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Relationships among initial hospital triage, disease progression, and mortality in community-acquired pneumonia

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Abstract

Background and objective—Appropriate triage of patients with severe community-acquired pneumonia (CAP) may improve morbidity, mortality, and use of hospital resources. Worse outcomes from delayed intensive care unit (ICU) admission have long been suspected but have not been verified.

Methods—In a retrospective study of consecutive patients with CAP admitted from 1996–2006 to the ICUs of a tertiary care hospital, we measured serial severity scores, intensive therapies received, ICU-free days, and 30-day all-cause mortality. Primary outcome was mortality. We developed a regression model of mortality with ward triage (and subsequent ICU transfer within 72 hours) as the predictor, controlled by propensity for ward triage and radiographic progression.

Results—Of 1,059 hospital-admitted patients, 269 (25%) were admitted to the ICU during hospitalization. Of those, 167 were directly admitted to the ICU without current requirement for life support, while 61 (23%) were initially admitted to the hospital ward, 50 of those undergoing ICU transfer within 72 hours. Ward triage was associated with increased mortality (OR 2.6, p=0.056) after propensity adjustment. The effect was less (OR 2.2, p=0.12) after controlling for radiographic progression. The effect probably increased (OR 4.0, p=0.08) among patients with ≥ 3 severity predictors at admission.

Conclusions—Initial ward triage among patients subsequently transferred to the ICU is associated with twofold higher 30-day mortality. This effect is most apparent among patients with ≥ 3 severity predictors at admission and is partially attenuated by controlling for radiographic progression. Intensive monitoring of ward-admitted patients with CAP seems warranted. Further research is needed to optimize triage in CAP.

Keywords

Intensive Care; Outcome Assessment; Pneumonia; Respiratory Tract Infections; Triage

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Introduction

Community-acquired pneumonia (CAP) is an important clinical and public health problem. When combined with influenza, CAP is the eighth-leading cause of death in the United States and the most common cause of death from infection in the developed world.[1–3] Approximately 500,000 adults are admitted to the hospital in the US annually for CAP.[4] Since appropriate site of care presumably improves outcome and is the major determinant of cost, optimal triage of these patients is considered important.[5, 6] While patients requiring mechanical ventilation or vasopressor infusion require immediate ICU admission, how best to triage patients with some markers of severity but no current need for mechanical ventilation or vasopressor infusion is not clear. Delayed triage to the intensive care unit (ICU) may place patients at risk for worse outcomes, including prolonged ICU or hospital stay and premature mortality, while unnecessary ICU admission is costly and may expose patients to other risks, e.g. hospital-acquired infection or delirium. Previous studies have yielded conflicting conclusions about the risks of delayed ICU triage.[7–13]

Regardless of ICU triage, radiographically progressive pneumonia is more lethal than pneumonia associated with stable radiographic infiltrates.[14, 15] Radiographic progression of CAP accords with the common clinical understanding that a subset of patients has progressive disease regardless of therapy, due to predisposition for ARDS or unmeasured microbe-specific factors. Recent studies of delayed ICU admission did not control for radiographically progressive pneumonia, which may have confounded their finding of worse outcome with delayed ICU admission.[16–18]

Worse outcomes from delayed intensive care unit (ICU) admission have long been suspected but not certain. To evaluate the effect of initial ward triage on mortality and length of stay, after controlling for radiographic progression and propensity for initial ward triage, we studied a cohort of patients with severe CAP (SCAP) whose triage was not dictated by a current requirement for mechanical ventilation or vasopressor infusion.

Methods

Setting

We have reported our general methods previously.[19] Briefly, the study was performed at LDS Hospital, a tertiary care, university-affiliated teaching hospital, with 520 total and 68 ICU beds. There are approximately 26,500 Emergency Department (ED) visits per year, resulting in approximately 7,000 hospital admissions. In 1995, the LDS Hospital ED initiated a standardized pneumonia therapy protocol; severity assessment and triage guidelines based on the 1993 ATS guidelines were available on a paper form that was rarely utilized by ED staff.[20–22] Hospital policy required ICU admission for any patient requiring ≥ 60% inspired oxygen unless advanced directives limiting care were in place.

