

ORIGINAL RESEARCH

Adverse Outcomes Associated With Delayed Intensive Care Unit Transfers in an Integrated Healthcare System

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BACKGROUND: Patients with intensive care unit (ICU) transfers from hospital wards have higher mortality than those directly admitted from the emergency department.

OBJECTIVE: To describe the association between the timing of unplanned ICU transfers and hospital outcomes.

DESIGN, SETTING, PATIENTS: Evaluation of 6369 early (within 24 hours of hospital admission) unplanned ICU transfer cases and matched directly admitted ICU controls from an integrated healthcare system. Cohorts were matched by predicted mortality, age, gender, diagnosis, and admission characteristics. Hospital mortality of cases and controls were compared based on elapsed time and diagnosis.

RESULTS: More than 5% of patients admitted through the emergency department experienced an unplanned ICU transfer; the incidence and rates of transfers were highest within the first 24 hours of hospitalization. Multivariable matching produced 5839 (92%) case-control pairs. Median

length of stay was higher among cases (5.0 days) than controls (4.1 days, $P < 0.01$); mortality was also higher among cases (11.6%) than controls (8.5%, $P < 0.01$). Patients with early unplanned transfers were at an increased risk of death (odds ratio, 1.44; 95% confidence interval, 1.26-1.64; $P < 0.01$); an increased risk of death was observed even among patients transferred within 8 hours of hospitalization. Hospital mortality differed based on admitting diagnosis categories. While it was higher among cases admitted for respiratory infections and gastrointestinal bleeding, it was not different for those with acute myocardial infarction, sepsis, and stroke.

CONCLUSIONS: Early unplanned ICU transfers—even within 8 hours of hospitalization—are associated with increased mortality; outcomes vary by elapsed time to transfer and admitting diagnosis. *Journal of Hospital Medicine* 2012;7:224-230. © 2011 Society of Hospital Medicine.

Hospitalized patients who require transfer from medical wards to the intensive care unit (ICU) have high in-hospital mortality, in some reports exceeding 55%.¹⁻⁴ In a previous report in this journal, we found that while these “unplanned ICU transfers” occurred in only 4% of hospitalizations, they were present in nearly one-quarter of fatal hospitalizations and were associated with substantial increases in resource utilization.⁴ For these reasons, interventions aimed at identifying and treating this high-risk group have received considerable attention and have been proposed as measures of inpatient safety.^{2,4-9}

Notably, mortality among patients with unplanned ICU transfers exceeds mortality among patients admitted to the ICU directly from the emergency department (ED)—a group traditionally considered to have the highest risk of death.^{1-3,10} Previous single-center studies suggest that increased mortality rates are pres-

ent even among patients transferred within 24 hours of hospital admission, and reinforce the notion that earlier recognition of critical illness may result in improved outcomes.¹¹⁻¹³ However, these studies have been performed primarily in small cohorts of heterogeneous patients, and may obscure the independent effect of unplanned transfers on mortality and hamper efforts to use unplanned transfer rates as a metric of healthcare quality.^{1,2,4,9}

In this study, we evaluated early unplanned ICU transfers drawn from a cohort of 499,995 hospitalizations in an integrated healthcare delivery system. Using patient data, extracted from the automated electronic medical record, we matched unplanned transfer cases to patients directly admitted to the ICU and described the association between delayed ICU transfers and adverse outcomes.

METHODS

Setting and Participants

We performed a retrospective analysis of adult patient (age ≥ 18 years) hospitalizations at 21 Northern California Kaiser Permanente (KP) Medical Care Program hospitals between January 2007 and December 2009. This work expanded on our previous report of hospital stays from November 2006 to January 2008.⁴ The 21 study hospitals used the same electronic health information systems; databases captured admission,

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discharge, and bed history data. The use of these databases for research has been described in our previous study and other reports; hospital characteristics, unit staffing, and resource levels have also been detailed previously.^{4,14–17} This study was approved by the KP Institutional Review Board.

