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Original Research

Mortality of Patients Requiring Escalation to Intensive Care within 24 Hours of Admission in a Mixed Medical-Surgical Population

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Abstract

Objective: Delayed intensive care unit admissions are associated with increased mortality. We present a retrospective study looking at whether indirect admissions to the ICU within 24 hours of hospital admission were associated with increased mortality.

Design: Retrospective cohort study

Setting: Mixed medical-surgical ICU at a large tertiary United States Veterans Affairs (VA) Hospital System

Population: The patients were a mix of medical and surgical patients. Patients included both those directly admitted from the operating room as well as those escalated to the ICU after initial admission to the ward (indirect admission).

Methods: All admissions to a medical-surgical ICU from 2008 to 2013 were included in the study. The database was queried for time and location where the admission originated. Separate lists were created for patients with severe sepsis, patients who transferred to the ICU within the first 24 hours, and patients who had rapid response or code team activations. Analysis was applied to the whole group and to medical and surgical subpopulations.

Results: A total of 3,862 ICU admissions were studied. Univariate analysis indicated an impact of delayed admission on whole group and surgical patients, however multivariate analysis indicated a significant effect of delayed admission on 1-year surgical mortality. Multivariate analysis also showed a consistent effect of age, ICU length of stay and cardiac arrest on mortality of both medical and surgical ICU patients.

Conclusion: In a large retrospective study, surgical patients had increased 1-year mortality if they required escalation to the ICU within 24 hours of hospital admission. This result was not replicated in medical patients, possibly related to a burden of illness that could not be altered by earlier care.

Keywords: Intensive care, triage, mortality, deterioration

Background

Intensive care units (ICUs) receive critically ill patients at all hours, both directly admitted from the emergency department (ED) or operating room (OR), and also on an unexpected basis from medical-surgical wards following a critical event or deterioration. An early impression of a patient's illness severity and expected course influences whether the patient is admitted to an ICU or ward. These triage decisions are important as ICU care is a limited resource within any healthcare facility and should be used judiciously [1]. Studies have shown that patients who have a delay in physical transfer to the ICU due to bed availability have poorer outcomes [2-4]. It is possible that early triage to a non-ICU unit and eventual transfer may be harmful.

A recent study that looked at ICU utilization in a post-operative surgical population and found that indirect admissions to the ICU, defined as patients first being admitted to the floor then transferred to the ICU, was associated with higher mortality and morbidity [5]. Similar findings were noted in a 2014 study of medical patients where patients who were indirectly admitted to the ICU had higher in-hospital mortality and death within 60 days [6]. Another study showed that in patients with unplanned ICU transfers within 48 hours of admission from an ED who received critical interventions had increased morbidity and mortality. [7]

Different factors associated with ICU admissions have also been associated with higher mortality rates. These characteristics can be split between organizational factors such as time and day of admission, time "delays" in admission to the ICU,[8] staffing models such as "closed" vs "open" ICUs [9] as well as different levels of nursing staffing[10] and patient-specific factors such as a age, being a medical or surgical patient (due to differing co-morbidities and health status), being admitted to the ICU for severe sepsis/shock, admission immediately following a respiratory or cardiac arrest, or after a rapid response activation for an acute decompensation. These factors have previously been evaluated for their effects on triage of admissions between intensive care units and other units in the hospital with the goal of identifying patients at risk for poor outcomes.

We report findings of our own retrospective cohort study of a mixed medical-surgical ICU in which we studied the association between indirect ICU admissions within 24 hours of hospital admissions and mortality. This short timeframe (< 24 hours) was selected based on prior studies on delays, and also because this is likely to represent deterioration from the initial presenting illness or an incorrect perception of the illness severity and course. This also potentially includes a high-risk patient population that could likely have been triaged to the ICU upon initial presentation.

Methods

This study was a retrospective analysis of admissions to a mixed medical-surgical Intensive Care Unit (ICU) at a tertiary referral 325-bed VA hospital for the 64 months between January 1, 2008 and April 30, 2013. This period was chosen because the availability and fidelity of data for ICU admissions, delayed admission, mortality and sepsis for these five years. The VA Research Committee and the Stanford University Human Subjects panel approved the study.

