Time of Admission to the PICU and Mortality*

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Objectives: To evaluate for any association between time of admission to the PICU and mortality.

Design: Retrospective cohort study of admissions to PICUs in the Virtual Pediatric Systems (VPS, LLC, Los Angeles, CA) database from 2009 to 2014.

Setting: One hundred and twenty-nine PICUs in the United States.

Patients: Patients less than 18 years old admitted to participating PICUs; excluding those post cardiac bypass.

Interventions: None.

Measurements and Main Results: A total of 391,779 admissions were included with an observed PICU mortality of 2.31%. Overall mortality was highest for patients admitted from 07:00 to 07:59 (3.32%) and lowest for patients admitted from 14:00 to 14:59 (1.99%). The highest mortality on weekdays occurred for admissions from 08:00 to 08:59 (3.30%) and on weekends for admissions from 09:00 to 09:59 (4.66%). In multivariable regression, admission during the morning 06:00–09:59 and midday 10:00–13:59 were independently associated with PICU death when compared with the afternoon time period 14:00–17:59 (morning odds ratio, 1.15; 95% CI, 1.04–1.26; $p = 0.006$ and midday odds ratio, 1.09; 95% CI; 1.01–1.18; $p = 0.03$). When separated into weekday versus weekend admissions, only morning admissions were associated with increased odds of death on weekdays (odds ratio, 1.13; 95% CI, 1.01–1.27; $p = 0.03$), whereas weekend admissions during the morning (odds ratio, 1.33; 95% CI, 1.14–1.55; $p = 0.004$), midday (odds ratio, 1.27; 95% CI, 1.11–1.45; $p = 0.0006$), and afternoon (odds ratio, 1.17; 95% CI, 1.03–1.32; $p = 0.01$) were associated with increased risk of death when compared with weekday afternoons.

Conclusions: Admission to the PICU during the morning period from 06:00 to 09:59 on weekdays and admission throughout the day on weekends (06:00–17:59) were independently associated with PICU death as compared to admission during weekday afternoons. Potential contributing factors deserving further study include handoffs of care, rounds, delays related to resource availability, or unrecognized patient deterioration prior to transfer. (*Pediatr Crit Care Med* 2017; 18:915–923)

Key Words: child; mortality; patient admission; pediatric intensive care; time factors

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Critically ill and unstable patients may be admitted to the ICU at any time. However, aspects of care provided in the ICU, as well as in other locations prior to ICU transfer, may differ by day of the week and time of day. Possible temporal differences in care in the ICU that could affect patient outcome include variable presence of an attending intensivist (1–3), accessibility of diagnostic services, availability of consultants and surgical staff, circadian rhythm disruption and fatigue (4–7), distraction due to morning rounds (8–10), and trainee experience level (11). Similar factors may affect patients prior to ICU arrival as well; diurnal variation in activation of medical emergency teams or rapid response systems (12, 13) and variations in transfer delays to the ICU from various locations by time of day (14) have been described.

Many previous studies have focused on outcomes of night and weekend admissions to the adult ICU and PICU with varying results. In adults, nighttime ICU admissions were found to have similar mortality compared with daytime in two large registry studies and a meta-analysis (14–16), whereas weekend admissions had higher mortality than weekdays in a meta-analysis (15) and one large registry study (16) but not in another registry study (14). For PICU admissions, one study showed increased risk-adjusted mortality for nighttime admissions (17), whereas several subsequent studies have shown no increased risk of death for night or weekend admissions (18–22).

Few studies have evaluated admission time periods outside of the night or weekend aggregated periods. In those studies reporting mortality by individual hour, peak mortality has been described to occur for admissions to the ICU in the morning in adults (05:00–08:00) (16, 23) and children (07:00) (18) rather than at night. In severity-adjusted analyses, admission during the morning time period was independently associated with increased ICU mortality in large studies in adults (odds ratio [OR], 1.19, 1.32) (8, 10) and children (OR, 1.27) (18); however, one smaller study in adults did not show similar findings (9).

The purpose of this study was to evaluate for any association between admission time and mortality in a large, recent sample of US PICUs. As many care processes may vary by time of day and day of the week, we sought to evaluate time periods throughout the day in the overall sample as well as separately for weekdays and weekends. Furthermore, we sought to identify any patient, disease process, or system factors which could affect any such association.

MATERIALS AND METHODS

Study Population

Deidentified admission data from January 1, 2009, to December 31, 2014, were obtained from the Virtual Pediatric Systems (VPS, LLC) database, a multicenter clinical database used primarily for benchmarking and quality assurance. This represented the most recent period for which complete data were available in the fields of interest at the time of data retrieval. The VPS database defines a PICU as a physical space dedicated exclusively to the care of critically ill children. VPS data were provided by VPS (LLC); no endorsement or editorial restriction of the interpretation of these data or the opinions of the authors has been implied or stated.