Patients

In a retrospective analysis of prospectively acquired electronic data using a validated algorithm,[23] we identified all patients admitted to LDS Hospital with ICD-9 codes for primary diagnosis of pneumonia (480–487.x) or respiratory failure or organism-specific sepsis (518.x, 038.x) with a secondary diagnosis of pneumonia (480–487.x) from 1996 to 2006. A chest radiograph compatible with pneumonia was required within 48 hours of admission, as extracted manually from radiologist-dictated reports.

We included patients admitted to the ICU either directly or within 72 hours of hospital admission who were not undergoing mechanical ventilation or vasopressor support (the

IDSA/ATS 2007 major criteria[5]) at the time of transfer from the ED to the ICU. We thus studied patients who did not have an obvious, immediate indication for ICU admission.

We excluded a) patients with aspiration pneumonia or immune suppression (AIDS, solid organ or bone marrow transplantation, metastatic solid tumors, or present or past hematologic malignancies as defined by ICD-9 codes); b) patients residing in a skilled nursing facility; c) patients discharged from a hospital within the prior 90 days; d) patients receiving chronic hemodialysis;[5] e) patients with admission do-not-resuscitate/do-not-intubate (DNR/DNI) orders[24]; and f) patients who expired in the ED. Patients were included only once in any 12-month period.

We calculated admission IDSA/ATS 2007[5] and SMART-COP[25] pneumonia severity prediction scores as well as the admission SAPS-2 score.[26] We also calculated daily IDSA/ATS 2007 scores for the first 72 hours following admission and the IDSA/ATS 2007 score at the time of transfer to the ICU among ward-triage patients. Thirty-day all-cause mortality, the primary mortality endpoint based on consensus that it best reflects pneumonia-associated mortality[27–30], was determined from the Utah Population Database.[31] We defined intensive therapies per our published methodology.[19] We defined radiographic progression as an extension of infiltrates or development of new pleural effusion on the basis of radiologist reports.

Triage Definitions

We defined ward triage *a priori* as initial admission to the hospital ward followed by ICU transfer within 72 hours. We chose 72 hours as a compromise meant to capture progressive SCAP while excluding late complications and to follow other reports.[16, 17] We also evaluated patients who died within 72 hours of being admitted to the ward but were never transferred to the ICU. Patients in this group whose death was unrelated to decisions to limit use of intensive therapies were considered to have undergone initial ward triage.

Because we were interested in the triage decision itself, we defined ICU triage as admission directly from ED to ICU, without any intervening stay on the hospital ward. We considered patients transferred from the ward to the ICU within 24 hours to have undergone ward triage, contrary to other studies.[16, 18] Because we were interested in whether observation in the ICU setting is beneficial, we included all patients admitted to the ICU, regardless of receipt of intensive therapies.

Primary analysis

Primary outcome was 30-day mortality. Our primary analysis was to determine whether initial ward triage (as opposed to initial ICU triage) was associated with increased mortality among patients who did not have an immediate need for ICU admission at the time they left the ED. To this end, we developed a logistic regression model of the association between ward triage and 30-day all-cause mortality in patients evaluated in the ED, adjusted for propensity[32–34] of ward triage and radiographic progression. We built the propensity model on the basis of IDSA/ATS 2007 severity score, SAPS-2 score, age, and other relevant predictors. We incorporated the propensity score into a final backward stepwise logistic regression, excluding predictors with $p>0.1$. The ultimate outcome of interest was all-cause 30-day mortality; the defined predictor of interest was ward triage. A linear regression model of ICU-free days at 30 days was built in the same manner. Missing predictors were assumed to be normal if dichotomous. Statistical significance was defined as a two-tailed $p < 0.05$. Analyses were performed with Stata 10 (College Park, TX) and R 2.10.2 (Vienna, Austria).[35]

Sensitivity Analyses

We performed three sensitivity analyses. First, we stratified the cohort based on an initial IDSA/ATS 2007 severity score ≥ 3, a consensus threshold for defining SCAP.[19, 36, 37] This first sensitivity analysis sought to define the association between ward triage and mortality among patients who appear to have been mis-triaged on the basis of high admission severity scores. Second, we replicated the methodology of Renaud et al[16] by including patients transferred from the ward to the ICU within 24 hours of hospital admission with patients directly admitted to the ICU to assess the effect of this methodology on the estimate of the association between ward triage and mortality. Third, we stratified the cohort into two time periods to evaluate for secular trends in the association.