Patient population:

All patients admitted from the ward to the ICU were analyzed. The patients were a mix of medical and surgical patients. Patients included both those directly admitted from the operating room as well as those escalated to the ICU after initial admission to the ward (indirect admission).

Data:

The Veterans Affairs VISTA system was queried to generate separate lists of all patients admitted to the ICU, patients that met criteria for severe sepsis at any time during their hospitalization, mortality, all hospital admissions to a non-ICU location, and a list of all patients who passed away in the study timeframe. Additional VA databases were cross-referenced to obtain birth date and gender information. Code and rapid response team activations were logged into a local database. Patients who had any of the following were classified as having sepsis during that admission: ICD-9 codes for severe sepsis (995.92), septic shock (785.52), or the presence of an infection-related ICD-9 code plus a code for an organ failure or hypotension.

Dates of events such as rapid response activations were compared with ICU admission data to establish relevance to that admission. Rapid responses activations within 2 days of ICU admission were considered relevant as a surrogate for detected earlier clinical deterioration. Code events defined as a cardiac or respiratory arrest within 24 hours of ICU admission or during the ICU stay were recorded. Severe sepsis was considered present if the ICD-9 codes mentioned above were generated for the overall hospital admission. Patients admitted to a non-ICU location and subsequently transferred to the ICU within 24 hours of their admission were coded as a "24-hr indirect admissions". Weekend admissions (admission on Saturday or Sunday) were identified for analysis given prior work demonstrating an increased mortality with this finding [11,12]. Night admissions were classified as those occurring between 10pm and 7am. Death rates were analyzed as occurring within 30 days, 90 days, or 1-year following ICU admission.

Cases of multiple admissions during the study timeframe were handled in the following manner: If an ICU admission occurred more than 365 days following a prior ICU discharge, the admissions were considered as distinct entities. This convention was followed so that patients surviving a year or more following ICU discharge were appropriately classified as such. When multiple ICU admissions occurred within a year of death or discharge date, only the most recent was considered in analysis of survival; these patients were classified as readmissions for purposes of analysis. Thus the practice of counting only the most recent admission within a given year may inadvertently result in dropping some "24-hr indirect admissions" from analysis if such an event did not occur in the most recent of the multiple admissions.

Analysis:

Continuous data was analyzed by Analysis Of Variance (ANOVA) or with non-parametric tests for non-normally distributed data. Categorical data was organized into contingency tables and analyzed by Fisher's exact test using Graph Pad Prism (v8.2) software.

Stepwise multiple logistic regression was carried out to assess the impact of potentially important clinical variables on 30, 90, and 365-day mortality. Variables that showed significant association with bivariate analysis at $p < 0.25$ were combined and eliminated in a stepwise manner according to significance level. A correlation matrix was prepared to assess co-linearity of variables; any with a correlation coefficient >0.8 would be eliminated and described. Some clinical variables deemed to have clinical relevance, even if non-significant, were included in the final analysis. For multivariable analysis, discrete intervals for age were created as follows: 18-40, 41-55, 56-75, 76-85, >85; intervals were based on progressive increases in crude 30-day and 1-year mortality for these groupings. Similarly ICU length of stay was divided into five intervals according as follows: 0-3.2, 3.3-7, 7-10.5, 10.5-14, and >14 days; the reference category was based on the upper confidence interval of the median LOS for all patients studied. Separate analyses were conducted for medical and surgical patients given the mixed medical-surgical nature of our ICU and the generally better survival of surgical ICU patients. Analyses were performed using STATA version14.0 (Stata Corp).

Results

Medical versus Surgical Patients

3,862 ICU patient encounters were analyzed of which 1,301 were medical and 2,561 were surgical admissions. Demographics and clinical characteristics are shown in **Table 1.** Overall, medical (vs. surgical) ICU patients had higher illness severity indicators at baseline with higher rates of 30-day mortality (25% vs. 3%), 90-day mortality (31% vs. 5.5%), and 1-year mortality (41% vs. 11%; p<0.001

for all). Medical patients also had a higher frequency of 24-hr indirect admissions (18% vs. 7.1%, OR 2.6, p<0.001), readmissions (23% vs. 16.%, OR 1.4, p<0.001), code blue events (4.2% vs. 0.4%, OR 10.5, p<0.001), rapid response calls (16.3% vs. 2.7%, OR, 6.0, p<0.001) and presence of severe sepsis (27% vs. 19%, OR 1.4, p<0.001). Given that surgical patients tend to have more planned ICU admissions during regular work hours, there was more variability in times of admission for medical patients. The differing rates in off-hour admissions were seen in both evening (25% vs 12%, p<0.001) and weekend admissions (17% vs 8.8%, p<0.0001).