Data were collected for each patient admission less than 18 years old to a PICU in the United States participating in VPS during any part of the study period. Unit characteristics included bed size, academic center designation, and 24/7 in-house attending intensivist coverage (yes/no for each admission). Patient demographics, diagnosis, severity of illness by Pediatric Index of Mortality 2 (PIM2) (24) and Pediatric Risk of Mortality 3 (PRISM 3) (25), and outcome (ICU mortality) were collected for each admission. Dates and times of ICU admission and discharge with ICU length of service were also collected, as well as origin of admission (emergency department [ED], inpatient ward, etc) and diagnosis category (respiratory, cardiovascular, etc). For specific diagnoses, patients admitted following cardiac arrest were identified from the PIM2 high-risk diagnosis "cardiac arrest" field. Congenital heart disease patients were identified from the VPS diagnosis subcategory field. Patients with shock were identified from *International Classification of Diseases,* 9th Edition codes; please see **Supplemental Data File** (Supplemental Digital Content 1, http://links.lww.com/PCC/A489) for further details on data grouping.

Study Design

This was a retrospective cohort study designed to evaluate any association between time of admission to the PICU and mortality. The primary outcome was ICU mortality. The main exposure of interest was hour of admission, which had been collected in the VPS database in 1-hour increments. Each hour was evaluated individually for observed mortality, expected mortality (by PIM2), and standardized mortality ratio (SMR) (by PIM2). For the multivariable analysis, the morning time period 06:00–09:59 was used as it was of a priori interest due to previous data indicating increased risk-adjusted mortality during this time period (8, 10, 18) and was also found on initial data review to be the four highest hours for observed mortality and SMR. The remaining hours were also divided into 4-hour increments: midday (10:00–13:59), afternoon (14:00–17:59), evening (18:00–21:59), night (22:00–01:59), and early morning (02:00–05:59) for comparison. For the secondary analysis, weekdays were defined as admission day on Monday through Friday, whereas weekends were defined as admission day on a Saturday or Sunday. An additional a priori designated secondary analysis was performed using earlier (January 1, 2009 to September 30, 2012) and later (October 1, 2012 to December 31, 2014) epochs of data with similar numbers of admissions to evaluate for trends over time. These epochs also represented a division between data that were analyzed in part in a previous study on admission time (18) in this population, so they were compared with ensure that any association found in this study was not driven solely by the findings in the older data. A secondary analysis by quartiles of the year (quartile 1: January 1 to March 3; quartile 2: April to June 30; quartile 3: July 1 to September 30; and quartile 4: October 1 to December 31) was also performed to evaluate for trends related to seasonality or changes in trainee experience.

Analyses

Descriptive data including demographics, origin of admission, and diagnosis category were compared between different time periods of admission using Student *t* test or analysis of variance for means, Wilcoxon rank-sum test or Kruskal-Wallis test for medians, and Pearson's chi-square test for proportions. For the multivariable analysis, a mixed-effects logistic regression model was used with individual PICU as a random effect and all other independent variables as fixed effects. Independent variables selected a priori for inclusion included time period of admission, age category, risk of mortality by PIM2, gender, origin of admission (26), trauma status, academic center designation, and 24/7 in-house attending intensivist presence. The afternoon hours (14:00–17:59) were used as the reference for the multivariable model, as this is a time period when most resources (e.g., staff, diagnostic studies) are readily available; this period also had the lowest observed mortality and highest number of admissions on initial review of the data. For the secondary analysis separating weekend and weekday admissions, the weekday afternoon period (Monday to Friday 14:00–17:59) was used as the reference for all multivariable analyses to consistently compare with a time period that typically is associated with higher resource availability in clinical practice. PIM2 was used to adjust for severity of illness for the primary analysis as it is a required data field in VPS; PRISM 3 was used for a sensitivity analysis. PIM2 risk of mortality was multiplied by 100 prior to inclusion in the model for the purposes of scale. A p value of less than 0.05 was considered statistically significant.

Data were analyzed using SAS software version 9.4 (SAS Institute, Cary, NC). The Institutional Review Board of Wake Forest University Health Sciences approved this study.

RESULTS

A total of 391,779 admissions to 129 PICUs in the United States were included over the time period 2009–2014. PICUs ranged in size from less than 10 to greater than or equal to 35 beds, with a median category of 20–24 beds; 83 (64%) were designated as academic centers, and 72 (56%) had 24/7 intensivist coverage for at least part of the study period (43% for the entire study period). The overall sample was 44% female with a median age of 4.8 years. Characteristics of patients admitted during each prespecified time period of admission shown in **Table 1**. The morning time period 06:00–09:59 had the lowest number of admissions and the highest expected (2.61%) and observed mortality (3.13%), whereas the afternoon time period 14:00–17:59 had the highest number of admissions and the lowest expected (2.02%) and observed mortality (2.07%). Scheduled admissions were more common during the midday and afternoon time periods, while trauma admissions were more common during the evening, night, and early morning periods.