Identifying Unplanned Transfers

We evaluated patients with “medical” hospitalizations—defined as those whose first hospital location was not in a surgical setting such as the operating room or post-anesthesia recovery area—whose admission originated in the ED; patients admitted for surgery were removed because of significant differences in observed mortality (see Supporting Information Appendix Figure 1 and Appendix Table 1 in the online version of this article). Patients whose admission did not originate in the ED were excluded to eliminate confounding resulting from differences in preadmission care. We also excluded patients admitted for gynecological and pregnancy-related care because of low hospital mortality.

Initial patient locations included the medical wards (wards); the transitional care unit (TCU); and the intensive care unit (ICU). Bed history data, based on time stamps and available for all patients, were used to track patient locations from the time of admission, defined as the first non-ED hospital location, until discharge. Patient length of stay (LOS) was calculated at each location and for the entire hospitalization.

Transfers to the ICU after a patient’s initial admission to the ward or TCU were termed “unplanned (or delayed) ICU transfers”; patients admitted from the ED to the ICU were termed “direct ICU admit” patients. Direct ICU admit patients were excluded from the unplanned transfer group even if they required a readmission to the ICU later in their hospital course. We focused on patients with unplanned ICU transfers early after hospitalization to identify those in whom prompt recognition and intervention could be effective; thus, our primary analyses were on patients with transfers within 24 hours of admission. In secondary analysis, we also evaluated patients with unplanned ICU transfers occurring within 48 hours after hospital admission.

Admission Severity of Illness

To account for severity of illness at admission, we used a predicted mortality measure developed at KP.¹⁴ This method strictly utilizes information available prior to hospital admission—including that from the ED; variables included age, gender, admitting diagnosis, and measures of laboratory test and comorbid disease burden. The method, derived using 259,669 KP hospitalizations, produced a c-statistic of 0.88 for inpatient mortality; external validation, based on 188,724 hospitalizations in Ottawa, produced a c-statistic of 0.92.^{14,18}

Admitting diagnoses were based on admission International Classification of Diseases, 9th revision (ICD-

9) codes, and grouped into 44 broad “Primary Conditions” based on pathophysiologic plausibility and mortality rates.¹⁴ The method also quantified each patient’s physiologic derangement and preexisting disease burden based on automated laboratory and comorbidity measures—the Laboratory Acute Physiology Score (LAPS) and the Comorbidity Point Score (COPS).¹⁴

In brief, the LAPS was derived from 14 possible test results obtained in the 24-hour time period preceding hospitalization, including: anion gap; arterial pH, PaCO₂, and PaO₂; bicarbonate; serum levels of albumin, total bilirubin, creatinine, glucose, sodium, and troponin I; blood urea nitrogen; creatinine; hematocrit; and total white blood cell count.¹⁴ The COPS was calculated from each subject’s inpatient and outpatient diagnoses, based on Diagnostic Cost Groups software,¹⁹ during the 12-month period preceding hospitalization.¹⁴ Increasing LAPS and COPS values were associated with increases in hospital mortality; detailed information about the development, application, and validation are available in previous work.^{14,18}

Statistical Analysis

Evaluating excess adverse outcomes associated with unplanned transfers requires adequate control of confounding variables. Our approach to reduce confounding was multivariable case matching—a technique used for assessing treatment effects in observational data.^{20,21} Patients with unplanned transfers—identified as cases—were matched with similar controls based on observed variables at the time of hospital admission.

We first matched patients with unplanned ICU transfers within 24 hours of hospital admission to direct ICU admit controls based on predicted in-hospital mortality (to within 1%); age (by decade); gender; and admitting diagnosis. If a case was matched to multiple controls, we selected 1 control with the most similar admission characteristics (weekday or weekend admission and nursing shift). The risk of death associated with unplanned transfers was estimated using multivariable conditional logistic regression. In secondary analysis, we repeated this analysis only among case-control pairs within the same hospital facilities.

To cross-validate the results from multivariable matching techniques, we also performed mixed-effects multivariable logistic regression including all early unplanned transfer patients and direct ICU admit patients, while adjusting for predicted hospital mortality, age, gender, admitting diagnosis, LAPS, COPS, weekend versus weekday admission, nursing shift, and hospital facility random effects. We repeated these same analyses where cases were defined as patients transferred to the ICU within 48 hours of hospitalization.