Finally, we performed an exploratory matching procedure based on serial IDSA/ATS 2007 scores, intended to assess whether the effect of ward triage was mediated by clinical deterioration. Clinical deterioration was defined as an increase in the IDSA/ATS 2007 score over time. Ward-triage patients were matched to ICU-triage patients based on admission IDSA/ATS 2007 score as well as IDSA/ATS 2007 score at the time of transfer to the ICU. Because ICU-triage patients did not have a corresponding time of transfer, we used the IDSA/ATS 2007 score for the hospital day that matched the transfer time of the matched ward-triage patient. For example, if the ward-triage patient was transferred to the ICU 36 hours after admission, the ICU-triage patient's day 2 IDSA/ATS 2007 score was used for matching.

Ethical considerations

This study was approved by the Intermountain Healthcare Institutional Review Board (#1008505); individual patient consent was not required.

Results

Clinical and Demographic Findings

Two-hundred seventeen patients met inclusion criteria (Figure 1). Table 1 presents admission data on this cohort. Overall 30-day mortality was 5.8% (61 of 1,059) for admitted, ED-evaluated patients. Among patients in the study cohort, 15% (32 of 217) died; of ward-triage patients, 22% (11 of 50) died, while of ICU-triage patients, 12.6% (21 of 167) died. Ward-triage patients (N=50) had a mean IDSA/ATS 2007 score of 1.9 (median 2, IQR 1–3) at the time of admission. At the time of transfer from the ward to the ICU, the mean IDSA/ATS 2007 score was 3.9 (median 4, IQR 3–5), a significant increase ($p<0.001$). ICU-triage patients (N=167) had a mean IDSA/ATS 2007 score of 2.3(median 2, IQR 2–3) at time of admission, which was stable through the second hospital day. An admission IDSA/ATS 2007 score ≥ 3 was associated with significantly higher odds of death across all patient strata—mortality was highest (43%) among ward-triage patients with an admission score ≥ 3.

The distribution of intensive therapies among patients based on their initial triage is displayed in Table 2. Ward-triage patients were much more likely to receive intensive therapies following ICU transfer than ICU-triage patients. The total volume of crystalloid infused in the first 12 or 24 hours, a marker of the adequacy of resuscitation, did not differ significantly between ICU-triage and ward-triage patients.

Death on the ward within 72 hours of admission but without transfer to the ICU affected four patients (median age 87 years), all of whom were excluded for newly instituted limitations of care that prohibited ICU transfer. By comparison, all patients directly admitted

to the ICU who died within 72 hours of admission received aggressive support, including vasopressors and mechanical ventilation.

Primary Analysis

The results of the final regression model for the primary analysis are displayed in Table 3, controlling for admission severity scores. In the propensity-adjusted model, initial ward triage had an OR of 2.6 (p= 0.056). When this effect was controlled for radiographic progression, OR was 2.2 (p=0.1). The linear regression model of ICU-free days at 30 days associated initial ward triage with approximately 3.3 fewer ICU-free days after controlling for propensity (p=0.02). Controlling for radiographic progression (the model displayed in Table 4) reduced the estimate to 2.3days (p=0.1).

Sensitivity Analyses

Stratifying the cohort based on admission IDSA/ATS 2007 score suggested a difference in the effect of initial ward triage on 30-day mortality. When restricted to patients with an admission score ≥ 3, the odds ratio was 4.1 (p=0.07), while among patients with an admission score < 3, the odds ratio was 1.6 (p=0.5). The sensitivity analysis applying the methodology of Renaud et al to our cohort yielded an OR of 3.7(p=0.04) for initial ward triage. Controlling for radiographic progression yielded an OR of 2.9 (p=0.1).

Discussion

Initial ward triage of patients subsequently transferred to the ICU within 72 hours was associated with higher 30-day mortality after controlling for propensity for ward triage. The significance of this association was attenuated by controlling for radiographic progression, though the effect estimate was reasonably stable. This association depends strongly on baseline severity: patients who met IDSA/ATS 2007 criteria for severe pneumonia (≥ 3 predictors) in the ED had a fourfold increased risk of death if triaged to the ward, an effect that almost reached statistical significance (p=0.07) despite the low size of this predefined subgroup.