Overall observed PICU mortality was 2.31% with a SMR by PIM2 of 1.03. Observed and expected (by PIM2) mortality for each hour of admission is shown in **Figure 1**. Observed mortality was highest for admissions from 07:00 to 07:59 (3.32%) and lowest for admissions from 14:00 to 14:59 (1.90%). Admissions during each hour of the morning period 06:00–09:59 had a higher observed mortality (≥ 2.7%) than any other hour outside of the morning period (all ≤ 2.5%), and these hours also had the four highest SMRs (1.18–1.23). Observed mortality on weekdays (n = 306,674 admissions) was 2.13% with SMR equal to 1.02 and on weekends (n = 85,105) was 2.99% with SMR equal to 1.07. Peak observed mortality occurred for admissions from 07:00 to 07:59 on weekdays (3.32%) and 09:00–09:59 on weekends (4.66%, the highest observed mortality for any hour-long period). Admissions during the 14:00–14:59 hour on weekdays had the lowest mortality for any hour-long period (1.58%).

The results of mixed-effects multivariable logistic regression evaluating for association of each independent variable at the time of admission with PICU mortality is displayed in **Table 2**. In the overall sample, morning admission 06:00–09:59 (OR, 1.15 [95% CI, 1.04–1.26]; p = 0.006) and midday admission 10:00–13:59 (OR, 1.09 [1.01–1.18]; p = 0.03) were associated with increased mortality as compared to admissions during the afternoon period from 14:00 to 17:59. Other factors associated with increased mortality included being a newborn, a trauma admission, or an admission from the inpatient ward, another hospital's ED, or another ICU. When weekdays and weekends were evaluated separately (**Table 3**), weekday mornings remained similarly associated with mortality (OR, 1.13 [1.01–1.27]; p = 0.03), whereas weekend mornings had the highest association with mortality (OR, 1.33 [1.14–1.55]; p = 0.004). Weekend midday (OR, 1.27 [1.11–1.45]; p = 0.0006) and afternoon (OR, 1.17 [1.03–1.32]; p = 0.014) admissions were also associated with increased mortality compared with weekday afternoons. Each time period associated with increased mortality had a higher proportion of admissions from an inpatient location (17.8–26.4%) than all other time periods (10.7–15.2% inpatient origin). Outside ICU admissions were more common during the weekend midday and afternoon time periods versus other times (3.5% vs 1.5–3%) (**Supplemental Tables 1** and **2**, Supplemental Digital Content 1, http://links.lww.com/PCC/A489).

A sensitivity analysis using PRISM 3 instead of PIM2 (n = 391,776) resulted in the morning and midday time periods no longer being statistically significantly associated with mortality for the overall sample (morning OR, 1.06 [0.96–1.08]; midday OR, 1.06 [0.98–1.15]) or the weekday sample (morning OR, 1.05 [0.93–1.19]; midday OR, 1.06 [0.97–1.07]). However, for the weekend sample, the morning (OR, 1.22 [1.03–1.44]; p = 0.02), midday (OR, 1.23 [1.07–1.42]; p = 0.005), and afternoon (OR, 1.17 [1.03–1.34]; p = 0.02) time periods remained significantly associated with mortality.

A plot showing the OR for admission during the time periods associated with increased mortality (morning 06:00–09:59 and midday 10:00–13:59) compared with afternoon admission by admission subcategory is depicted in **Figure 2**. The groups with significantly increased odds of death for morning admission were admissions from the inpatient floor (OR, 1.21 [1.03–1.42]; p = 0.02) or another ICU (OR, 1.41 [1.03–1.93]; p = 0.03), admissions with an "other" diagnosis category (OR, 1.15 [1.04–1.26]; p = 0.006), and admissions in the third quartile of the calendar year (July to September; OR, 1.24 [1.03–1.48]; p = 0.02). The groups with significantly increased odds of death for midday admissions were admissions from the ED (OR, 1.19 [1.01–1.41]; p = 0.04) or an outside ED (OR, 1.28 [1.06–1.55]; p = 0.01), admissions with a "respiratory" (OR, 1.29 [1.09–1.51]; p = 0.003) or "other" diagnosis category (OR, 1.09 [1.01–1.18]; p = 0.03), and admissions in the fourth quartile of the calendar year (October to December; OR, 1.19 [1.02–1.39]; p = 0.03). Admission during the morning or midday hours did not significantly increase odds of death for the high-risk subgroups of trauma (morning OR, 1.22 [0.85–1.75]; midday OR, 1.10 [0.81–1.49]), postcardiac arrest (morning OR, 1.23 [0.96–1.57]; midday OR, 1.07 [0.89–1.30]), congenital heart disease (morning OR, 1.05 [0.62–1.79]; midday OR, 0.85 [0.50–1.11]), or shock (morning OR, 1.27 [0.90–1.81]; midday OR, 1.26 [0.91–1.73]).