The association between a number of clinical conditions and 30 and 90-day mortality are shown in **Table 2**. Except for septic shock, all variables were associated with increased mortality compared to patients without the condition. When medical and surgical patients are considered separately, only rapid response calls (46% vs. 38%, *p=0.021*) and code blue events (69% vs 38%, *p <0.0001*) were associated with a higher 30-day mortality in medical patients. In contrast, an increased 30-day mortality was associated with both medical and surgical patients with evening admissions (6.9% vs. 2.6%, p<0.01), and ICU readmissions (7.3% vs. 2.3%, p <0.01), as well as code blue events (55% vs. 3.2%, p<0.01) and rapid response calls (12% vs. 2.8%, p< 0.01; **Table 2A**). This general difference between medical and surgical patients was maintained in analysis of 90-day mortality (**Table 2B**) and in 1-year mortality (Supplementary data file) except for the emergence of an apparent decrease in mortality associated with 24h indirect admissions in medical patients for both of these time periods. For mortality at 90-days, medical patients with indirect ICU admissions had a 24% mortality vs. 33% in patients with regular admissions (OR 0.63, p = 0.003); 1-year mortality was 33% vs. 41%, OR 0.65; p = 0.003).

Indirect Admissions

A total of 420 patients, both medical (n=239) and surgical (181) patients, were admitted to the ICU from other hospital locations where they stayed for less than 24 hours, and are referred to here as 24-hr indirect or delayed admissions. 24-hr indirect admissions had a higher 30-day mortality of 15% compared to a 9.9% mortality in regular admissions (OR 1.39, p=0.03). The 90d mortality difference was similar (20% vs. 13%, OR 1.46; p= 0.005). **Table 3** looks at the presence of weekend and evening admissions, codes, sepsis and emergency team calls in patients with direct vs. indirect admissions, and shows that with the exception of sepsis, there is a concentration of these factors in delayed admissions. Rapid response were seven fold higher in surgical patients with delayed admissions (p=0.0001) and approximately 2.5-fold higher in medical patients p<0.0001; see **Table 3**). Otherwise, the higher concentration of weekend and evening admissions and codes, increases calls were only found in surgical patients **Table3.**

Of the 420 patients with delayed admissions, 181 (43%) were surgical and had a significantly higher 90-day and 1-year mortality than direct admits (11% vs. 5.1% at 90-days p=0.006, and 18% vs 11% at 1-year, p=0.003).

Multivariable analysis

Given the coincidence of factors influencing mortality stepwise regression analysis was carried out to analyze clinical variables influencing short and long term mortality in the study population. In addition to the variables considered in the data presented above, age and ICU length of stay (LOS) were entered in as additional variables to control for mortality. Age strata described had a stepwise increase in mortality as shown in the data supplement; LOS was also stratified as described above. Analysis of the whole population found LOS, age, medical admission, cardiac arrest, ICU readmission and RRT to be independent predictors of 30-day mortality (**Table 4A**). Delayed admissions did not predict mortality in the whole group analysis. This pattern remained largely unchanged when 90-day and 1-year mortality were examined (supplemental data file), however, the odds ratios associating the variables with mortality decreased. Also the significance of an RRT call as an independent predictor of mortality was lost at 1-year.

With medical admissions indicating one of the largest independent risks for mortality in the study (OR 8,4, P<0.0001; **Table 4A**), separate analyses were therefore conducted for medical and surgical subjects. Multivariable analysis of medical patients indicated that only code blue activation, age strata and ICU LOS predicted 30-day mortality (**Table 4B**). Analysis of surgical mortality was also predicted by age, arrest, and ICU LOS, but also ICU readmission, and evening admission (**Table 4C**). 24-hour delayed admission was not a significant predictor of 30-day mortality.