Our study expands prior observations[16–18] in several ways. First, we estimated the influence of progressive pneumonia, a distinct clinical entity that likely confounded prior studies.[14, 15] Second, we studied actual triage rather than merging patients transferred from the ward to the ICU within 24 hours.[16, 18] (Merging patients transferred within 24 hours inflates the risk of ward triage, as demonstrated by a sensitivity analysis in our cohort.) Third, we evaluated the effect of ward triage in a hospital with respiratory protocols, low thresholds for ICU transfer, and low overall mortality from CAP, a setting in which ward triage should be relatively safe. Fourth, we explicitly investigated patients who died before ICU transfer but within 72 hours. Our study thus increases the confidence of inferences about worse outcomes among patients initially triaged to the hospital ward.

The issue of confounding by progressive pneumonia is important to consider in assessing the risk of ward triage of patients with CAP. The development of ARDS or a systemic cytokine response to bacteriolysis in patients with a high titer of genomic bacterial DNA[38] could cause rapid progression of CAP in a patient who initially appears well. Similarly, late-appearing shock is generally more lethal than early-appearing shock in infected patients.[15, 39, 40] This study helps address the concern that the association between ward triage and poor outcome is confounded by the entity of progressive CAP. First, the association between ward triage and mortality persisted as a trend (p=0.1) after control for radiographic progression. Second, the association between ward triage and mortality is large (OR 4.0, p=0.08) among patients with severe pneumonia at admission. Though the small

number of such patients limits certainty about this conclusion, our patient cohort suggests that progressive CAP only partially accounts for the association between ward triage and mortality.

Mortality associated with ward triage may be related to physiological deterioration. Patients who deteriorate die more frequently; our primary analysis suggests that this clinical deterioration may be related to initial ward triage. That deteriorating patients have higher mortality is not surprising, but our study suggests that ward triage may contribute to this deterioration.

There are limits to the generalizability of our findings. Progressive respiratory failure is monitored closely on the wards of the study hospital, often with continuous pulse oximetry, and ICU transfer is usually undertaken before mechanical ventilation is immediately required. In institutions where the clinical course of CAP patients cannot be monitored frequently, the deleterious effect of initial ward triage may be substantially worse. In addition, the use of a treatment guideline for CAP might alter results compared to a setting where care is more variable. Our study was retrospective, though clinical data were recorded prospectively throughout the duration of the study, and the retrospective design avoided the risk of a Hawthorne effect (clinicians behaving differently when they believe they are being observed). Our mortality is consistent with other studies. Our ICU admission rate is somewhat higher and our ED stays shorter than at some other US hospitals.[28, 41, 42] We were unable to gather data on how often bed availability affected triage decisions. Relatively few patients in eleven years underwent discordant triage; the modest sample size may limit generalizability of the present study.

We propose that healthcare systems provide careful scrutiny of moderately ill patients (≥ 2 IDSA/ATS severity criteria, with special emphasis on patients with ≥ 3 criteria) with CAP, a group whose triage is not straightforward. Data from multiple centers now provide evidence to justify prospective evaluation of explicit triage strategies. Such triage strategies should include objective assessment of CAP severity in the ED. A triage protocol might recommend ICU admission for patients with ≥ 3 minor criteria, particularly those with hypoxemia, and careful monitoring on a hospital ward for patients with ≥ 2 minor criteria. We also propose development of models for predicting deterioration on the hospital ward among patients with pneumonia. Better models should improve the efficiency and generalizability of the prospective studies that should be performed to confirm our findings. Until results from rigorous, prospective studies become available, we believe that early ICU admission or better-than-usual monitoring on the floor should be implemented for moderately ill patients admitted with CAP.

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Summary at a Glance

It is unclear whether admitting a patient with severe pneumonia to the hospital ward has a negative effect on outcome. Attempts to answer this question have been confounded by the entity of progressive pneumonia. In this study we suggest that some of the association of initial ward triage with mortality is accounted for by progressive pneumonia.