TABLE 1. Patient Characteristics by Time Period of Admission

Patient Characteristics	Morning (06:00–09:59), n = 30,752	Midday (10:00–13:59), n = 68,944	Afternoon (14:00–17:59), n = 100,729	Evening (18:00–21:59), n = 85,943	Night (22:00–01:59), n = 64,913	Early Morning (02:00–05:59), n = 40,948
Age (yr), median (IQR)	4.1 (1.0–11.2)	3.9 (0.9–11.1)	5.1 (1.2–12.4)	5.2 (1.3–12.4)	5.2 (1.3–12.5)	5.1 (1.2–12.6)
Age categories, %						
< 1 mo	3.9	3.1	3.2	3.6	3.6	3.9
1–23 mo	33.2	34.2	29.9	28.9	28.3	28.8
2–5 yr	21.6	22.1	20.6	21.1	21.4	21.1
6–12 yr	22.0	21.5	24.0	24.3	23.6	22.5
13 to < 18 yr	19.5	19.1	22.5	22.5	23.1	23.7
Female, %	43.7	44.6	45.2	44.3	43.6	44.2
Pediatric Index of Mortality 2 risk of mortality, mean % (SD)	2.61 (0.10)	2.10 (0.08)	2.02 (0.08)	2.32 (0.09)	2.38 (0.09)	2.31 (0.08)
Scheduled (≥ 12 hr in advance), %	11.0	36.3	35.2	18.4	4.2	1.6
Postoperative, %	14.0	39.9	41.7	27.4	13.1	9.4
Mechanical ventilation at admission[a] %	26.4	24.4	24.5	26.4	25.7	24.9
Cardiac arrest prior to admission, %[a]	2.1	1.9	1.7	2.1	2.0	1.7
Trauma, %	5.8	3.9	5.6	10.4	14.2	11.6
Origin of admission, %						
ER same hospital	35.2	21.0	25.5	36.9	48.2	47.8
ER outside hospital	20.3	12.6	13.5	19.3	25.9	26.9
Inpatient	26.0	16.9	11.9	12.8	12.5	16.2
Operating room	7.4	21.7	19.8	11.3	4.8	3.1
Postanesthesia care unit	2.4	14.5	18.0	11.6	3.5	1.5
Other origin[b]	6.7	10.3	8.4	5.4	3.2	2.8
Other ICU	1.9	3.1	2.9	2.7	1.9	1.6
Diagnosis category, %						
Respiratory	41.2	31.9	27.5	26.9	28.9	35.1
Neurologic	12.9	17.5	16.0	15.9	15.7	14.0
Injury/poisoning/adverse effects	9.8	6.8	8.6	15.0	20.8	17.9
Cardiovascular	5.2	7.7	6.7	5.7	4.7	4.4
Hematology/oncology	3.4	5.5	6.9	6.9	4.3	3.1
Infectious	6.7	4.4	4.0	5.0	5.6	6.3
Other[b]	20.7	26.2	29.7	22.0	13.4	8.2
Academic center, %	74.2	71.9	73.7	73.9	74.4	75.0
24/7 intensivist, %	59.4	59.3	59.7	59.9	59.8	60.0
Observed mortality, %	3.13	2.35	2.07	2.31	2.26	2.35

ER = emergency department, IQR = interquartile range.

[a]From components of Pediatric Index of Mortality 2; mechanical ventilation includes invasive and/or noninvasive mechanical ventilation within 1 hr of admission.

[b]Please see supplemental data file for further details.

$p < 0.0001$ for all comparisons across categories except 24/7 intensivist, for which $p = 0.09$.