Analysis of 90-day and 1-year mortality in medical patients did not indicate any additional significant predictors of mortality (supplemental file, table 3c,d). In the analysis of surgical patients mortality at 90-days and 1-year, the most consistent predictors of mortality continued to be LOS, Age, code and ICU readmission (supplement 3 e,f); night time admission became an insignificant factor in the longer term mortality, but 24h-delaped admission gained significance in the analysis of 1-year mortality (OR1.6s, p=0.025).

Discussion

While previous studies have reported higher mortality with delayed ICU admission and indirect ICU admissions, [3,5,6,8] we conducted this study to evaluate potential differences of this effect between medical and surgical patients, and to evaluate the impact of delayed admission on both short and long-term mortality.

In a multivariate analysis, our study showed only a difference in 1-year mortality in surgical patients attributable to indirect 24-hr admissions to the ICU. Interestingly, this was not true of the medical patient population, probably related to their high overall 1-year mortality rate compared to surgical patients (41% vs. 11% ; Table 1). There are many possible reasons for this finding. First, given the higher mortality rate of medical patients in our study we could have been inadequately powered to see a difference. Second, we are assuming that critical care interventions are initiated solely in the ICU. While this is largely true for multiple vasopressors and invasive ventilation, it is likely that early appropriate interventions such as fluid administration, non-invasive ventilation and early titration of vasopressors did take place prior to the transfer of medical patients to the ICU, as a large number of indirect medical admissions originated from a step down unit where these capabilities exist and are commonly used. of Lastly there may be some inherent difference in patients triaged as stable enough to be admitted to the floor first as compared to patients who were deemed unstable upon arrival to the ED prompting a direct ICU admission.

A VA study has inherent issues with generalizability given the predominantly male population with similar co-morbidities. [13-15] However, we believe that this was a strength in our study as using a relatively homogenous population allowed us to evaluate system-based factors as well as differences between medical and surgical population with fewer confounding factors.

Admissions on weekends for medical and surgical patients trended toward but did not show a significant association with 1-year mortality in our study. A prior large meta-analysis looking at over 97 studies (over 51 million patients) found an association between being admitted on the weekend versus weekday and higher mortality. [12] This study concluded that weekend admissions were an independent predictor of higher mortality even when taking into account staffing levels and reduced frequency of procedures done on the weekend. Our study could have been inadequately powered to see this association.

We found that surgical patients had higher 1-year mortality for patients who had one of many characteristics including transfer of care to the ICU within 24 hours of admission, being admitted during the night, having a rapid response activation, or a cardiac arrest in comparison to medical patients who only had a higher 1-year mortality for code and rapid response. Overall the incidence of these characteristics was much higher for medical patients overall suggesting a population with a higher severity of illness. Surgical patients had much lower incidence of these characteristics but when present did lead to higher 1-year mortality. The differences noted again likely speak to differences between medical and surgical patients, wherein the latter are generally healthier and changes in condition may respond better to early aggressive interventions. This may account for why indirect and nighttime admissions had an impact on mortality. Despite best efforts, the disease at hand and the patient's physiologic reserve likely have the greatest impact on survival of medical patients.

A limitation of the present study is the small set of variables available for mortality adjustment. While several computational methods for risk adjustment of ICU patients such as APACHE, SOFA and a VA-developed tool exist, [16-19] we did not have access to these tools for this study. We do however, acknowledge that they may have helped immeasurably in accounting for co-morbidities and disease burden in our patients.

While our study is limited by confounders present in most retrospective studies, [9,10] this study does shed some valuable insights into future areas of investigation. First, it appears that ICU admission delays are a separate phenomenon than indirect ICU admissions within 24 hours of presentation. Second, direct admissions postoperatively to the ICU is a practice that varies from institution-to-institution and country of practice due to the limited ICU resources and no true standardization of which patients warrant direct ICU admission post-operatively. [20-22] Our study found that our surgical population, which included planned post-operative admissions, had higher 1-year mortality associated with 24-hour indirect admissions. This represents the subset of surgical patients who were initially deemed stable enough to be admitted to the floor postoperatively and then required a transfer to the ICU within the first 24 hours. Thus, one could hypothesize that having a deliberate system in place to determine which patients or procedures are high-risk enough requiring planned post-operative ICU admissions could improve outcomes. This observation has been made before in other countries [5] but to our knowledge our study is the first study looking specifically at mortality trends of patients transferred within the first 24 hours post-operatively, when a patient is likely most vulnerable. It is unclear what drives this increase, whether it is from a "failure to rescue" which has been previously studied in surgical patients [21-23] that would have been picked up earlier had they already been admitted to the ICU. Another possible explanation is that surgical patients that end up requiring transfer from the ward to the ICU suffer from devastating complications such as a massive pulmonary embolism, post-operative myocardial infarction, hemorrhagic shock, or other complication accounting for higher mortality. Future studies are needed to determine if there are identifiable risk factors (surgical, patient-specific co-morbidities, emergency nature of surgical intervention, etc.) that could help guide triage decisions regarding appropriateness of direct ICU admissions from the operating room.

