) and most cases of organ failure associated with pneumonia occur early (3), which contrasts with late ICU admissions that may be associated with factors other than the severity of pneumonia itself (26, 35). Our findings confirm that even after excluding patients who present with an obvious indication for immediate ICU transfer, a majority of CAP patients (303 of 378; 80.2%) who require critical care are transferred within the first 3 days of presentation. Organ failure is likely to be influenced by the initial management, rendering our findings highly relevant to patient management and potential ICU referral in the ED. Second, we assessed the robustness of our findings by excluding patients with obvious reasons for immediate transfer to an ICU from the ED. Including patients presenting with such clinically apparent features was of limited value because the indication for ICU transfer is almost mandatory (20, 36). Third, we elected not to exclude patients with severe advanced comorbid conditions, even though such patients might be considered poor candidates for ICU admission (30, 37); policies and practices in this regard may vary across institutions and countries. It should be noted that retaining those patients likely resulted in an underestimation of the actual benefit of direct ICU transfer (36).

Several potential limitations of our study must be acknowledged. First, the findings of our study are based solely on patient characteristics at presentation and do not take into account causative pathogens or processes of care (e.g., timely administration of antibiotics, type of antibiotics), which may have confounded the relationship between study groups and patient outcomes. Second, patients who died or improved without admission to the ICU were not captured by the methodology of this study and may account for a substantial group of patients. However, in the absence of validated criteria to qualify the need for ICU admission it was not possible to prevent this limitation. Third, we did not assess the causes that led to a delayed transfer to the ICU, which might have confounded the interpretation of the differences in medical outcomes between direct-transfer and delayed-transfer patients. Fourth, we were not able to assess the process of care during the time patients stayed in the ED, and whether intensive care was initiated in the ED setting, a fact that in some cases might have confounded the actual day of intensive care initiation.

CONCLUSIONS

In summary, this study suggests that earlier identification of patients without major severity criteria at ED presentation but at high risk for requiring admission to the ICU could provide substantial improvement of quality of care and thereby positively influence their medical outcomes. A better understanding of delayed ICU transfer of pneumonia patients could be used to refine the criteria for severe CAP as defined by the 2007 Infectious Diseases Society of America/American Thoracic Society consensus guideline (16). Consistent with the latest update of the Surviving Sepsis Campaign, these findings support the development of predictive models to identify patients with incipient severe CAP.

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