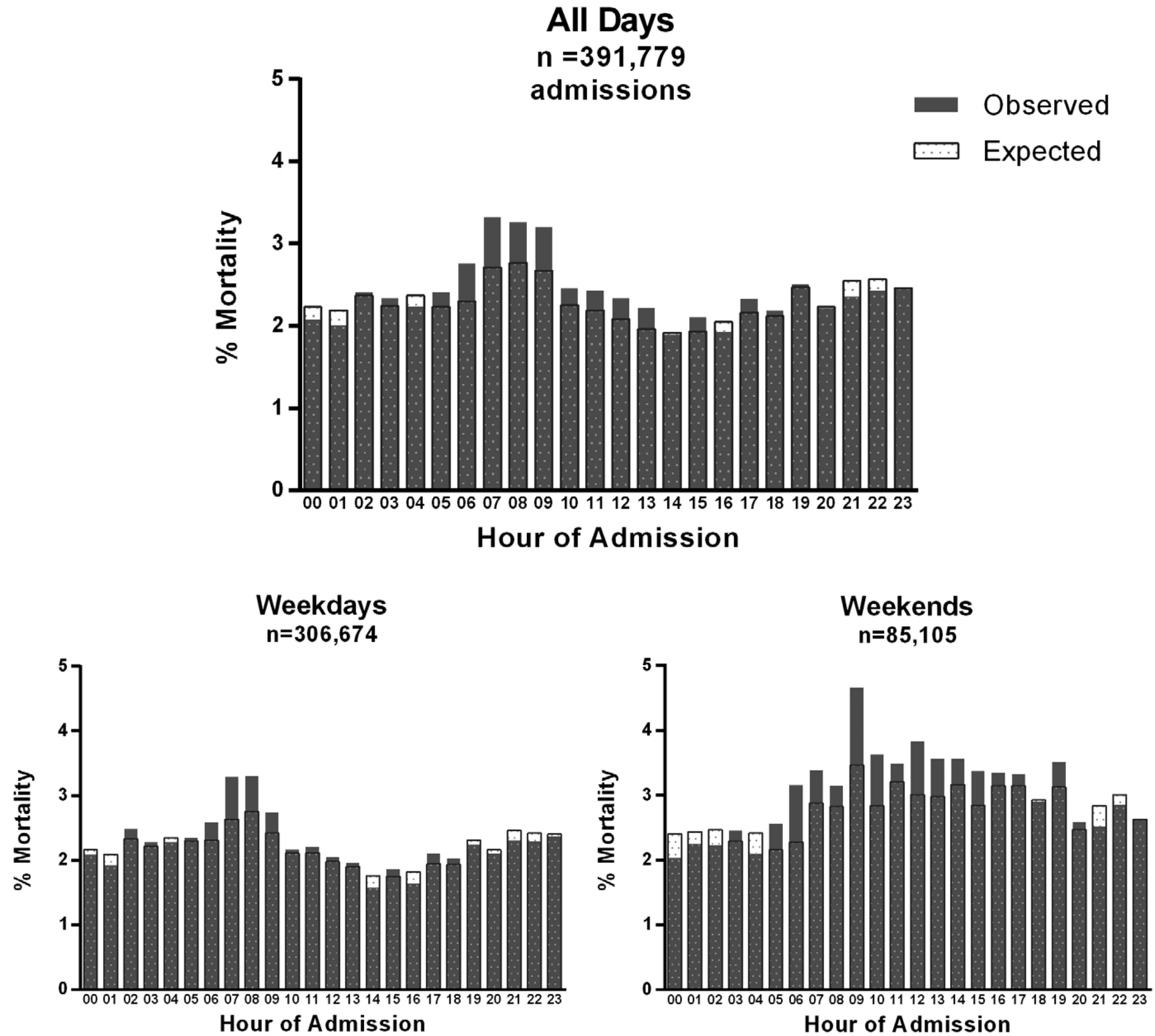

Figure 1. PICU mortality by hour of admission. Observed mortality is compared with predicted mortality (by Pediatric Index of Mortality 2) for admissions during each hour of the day.

Median time from admission until death for patients who died after being admitted during the different time periods of admission was as follows: median days until death (inter-quartile range): morning (3.6 [1.4–11.3]), midday (4.2 [1.5–12.3]), afternoon (4.0 [1.5–11.0]), night (3.1 [1.3–7.7]), and early morning (3.2 [1.2–8.1]; $p < 0.0001$). A post hoc analy-sis revealed that approximately one third of deaths occurred in each of the time periods of less than 48 hours (33.0%), 48 hours to less than 7 days (35.0%), and greater than or equal to 7 days (33.0%) after admission. Using each tertile separately as the outcome variable in the multivariable analysis, morn-ing admission was only significantly associated with death occurring in less than 48 hours (death < 48 hr from admis-sion: morning OR, 1.20 [1.02–1.41], $p = 0.03$, midday OR, 1.03 [0.89–1.19]; death 48 hr to < 7 d: morning OR, 1.10, [0.95–1.27], midday OR 1.12 [0.99–1.26]; death ≥ 7 d: morning OR, 1.04 [0.91–1.19], midday OR, 1.05 [0.94–1.17]).

A secondary analysis was also done evaluating admissions earlier in the time period sampled (epoch 1: January 1, 2009 to September 1, 2009; $n = 199{,}438$) versus later (epoch 2: October 1, 2012 to December 31, 2014; $n = 192{,}341$) to evaluate for any change in characteristics of the association between admission time and mortality over time. Around-the-clock (24/7) intensivist coverage was present for a higher percentage of admissions in the later time period (epoch 1: 55%; epoch 2: 64%). Overall mortality was lower in the later time period (epoch 1: 2.44% mortality; epoch 2: 2.18% mortality), with peak mortality occurring for admissions from 07:00 to 07:59 in epoch 1 (observed mortality 3.8%) and for admissions from 08:00 to 08:59 in epoch 2 (3.1%) (**Fig. 3**). For the overall samples,

TABLE 2. Association With PICU Mortality by Multivariable Analysis

Independent Variables	OR (95% CI)	p
Admission time		
Morning (06:00–09:59)	1.15 (1.04–1.26)	0.006
Midday (10:00–13:59)	1.09 (1.01–1.18)	0.03
Afternoon (14:00–17:59)	Reference	
Evening (18:00–19:59)	0.95 (0.88–1.03)	0.18
Night (20:00–01:59)	0.87 (0.80–0.95)	0.002
Early morning (02:00–05:59)	0.91 (0.83–1.00)	0.05
Age categories		
< 1 mo	1.16 (1.03–1.31)	0.02
1–23 mo	1.02 (0.95–1.09)	0.64
2–5 yr	0.87 (0.80–0.94)	0.0009
6–12 yr	0.95 (0.87–1.02)	0.17
13 to < 18 yr	Reference	
Female	1.03 (0.98–1.09)	0.22
Pediatric Index of Mortality 2 risk of mortality	1.09 (1.09–1.09)	< 0.0001
Trauma = yes	1.68 (1.55–1.83)	< 0.0001
Origin of admission		
Inpatient	2.77 (2.58–2.98)	< 0.0001
Outside hospital ER	1.40 (1.30–1.51)	< 0.0001
Operating room	0.53 (0.47–0.60)	< 0.0001
Postanesthesia care unit	0.18 (0.14–0.22)	< 0.0001
Other ICU	3.45 (3.10–3.85)	< 0.0001
Other origin[a]	1.07 (0.94–1.21)	0.29
ER same hospital	Reference	
Academic center	1.04 (0.88–1.22)	0.66
24/7 intensivist	1.07 (0.95–1.19)	0.27

ER = emergency department, OR = odds ratio.