Unplanned Transfer Timing

Using bed history data, we identified the “elapsed time” from admission to unplanned transfer, and categorized

TABLE 1. Baseline Characteristics of Patients by Initial Hospital Location and Need for Unplanned ICU Transfer

Variable	Overall	Early Delayed ICU Transfer (by Elapsed Time Since Hospital Admission)		Direct ICU Admit
		Within 24 hr	Within 48 hr	
No. (%)	313,797	6,369 (2.0)	9,816 (3.1)	29,929 (9.5)
Age*	67 ± 18	67 ± 16	68 ± 16	64 ± 17
Female*	169,358 (53.7)	3,125 (49.1)	4,882 (49.7)	14,488 (48.4)
Weekend admission*	83,327 (26.6)	1,783 (28.0)	2,733 (27.8)	8,152 (27.2)
Nursing shift at admission*				
Day (7 AM–3 PM)	65,303 (20.8)	1,335 (21.0)	2,112 (21.5)	7,065 (23.6)
Evening (3 PM–11 PM)	155,037 (49.4)	2,990 (47.0)	4,691 (47.8)	13,158 (44.0)
Night (11 PM–7 AM)	93,457 (29.8)	2,044 (32.1)	3,013 (30.7)	9,706 (32.4)
Initial hospital location*				
Ward	234,915 (82.8)	5,177 (81.3)	7,987 (81.4)	...
Transitional care unit	48,953 (17.2)	1,192 (18.7)	1,829 (18.6)	...
LAPS*	24 ± 19	28 ± 20	28 ± 20	35 ± 25
COPS*	98 ± 67	105 ± 70	106 ± 70	99 ± 71
Length of stay (days)	4.6 ± 7.5	8.4 ± 12.2	9.1 ± 13.4	6.4 ± 9.5
In-hospital mortality	12,686 (4.0)	800 (12.6)	1,388 (14.1)	3,602 (12.0)

NOTE: Values are mean ± SD or number (%). Abbreviations: COPS, Comorbidity Point Score; ICU, intensive care unit; LAPS, Laboratory Acute Physiology Score. * $P < 0.001$ for comparison by analysis of variance (ANOVA) or chi-squared test between groups.

patients in increments of elapsed time from admission to unplanned transfer. Time-to-unplanned transfer was summarized using Kaplan-Meier curve.

All analyses were performed in Stata/IC 11.0 for Mac (StataCorp LP, College Station, TX). Continuous variables were reported as mean ± standard deviation (SD). Cohort comparisons were performed with analysis of variance (ANOVA). Categorical variables were summarized using frequencies and compared with chi-squared testing. A P value < 0.05 was considered statistically significant.

RESULTS

During the study period, 313,797 medical hospitalizations originated in the ED (Table 1). Overall, patients' mean age was 67 ± 18 years; 53.7% were female. Patient characteristics differed significantly based on the need for ICU admission. For example, average LAPS was highest among patients admitted directly to the ICU and lowest among patients who never required ICU care ($P < 0.01$). Patients with unplanned ICU transfers during hospitalization had longer length of stay and higher hospital mortality than direct ICU admit patients ($P < 0.01$). Overall, more than 1 in 15 patients experienced an unplanned transfer to the ICU.

The majority of unplanned transfers occurred within the first 48 hours of hospitalization (57.6%, Figure 1); nearly 80% occurred within the first 4 days. The rate of unplanned transfer peaked within 24 hours of hospital admission and decreased gradually as elapsed hospital LOS increased (Figure 1). While most patients experienced a single unplanned ICU transfer, 12.7% required multiple transfers to the ICU throughout their hospitalization.

Multivariable case matching between unplanned transfer cases within 24 hours of admission and direct

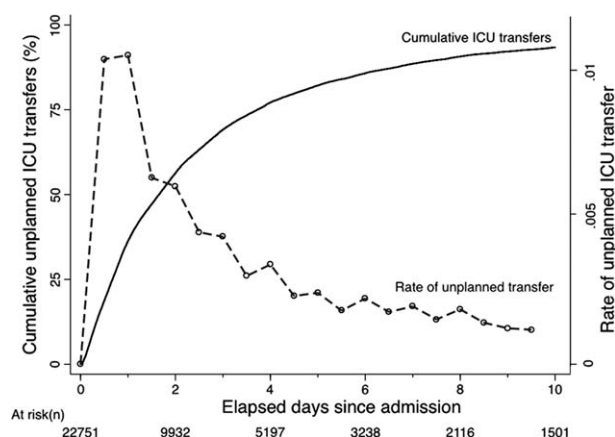


FIG. 1. Cumulative incidence (solid line) and 12-hour rate (dashed line) of unplanned intensive care unit (ICU) transfers.