Many societies such as the Society of Critical Care Medicine have created guidelines for admissions and a prioritization framework for who should be admitted to the ICU, however many of them were created with a limited amount of high-quality evidence and have not been validated. While a smaller proportion of ICU admissions have clear ICU indications, such as requiring life support from single or multiple organ failure, many ICU admissions fall into a grey zone. Results from our study can hopefully guide future areas of research with regards to ICU admission, triage, and long-term outcomes to help stratify these admissions to best optimize patient outcomes and critical care resource utilization.

Conclusion

In a large retrospective study of survival of ICU patients, factors such as age, ICU lengths of stay, and arrests had the greatest independent impacts on survival. Some situational variables such as nighttime admission and indirect admission and re-admission to the ICU impacted the survival of surgical patients. Surgical patients also had increased 1-year mortality if they required escalation to the ICU within 24 hours of hospital admission; this result was not replicated in medical patients, a finding possibly related to unmeasured factors including disease burden.

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Table 1. Demographics and study clinical variables of ICU patients reviewed in the study

Patient Characteristic	**All patients N=3862**	**Medical patients N=1301**	**Surgical patients N=2561**	***P*-value (Med vs. Surg.)**
Age (years ± SD)	66.6 (12.1)	67.2 (13.6)	66.3 11.2)	<0.005*
Gender (% male)	96.8	95.8	97.4	0.010§
ICU LOS (Median, CI)	3 (2.9-3.2)	3 (2.9-3.3)	2.7 (2.4-2.9)	<0.0001**
30d Mortality n (%)	403 (10)	324 (25)	79 (3.1)	<0.0001§
90d Mortality n (%)	542 (14)	401 (31)	141 (5.5)	<0.0001§
1-year mortality n (%)	809 (21)	527 (41)	282 (11)	<0.0001§
24-hr indirect admission	420 (11)	239 (18)	181 (7.1)	<0.0001§
Code blue events	65 (1.7)	54 (4.2)	11 (0.4)	<0.0001§
Rapid response call	280 (7.3)	212 (16)	68 (2.7)	<0.0001§
Weekend admissions	440 (11)	215 (17)	225 (8.8)	<0.0001§
Evening admissions	630 (17)	328 (25)	302 (12)	<0.0001§
Severe sepsis	831 (22)	349 (27)	482 (19)	<0.0001§
Readmission	703 (18)	293 (23)	411 (16)	<0.0001§

Table 2. Mortality among the medical and surgical ICU patient population by admission characteristics

A. 30-day mortality

Variable	All Patients n (%)	*P*§	Surgical Patients n (%)	*P*§	Medical Patients n (%)	*P*§
24-hr indirect admission	63/474 (13)	0.0366	9 (4.9) vs. 70 (2.9)	0.17	54 (24) vs. 270 (27)	0.41
Code blue event	41/65 (63)	<0.0001	6 (55) vs. 73 (3.2)	<0.01	35 (69) vs. 289 (23)	<0.01
Rapid response call	73/280 (26)	<0.0001	8 (12) vs. 71 (2.8)	<0.01	65 (38) vs. 259 (24)	0.04
Weekend admissions	64/440 (15)	0.0037	12 (5.3) vs. 67 (2.9)	0.13	52 (32) vs. 272 (25)	0.86
Evening admissions	103/630 (16)	<0.0001	21 (6.9) vs. 58 (2.6)	<0.01	82 (30) vs. 242 (25)	1.0
Severe sepsis/ shock	102/831 (12)	0.054	19 (3.9) vs. 60 (2.9)	0.24	83 (28) vs. 241 (25)	0.61
ICU Readmission	109/704 (15)	<0.0001	30 (7.3) vs. 49 (2.3)	<0.01	79 (32) vs. 245 (24)	0.36