[a]Please see supplemental data file for further details.

TABLE 3. Association of Admission Time Period With PICU Mortality by Multivariable Analysis: Weekdays Versus Weekends

	Weekdays (n = 306,674 Admissions)		Weekends (n = 85,105 Admissions)	
Admission Time Periods	OR (95% CI)	p	OR (95% CI)	p
Morning (06:00–09:59)	1.13 (1.01–1.27)	0.03	1.33 (1.14–1.55)	0.004
Midday (10:00–13:59)	1.09 (1.00–1.20)	0.06	1.27 (1.11–1.45)	0.0006
Afternoon (14:00–17:59)	Reference		1.17 (1.03–1.32)	0.014
Evening (18:00–21:59)	0.97 (0.89–1.06)	0.51	1.02 (0.89–1.16)	0.80
Night (22:00–01:59)	0.90 (0.81–0.99)	0.03	0.91 (0.79–1.04)	0.18
Early morning (02:00–05:59)	0.94 (0.84–1.05)	0.25	0.95 (0.81–1.11)	0.50

OR = odds ratio.

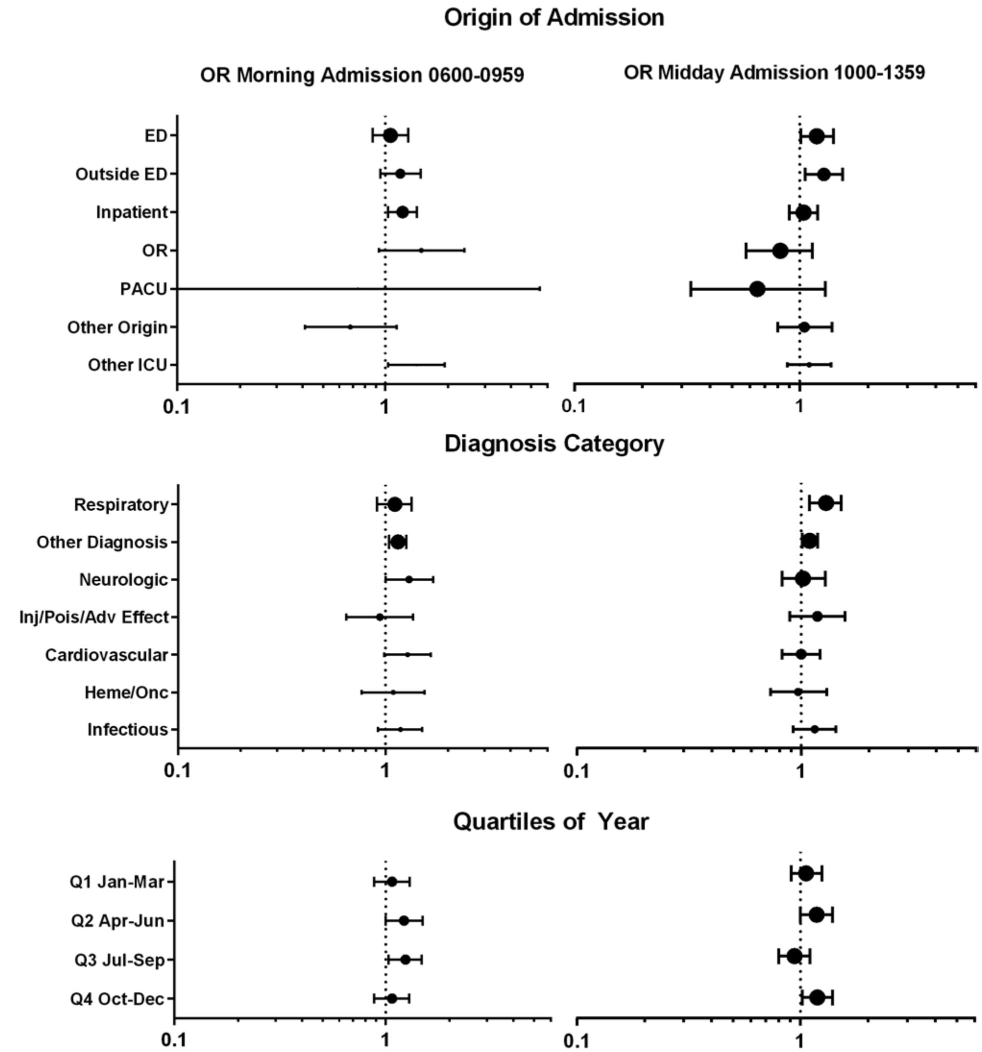

Figure 2. Odds ratio (OR) plots by subcategory. OR for mortality of morning and midday admission by admission subcategory. ED = emergency department, Inj/Pois/Adv = injury/poisoning/adverse, PACU = postanesthesia care unit.

morning and midday admissions were associated with mortality for the earlier period (epoch 1: morning OR, 1.23 [1.08–1.39], $p = 0.002$; midday OR, 1.15 [1.03–1.29], $p = 0.01$) but not for the later period (epoch 2: morning OR, 1.03 [0.90–1.19]; midday OR, 1.00 [0.89–1.13]) in the multivariable analysis. However, weekend admissions in epoch 2 during the morning (OR, 1.43 [1.14–1.80]; $p = 0.002$) and midday (1.43 [1.18–1.74]; $p = 0.0003$) were associated with increased mortality.