ICU admit controls resulted in 5839 (92%) case-control pairs (Table 2). Matched pairs were most frequently admitted with diagnoses in “Primary Condition” groups that included respiratory infections and pneumonia (15.6%); angina, acute myocardial infarction (AMI), and heart failure (15.6%); or gastrointestinal bleeding (13.8%).

In-hospital mortality was significantly higher among cases (11.6%) than among ICU controls (8.5%, $P < 0.001$); mean LOS was also longer among cases (8 ± 12 days) than among controls (6 ± 9 days, $P < 0.001$). Unplanned transfer cases were at an increased odds of death when compared with ICU controls (adjusted odds ratio [OR], 1.44; 95% confidence interval [CI], 1.26–1.64; $P < 0.001$); they also had a significantly higher observed-to-expected mortality ratio. When cases and controls were matched by hospital facility, the number of case-control pairs decreased (2949 pairs; 42% matching frequency) but the odds of death was of similar

TABLE 2. Characteristics and Outcomes of Patients With Unplanned ICU Transfers and Matched Patients Directly Admitted to the ICU

	ICU Cohorts (by Elapsed Time to Transfer Since Hospital Admission)			
	Within 24 hr (n = 5,839)		Within 48 hr (n = 8,976)	
	Delayed ICU Transfer (Case)	Direct ICU Admit (Control)	Delayed ICU Transfer (Case)	Direct ICU Admit (Control)
Age	67 ± 16	66 ± 16	67 ± 16	67 ± 16
Female	2,868 (49.1)	2,868 (49.1)	4,477 (49.9)	4,477 (49.9)
Admitting diagnosis				
Pneumonia	911 (15.6)	911 (15.6)	1,526 (17.0)	1,526 (17.0)
Heart failure or MI	909 (15.6)	909 (15.6)	1,331 (14.8)	1,331 (14.8)
Gastrointestinal bleeding	806 (13.8)	806 (13.8)	1,191 (13.3)	1,191 (13.3)
Infections (including sepsis)	295 (5.1)	295 (5.1)	474 (5.3)	474 (5.3)
Outcomes				
Length of stay (days)*	8 ± 12	6 ± 9	9 ± 13	6 ± 9
In-hospital mortality*	678 (11.6)	498 (8.5)	1,181 (13.2)	814 (9.1)

NOTE: Admitting diagnosis includes the 4 most frequent conditions. Pneumonia includes other respiratory infections. Abbreviations: ICU, intensive care unit; MI, myocardial infarction. * $P < 0.01$.

magnitude (OR, 1.43; 95% CI, 1.21-1.68; $P < 0.001$). Multivariable mixed-effects logistic regression including all early unplanned transfer and direct ICU admit patients produced an effect size of similar magnitude (OR, 1.37; 95% CI, 1.24-1.50; $P < 0.001$).

Results were similar when cases were limited to patients with transfers within 12 hours of admission; mortality was 10.9% among cases and 9.1% among controls ($P = 0.02$). When including patients with unplanned transfers within 48 hours of hospital admission, the difference in mortality between cases and controls increased (13.2% vs 9.1%, $P < 0.001$). The odds of death among patients with unplanned transfers increased as the elapsed time between admission and ICU transfer lengthened (Figure 2); the adjusted OR was statistically significant at each point between 8 and 48 hours.

When stratified by admitting diagnosis groups, cases with unplanned transfers within the first 48 hours had increased mortality compared with matched controls in some categories (Table 3). For example, for patients in the respiratory infection and pneumonia group, mortality was 16.8% among unplanned transfer cases and 13.0% among early matched ICU controls ($P < 0.01$). A similar pattern was present in groups including: gastrointestinal bleeding, chronic obstructive pulmonary disease (COPD) exacerbation, and seizure groups (Table 3). However, for patients with AMI alone, mortality was 5.0% among cases and 3.7% among matched controls ($P = 0.12$). Patients with sepsis had a mortality rate of 15.2% among cases and 20.8% among matched controls ($P = 0.07$). Similarly, patients with stroke had a mortality rate of 12.4% among unplanned transfer cases and 11.4% in the matched controls ($P = 0.54$).