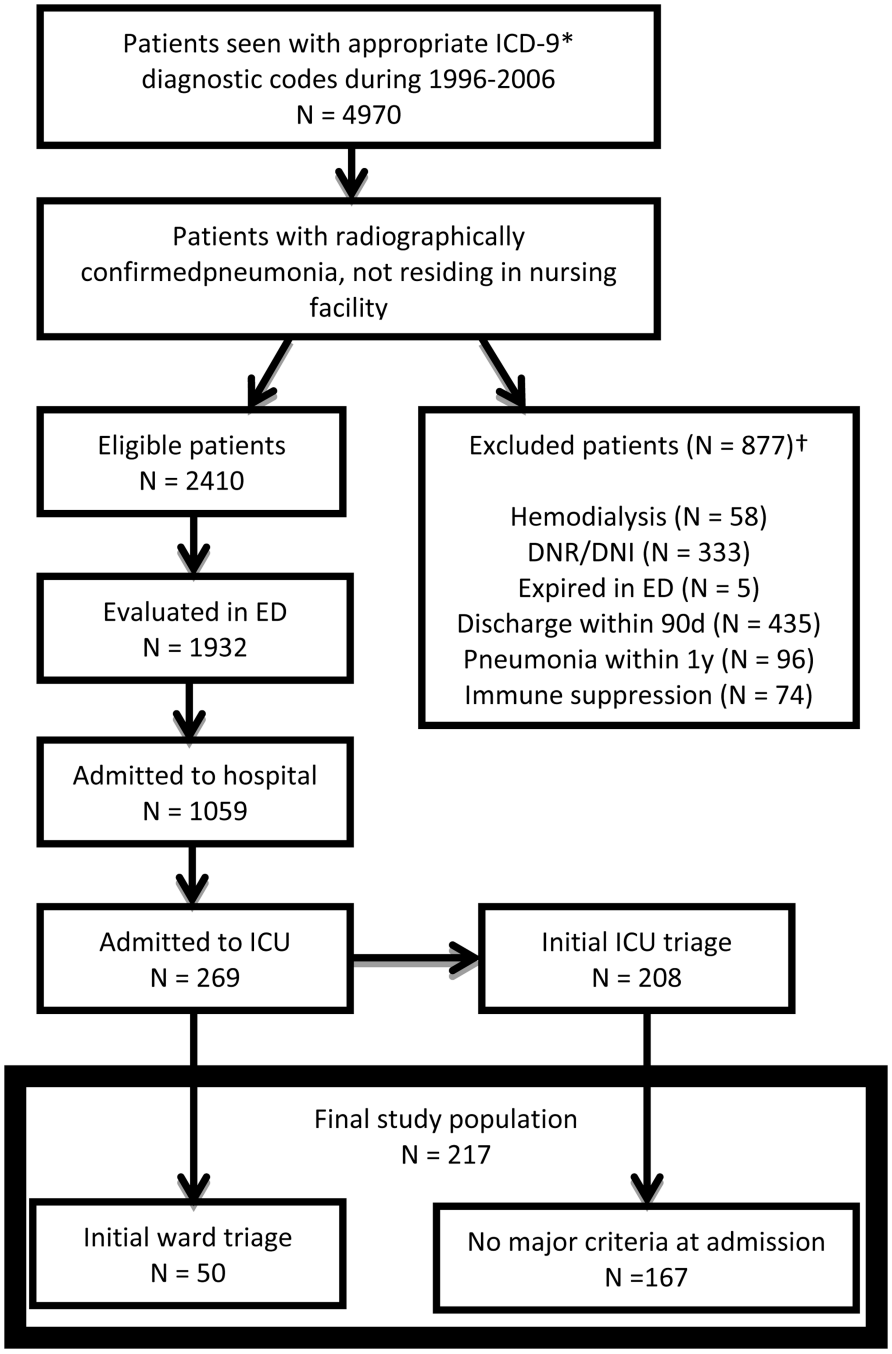

Figure 1.

Flow chart illustrating patient selection for the final study population.

*Primary ICD-9 code for pneumonia (480–487.x) or respiratory failure (518.x), organism-specific sepsis (0.38.x) with pneumonia (480–487.x) as secondary diagnosis.