DISCUSSION

In this large cohort of US PICUs, we have found that peak mortality occurred for admissions from 07:00 to 07:59, and admission during the morning time period from 06:00 to 09:59 was independently associated with mortality on both weekdays and weekends after adjustment for severity of illness, origin of admission, 24/7 intensivist presence, and other factors. On weekends, admission during the midday (10:00–13:59) and afternoon (14:00–17:59) time periods were also independently associated with increased mortality as compared to weekday afternoons.

Our findings are consistent with some previous published findings showing peak mortality for morning admissions to the ICU in adults (8, 10, 16, 23) and children (18). One smaller study in adults showed increased severity of illness but no significantly increased mortality for morning admissions (9). Although nighttime PICU admission was associated with death in one previous pediatric cohort (17), our study showed a decreased risk of death (OR, 0.87) for nighttime admissions from 22:00 to 01:59 and equivalent risk for evening (18:00–21:59) and early morning (02:00–05:59) admission compared with weekday afternoons. Our finding of increased risk of death for admissions throughout the weekend daytime periods (06:00–17:59) is similar to findings in adult studies showing increased risk of death for weekend admissions (15, 16); however, previous pediatric studies have not shown increased risk for admission during the aggregate weekend periods (17, 18).

Causes of the associations between time of admission and mortality can only be hypothesized given the limitations of the data available in a large, retrospective dataset. Differences in care in the ICU after patient arrival have been hypothesized to contribute to differences in outcomes for patients admitted during the morning and other time periods (8-10). Provider distraction may occur in the morning in the ICU due to handoffs, morning rounds, or other factors. On weekends, resources may not be as readily available such as ICU staff, consultants, and/or diagnostic and procedural services. Such distractions or limitations could lead to delays in management of unstable patients during a critical initial phase or "golden hour" of resuscitation (27). Differences in care at the time of admission could be hypothesized to lead to death relatively soon after admission, and morning admission was associated with death in less than 48 hours in our cohort. However, it is unclear why admission late at night would be associated with equivalent or lower mortality when resources would also likely be less available than on

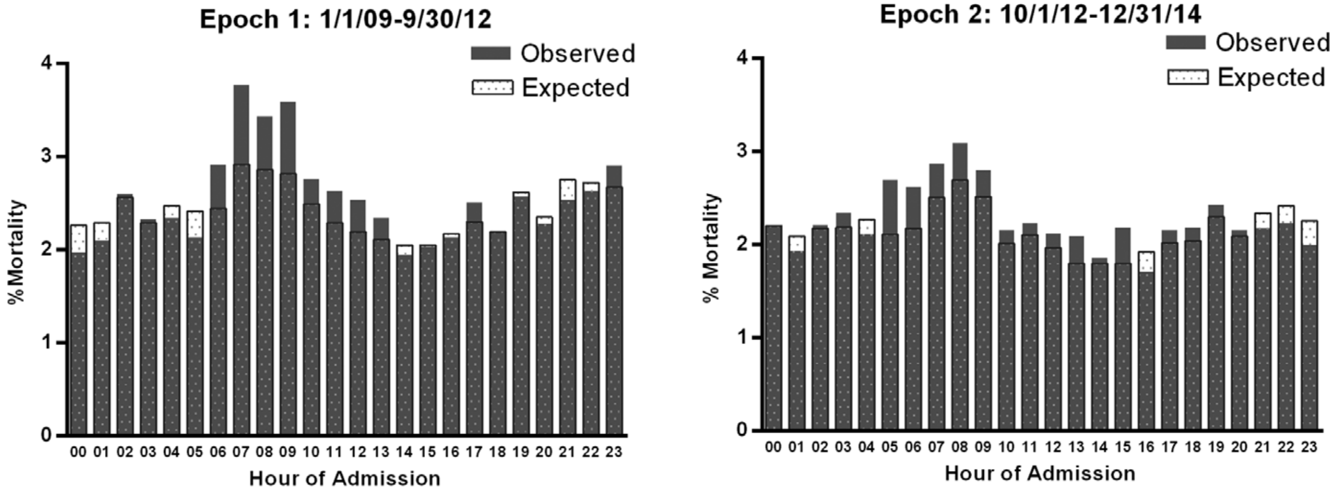

Figure 3. PICU mortality by hour of admission. Observed mortality is compared with predicted mortality (by Pediatric Index of Mortality 2) for admissions during each hour of the day separately for epoch 1 (January 1, 2009 to September 30, 2012; *n* = 199,438) and epoch 2 (October 1, 2012 to December 12, 2014; *n* = 192,341).

weekday afternoons. Furthermore, this effect might be expected to be most prominent for high-risk and time-sensitive admission diagnoses such as shock, postcardiac arrest, trauma, or congenital heart disease. The morning and midday time periods were not significantly associated with mortality for these subgroups in our study; however, admission numbers were relatively small and each point estimate for odds of mortality was greater than one.