DISCUSSION

This study found that unplanned ICU transfers were common among medical patients, occurring in 5% of all hospitalizations originating in the ED. The major-

ity of unplanned transfers occurred within 48 hours of admission; the rate of ICU transfers peaked within 24 hours after hospitalization. Compared with patients admitted directly from the ED to the ICU, those transferred early after admission had significantly increased mortality; for example, patients transferred within 24 hours were at a 44% increased odds of hospital death. The adverse outcomes associated with unplanned transfers varied considerably by admission diagnosis subgroups.

Our findings confirm previous reports of increased mortality among patients with unplanned ICU transfers. Escarce and Kelley reported that patients admitted to the ICU from non-ED locations—including wards, intermediate care units, and other hospitals—were at an increased risk of hospital death.¹ Multiple subsequent studies have confirmed the increased mortality among patients with unplanned transfers.^{2-4,10,13,22,23} We previously evaluated patients who required a transfer to any higher level of care and reported an observed-to-expected mortality ratio of 2.93.⁴

Fewer studies, however, have evaluated the association between the timing of unplanned transfers and inpatient outcomes; previous small reports suggest that delays in ICU transfer adversely affect mortality and length of stay.^{12,13,24} Parkhe et al. compared 99 direct ICU admit patients with 23 who experienced early unplanned transfers; mortality at 30 days was significantly higher among patients with unplanned transfers.¹³ The current multifacility study included considerably more patients and confirmed an in-hospital mortality gap—albeit a smaller one—between patients with early transfers and those directly admitted to the ICU.

We focused on unplanned transfers during the earliest phase of hospitalization to identify patients who might benefit from improved recognition of, and intervention for, impending critical illness. We found that even patients requiring transfers within 8 hours of hospital admission were at an increased risk of death.

Bapojé et al. recently reported that as many as 80% of early unplanned transfers were preventable and that most resulted from inappropriate admission triage.¹¹ Together, these findings suggest that heightened attention to identifying such patients at admission or within the first day of hospitalization—when the rates of unplanned transfers peak—is critical.

Several important limitations should be recognized in interpreting these results. First, this study was not designed to specifically identify the reasons for unplanned transfers, limiting our ability to characterize episodes in which timely care could have prevented excess mortality. Notably, while previous work suggests that many early unplanned transfers might be prevented with appropriate triage, it is likely that some excess deaths are not preventable even if every patient could be admitted to the ICU directly.

We were able to characterize patient outcomes by admitting diagnoses. Patients admitted for pneumonia and respiratory infection, gastrointestinal bleeding, COPD exacerbation, or seizures demonstrated excess mortality compared with matched ICU controls, while those with AMI, sepsis, and stroke did not. It is possible

that differences in diagnosis-specific excess mortality resulted from increasing adherence to well-defined practice guidelines for specific high-risk conditions.^{25–27} For example, international awareness campaigns for the treatment of sepsis, AMI, and stroke—“Surviving Sepsis,” “Door-to-Balloon,” and “F.A.S.T.”—emphasize early interventions to minimize morbidity and mortality.

Second, the data utilized in this study were based on automated variables extracted from the electronic medical record. Mortality prediction models based on automated variables have demonstrated excellent performance among ICU and non-ICU populations^{14,18,28}; however, the inclusion of additional data (eg, vital signs or neurological status) would likely improve baseline risk adjustment.^{5,10,29–31} Multiple studies have demonstrated that vital signs and clinician judgment can predict patients at an increased risk of deterioration.^{5,10,29–31} Such data might also provide insight into residual factors that influenced clinicians’ decisions to triage patients to an ICU versus non-ICU admission—a focus area of our ongoing research efforts. Utilizing electronically available data, however, facilitated the identification of a cohort of patients far larger than that in prior studies. Where previous work has also been limited by substantial variability in baseline characteristics among study subjects,^{1,2,12,13} our large sample produced a high percentage of multivariable case matches.