†Some patients had >1 exclusion; 11 (excluded) patients were transferred to ICU after >72 h

Table 1

Comparison of Admission Characteristics

Parameter	Ward triage N=50	ICU triage N=167	p-value for comparison
Age (years)	62	58	0.3
Sex (% female)	46	46	0.95
CURB-65 (points)	1.9	1.9	0.8
SMART-COP (points)	2.9	3.5	0.02
IDSA/ATS 2007 minor criteria (points)	1.9	2.4	0.01
SAPS-2 score (points)	25	26.4	0.4
Appropriate initial antibiotics (%)	72	71	0.9
Bacteremia (%)	8	8	0.96
Microbial etiology identified (%)	18	16	0.7
Confusion (%)	4	10	0.2
Multilobar disease (%)	50	58	0.3
Blood Urea Nitrogen > 20mg/dl (%)	64	54	0.2
Respiratory rate >= 30/min (%)	14	37	<0.01
Mean Arterial Pressure < 65mmHg (%)	16	23	0.3
P/F ratio<250 (%)*	30	44	0.07
Hypothermia—Temp<36C (%)	10	8	0.6
White Blood Cells < 4,000/mm3 (%)	6	3	0.3
Platelets<100,000/mm3 (%)	0	5	0.1
Hospital mortality (%)	20	12	0.1
30-day mortality (%)	22	13	0.1

*Adjusted for altitude of LDS Hospital (1400m, average barometric pressure 650 mmHg) CURB-65: Confusion, Urea, Respiratory Rate, Blood Pressure, Age>65 Score; SMART-COP: Systolic blood pressure, Multilobar pneumonia, low Albumin, Respiratory rate, Tachycardia, Confusion, low Oxygen, low PH Score; IDSA/ATS 2007: Infectious Diseases Society of America/American Thoracic Society 2007 Pneumonia Guidelines; SAPS-2: Simplified Acute Physiology Score.

Table 2

Intensive therapies received by initial triage decision

Intensive therapy	Ward triage % (95% CI) (N=50)	ICU triage % (95% CI) (N=167)	p value for comparison
Any intensive therapy	84 (74–94)	68 (61–75)	0.02
NIPPV	12 (3–21)	11 (6–15)	0.8
FiO2>=0.6	62 (49–75)	52 (45–60)	0.2
Mechanical ventilation	52 (38–66)	23 (17–30)	<0.01
Vasopressor support	34 (21–47)	19 (13–24)	0.02
Ventilation and vasopressors	30 (17–43)	14 (9–20)	0.01
Ventilation or vasopressors	56 (42–70)	28 (21–34)	<0.01
Central venous catheter	38 (25–51)	23 (17–29)	0.03
Arterial catheter	50 (36–64)	41 (33–48)	0.2
Aggressive fluid resuscitation*	22 (11–33)	12 (7–17)	0.08

NIPPV: Non-invasive positive pressure ventilation

* >=4L of crystalloid within 2 hours

Table 3

Regression models for 30-day mortality

Predictor	OR (95% CI; p value) unadjusted	OR (95% CI; p value) propensity-adjusted	OR (95% CI; p value) adjusted for radiographic progression
Initial Ward Triage (vs. Initial ICU Triage)	2.4 (0.95–5.9; 0.06)	2.6 (0.98–7.0; 0.056)	2.2 (0.8–6.0; 0.12)
Age (per year)	1.04 (1.01– 1.07; <0.01)	1.04 (1.01– 1.08; <0.01)	1.05 (1.02– 1.08; <0.01)
Minor Criteria Score (per point)	1.8 (1.3–2.5; <0.01)	1.8 (1.2–2.8; 0.01)	1.7 (1.1–2.7; 0.02)
Propensity Score	NA	1.6 (0.04–62; 0.8)	1.5 (0.04–60; 0.8)
Radiographic Progression (vs. no radiographic progression)	NA	NA	2.4 (0.92–6.3; 0.07)

95% CI: Ninety-five percent confidence interval for Odds Ratio

Table 4

Linear Regression of ICU-free days at 30 days (N=209)*

Predictor	Coefficient	95%CI	p value
Ward Triage	−2.3	−5.1-0.5	0.1
Age	−0.06	−0.13-0.001	0.06
Minor Criteria Score	−1.5	−2.6 -−0.4	< 0.01
Propensity Score	0.3	−9.1-9.1	0.9
Radiographic Progression	−3.8	−6.1-−1.5	<0.01
Intercept	34	29–39	<0.01

* The 8 patients with low platelet count were all admitted directly to the ICU so were excluded from the model.