Another possible mechanism for our findings could be characteristics of patients and their care prior to ICU admission that are systematically different at different times. All time periods significantly associated with mortality had a higher proportion of patients admitted from an inpatient origin, and outside ICU admissions were more common during weekend midday and afternoon time periods. On multivariable analysis, morning admissions (the time period most consistently and highly associated with mortality) were significantly associated with mortality only for admissions from the inpatient floor and outside ICU but not other locations. These inpatient ward or ICU patients may be more likely to be refractory to treatment and have had longer progression of their disease process without significant improvement, making them very different from a patient who has received initial care in the ED and then is sent to the ICU. Previous reports in adults and children have shown that transfers from the inpatient ward had higher odds of mortality (26, 28–30), and interhospital transfer admissions from non-ICU and ICU origins had longer lengths of stay (26, 31), even after adjustment for severity of illness. Furthermore, the length of time a patient spends in the hospital prior to ICU admission (32) has been associated with mortality.

The severity of illness scoring systems used for our study, PIM2 (24) and PRISM 3 (25), may not fully capture differences related to care prior to transfer. Although both incorporate vital sign and laboratory variables as well as certain high- and low-risk diagnoses, only PRISM 3 includes a field for admission from the inpatient floor and neither specifies duration/types of therapy administered prior to admission. When PRISM 3 was substituted for PIM2 in the multivariable analysis, only weekend day time periods and not weekday mornings remained significantly associated with increased mortality, perhaps reflecting better adjustment for some of the effects of transfer from an inpatient location.

The time periods of mornings and weekend daytime could also be hypothesized to be associated with delays in recognition of deterioration or transfer of these patients from inpatient or outside ICU locations. Transfer delays to the ICU have been associated with mortality in adults (33, 34). Delays in care or transfer overnight from the sending location could be related to decreased overnight staffing on the wards (8, 12, 13), fatigue/circadian rhythm disruption of night shift workers (4, 5, 7), or other factors. A study in pediatric inpatients showed increased overnight triggers of the rapid response system when a standardized early warning score was used instead of only provider or caregiver activation, supporting the hypothesis that some patients may be experiencing unrecognized deterioration overnight (12). Calls to medical emergency teams for inpatient ward patients have been shown to be increased in the morning and evening after nurse handoff (6, 13), suggesting that evaluation by a new provider reveals deterioration of a patient's condition that may have been ongoing and unrecognized. In one report, medical emergency team activations during the 07:00 hour had the highest rates of cardiac arrest and death at the time of medical emergency team activation (with another peak at 05:00), with overall in-hospital mortality being highest for activations during the 08:00 hour (13). Our finding of admissions in July to September having an amplified association between morning admission and mortality (OR, 1.24) could reflect trainee inexperience contributing to either gaps in care in the PICU or delays to intervention and ICU transfer on the inpatient wards overnight (11), with perhaps a more senior clinician evaluating and transferring the patient in the early morning.

Our study has several strengths including a relatively large number of patients (> 390,000) and PICUs (129) in a recent cohort, which allow study of the rare primary outcome of mortality and suggest generalizable results. The weaknesses of our study, however, make it difficult to establish a cause for the observed association between admission time period and mortality beyond generating further hypotheses. We have no information regarding therapies provided prior to ICU admission at other locations or any delays in these therapies or patient transfer which could be influenced by time of day. We also have no information regarding handoff practices, rounding times, or staffing patterns in the PICUs, all of which could influence initial care of patients. Finally, we have no information about mortality after PICU discharge.

CONCLUSIONS

In conclusion, admission to the PICU during the morning time period 06:00–09:59 was most strongly associated with mortality in this large retrospective cohort, with peak mortality occurring for admissions from 08:00 to 08:59 on weekdays and 09:00 to 09:59 on weekends. Weekend midday (10:00–13:59) and afternoon (14:00–17:59) admissions were also associated with mortality as compared to weekday afternoons. Patient factors not captured by severity of illness, delays in care or transfer prior to ICU arrival, or gaps in care in the ICU may contribute to this association. Regardless of the cause, providers in the ICU should be sensitive to the increased risk of mortality of this vulnerable group of patients and make efforts to ensure that admissions during this period receive careful attention. Studies of time of ICU admission should include consideration of morning and weekend day admissions rather than only evaluating the traditional "off-hour" time periods of nights and aggregate weekends. Future studies may also characterize ways to minimize delays in identifying and transferring deteriorating inpatients overnight (such as early warning scores or vital sign–based algorithms triggering rapid response teams), as well as strategies to ensure optimal care for admissions that occur during times of handoff or rounding in the ICU.

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