Third, we chose to match patients with a severity of illness index based on variables available at the time of hospital admission. While this mortality prediction model has demonstrated excellent performance in internal and external populations,^{14,18} it is calibrated for general inpatient, rather than critically ill, populations. It remains possible that case matching with ICU-specific severity of illness scores might alter matching characteristics, however, previous studies suggest that severity of illness, as measured by these scores, is comparable between direct ICU admits and early ICU transfers.¹³ Importantly, our matching procedure avoided the potential confounding known to

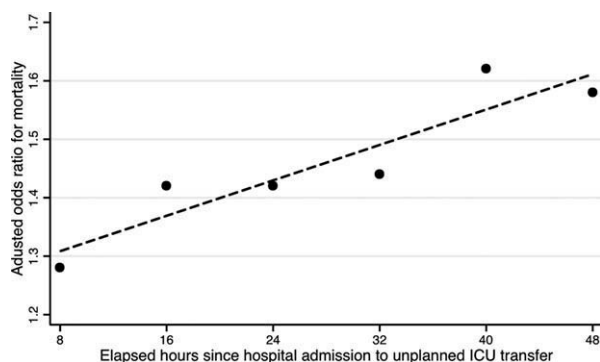


FIG. 2. Multivariable odds ratio for mortality among patients with unplanned intensive care unit (ICU) transfers, compared with those with direct ICU admissions, based on elapsed time between hospital admission and ICU transfer. Dashed line represents a linear regression fitted line of point estimates (slope = 0.08 per hour; model R^2 0.84). P value <0.05 at each timepoint.

TABLE 3. Hospital Mortality Among Selected Primary Condition Groups

Primary Condition Group	Mortality in ICU Case-Control Cohorts, No. (%)			
	Within 24 hr		Within 48 hr	
	Delayed ICU Transfer (Case)	Direct ICU Admit (Control)	Delayed ICU Transfer (Case)	Direct ICU Admit (Control)
Respiratory infections	143 (15.7)	126 (13.8)	493 (16.8)	380 (13.0)
Angina, heart failure, or MI	60 (6.6)	41 (4.5)	324 (7.7)	152 (3.6)
Acute MI alone	16 (5.7)	17 (6.1)	82 (5.0)	61 (3.7)
Gastrointestinal bleeding	96 (11.9)	55 (6.8)	549 (19.3)	188 (6.6)
Infections including sepsis	20 (9.8)	52 (11.2)	228 (14.8)	220 (14.2)
Sepsis alone	32 (18.9)	31 (18.3)	123 (15.2)	168 (20.8)
COPD exacerbation	20 (9.8)	12 (5.9)	74 (10.8)	43 (6.3)
Stroke	18 (10.2)	19 (10.8)	77 (12.4)	71 (11.4)
Seizure	21 (8.6)	9 (3.7)	68 (7.1)	34 (3.6)

Abbreviations: COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; MI, myocardial infarction.

exist with the use of prediction models based on discharge or intra-hospitalization data.^{32,33}

Finally, while we were able to evaluate unplanned transfer timing in a multifacility sample, all patient care occurred within a large integrated healthcare delivery system. The overall observed mortality in our study was lower than that reported in prior studies which considered more limited patient cohorts.^{1,2,12,13,22} Thus, differences in patient case-mix or ICU structure must be considered when applying our results to other healthcare delivery systems.

This hypothesis-generating study, based on a large, multifacility sample of hospitalizations, suggests several areas of future investigation. Future work should detail specific aspects of care among patients with unplanned transfer, including: evaluating the structures and processes involved in triage decisions, measuring the effects on mortality through implementation of interventions (eg, rapid response teams or diagnosis-specific treatment protocols), and defining the causes and risk factors for unplanned transfers by elapsed time.

In conclusion, the risk of an unplanned ICU transfer—a common event among hospitalized patients—is highest within 24 hours of hospitalization. Patients with early unplanned transfers have increased mortality and length of stay compared to those admitted directly to the ICU. Even patients transferred to the ICU within 8 hours of hospital admission are at an increased risk of death when compared with those admitted directly. Substantial variability in unplanned transfer outcomes exists based on admitting diagnoses. Future research should characterize unplanned transfers in greater detail with the goal of identifying patients that would benefit from improved triage and early ICU transfer.

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