B. 90-day mortality

Variable	All Patients n (%)	*P*§	Surgical Patients n (%)	*P*§	Medical Patients n (%)	*P*§
24-hr indirect admission	88/474 (19)	0.0037	19 (11) vs. 122 (5.1)	0.006	69 (24) vs. 232 (33)	0.003
Code blue event	43/65 (66)	<0.0001	6 (55) vs. 135 (5.3)	<0.0001	37 (69) vs. 364 (29)	<0.0001
Rapid response call	92/280 (33)	<0.0001	11 (16) vs. 130 (5.2)	0.001	81(38) vs. 320 (29)	0.012
Weekend admissions	84/440 (19)	0.0017	16 (7.1) vs. 125 (5.4)	0.282	68 (31) vs. 333 (31)	0.012
Evening admissions	125/630 (20)	<0.0001	25 (8.3) vs. 116 (5.1)	0.03	100(30) vs. 301 (31)	0.89
Severe sepsis/ shock	133/831 (16)	0.071	35 (7.3) vs. 106 (5.1)	0.075	98 (28) vs. 303 (32)	0.198
ICU Readmission	142/704 (20)	<0.0001	47 (11) vs. 94 (4.4)	<0.0001	95 (32) vs. 306 (30)	0.51

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Table 3. Prevalence of key study characteristics in patients with direct and 24-hr indirect ICU admissions

Admission Characteristic	Direct admissions N= 3,442	24-hr indirect admissions N = 420	*P*-value[§]
Severe sepsis n (%)	730 (21)	101 (24)	0.186
Medical	281 (26)	68 (28.	0.52
Surgical	449 (19)	33 (18)	0.92
Evening admissions	539 (16)	91 (22)	0.0026
Medical	271 (26)	58 (24)	0.74
Surgical	268 (11)	33 (18)	0.008
Weekend admissions	369 (11)	71 (17)	<0.001
Medical	179 (17)	36 (15)	0.56
Surgical	190 (8.0)	35 (19)	0.0001
Code blue	49 (1.4)	16 (3.8)	<0.001
Medical	41 (3.9)	13 (5.4)	0.28
Surgical	8 (0.3)	3 (1.7)	0.037
Rapid response call	183 (5.3)	97 (23)	<0.0001
Medical	139 (13)	73 (31)	<0.0001
Surgical	44 (1.8)	24 (13)	0.0001

Table 4. Multivariable analysis of 30-day mortality in ICU patients

A. All patients

Variable	OR	SE	95% Conf. Int.	*P* > [z]
LOS Strata	1.41	0.06	1.288 - 1.535	0.0000
Age Strata	1.87	0.13	1.622 - 2.146	0.0000
ICU Readmission	1.62	0.22	1.242 - 2.122	0.0000
Medical vs. Surgical	8.42	1.16	6.435 - 11.02	0.0000
RRT	1.42	0.24	1.018 - 1.991	0.0390
Code Blue	8.48	2.51	4.748 - 15.134	0.0000
24-hr Delay Admit	0.84	0.14	0.599 - 1.169	0.2960

B. Medical patients

Variable	OR	SE	95% Conf. Int.	*P* > [z]
LOS Strata	1.34	0.07	1.209 - 1.48	0.0000
Code Blue	6.09	1.85	3.349 - 11.055	0.0000
RRT	1.30	0.23	0.917 - 1.853	0.1390
24-hr Delay Admit	0.77	0.14	0.536 - 1.099	0.1480
Age Strata	1.68	0.13	1.438 - 1.958	0.0000

C. Surgical patients

Variable	OR	SE	95% Conf. Int.	*P* > [z]
LOS Strata	1.54	0.14	1.296 - 1.835	0.000
Age Strata	2.45	0.37	1.829 - 3.294	0.000
ICU Readmission	2.57	0.67	1.541 - 4.282	0.000
PM Admission	2.36	0.67	1.356 - 4.121	0.002
RRT	1.72	0.81	0.68 - 4.326	0.253
24-hr Delay Admit	0.97	0.41	0.426 - 2.225	0.950
Code Blue	30.33	20.33	8.154 - 112.838	0.000