Saving Patients' Lives Through Activating a Rapid Response System: Willing Is Not Enough, We Must Do*

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Rapid response systems (RRSs), as the first of the six patient safety improvement strategies advocated by the Institute of Healthcare Improvement's 100,000 lives campaign (1), have been widely adopted across the world. In the United States, since the recommendation by the Joint Commission, it has gained wide acceptance and has been implemented across many hospitals. However, despite the clear clinical intuition underlying the RRS concept and its popularity, several studies have failed to show a significant improvement in patient outcomes, in particular, in reduced patient mortality (2). Such results have led to controversy regarding its effectiveness. The RRS concept is a hospital-wide intervention with the intention and promise to save patient lives. However, among the 10 patient safety strategy systematic reviews commissioned by the Agency for Healthcare Research and Quality (3), the RRS, as a patient safety strategy, was not recommended or included in the list of "Strongly encouraged" strategies but only included in the list of "Encouraged" (4). This is despite strong evidence supporting its possible dose-response effect (more rapid response team [RRT] calls and lower hospital mortality) in the largest study ever conducted in this field (5) (i.e., a 23-hospital cluster randomized controlled trial) as well as the long raised issue of how the evidence related to complex system intervention in patient safety should be assessed and policy recommendations made (6).

In this light, in a recent issue of *Critical Care Medicine*, the study by Barwise et al (7), which found a significant relationship between delayed RRT activation and increased hospital mortality and morbidity as well as increased length of stay in a tertiary care hospital, is important in helping our understanding of the effectiveness and implementation of a RRS: 1) these findings are consistent with other similar studies (8–12) that all showed a significant relationship between delayed calls and increased hospital mortality (it was estimated that every 100 delayed calls were associated with an extra 13 deaths by a multicenter study) (12); 2) the consistency and robustness of such findings across different studies conducted at different settings provided pivotal evidence that nondelayed RRT activation could save more patient lives and support the notion that a RRS actually can save patient lives; 3) the rate of delayed calls in the current study is high (57%, in comparison with 29% reported in a large multicenter study which was based on a more relaxed delay call definition [> 15 min given the exist calling criteria (12) compared with the current study of using > 1 hr as the cutoff]); 4) the substantial proportion of delayed calls highlighted that despite the promises, much more could be done to improve the compliance of RRTs and RRSs to save patient lives; 5) the study included a large number of RRT calls (1,227) in 2012 in an institution with an RRS since 2007. It is especially important to recognize that delayed calls to a RRT not only occurred in a hospital with a newly implemented RRS. Even for a mature RRS hospital, such a problem can be substantial and can persist; 6) the results reinforce the concept that not only failing to call (5) but also failing to call early can be fatal and defeats the purpose of a RRS.

The authors should be commended for their efforts in providing more detailed data on the relationship between delayed calls and associated morbidity as well length of stay in ICU in hospital. The study also provided more detailed data on patients who had a RRT call and were transferred to the ICU. The results showed that those patients with a delayed call and transferred to the ICU were generally sicker, had more intensive treatment, had higher ICU mortality, and stayed longer both in ICU and hospital. One implication from these results is that a timely RRT call could also save more hospital resources. However, as a single-center observation study, no causality among the association could be assured and the results also need confirmation in a similar setting.

The study, like many similar studies, did not provide data on reasons behind the delayed calls. Further research should shed more light on the underlying causes of delayed calls. Was it due to a lack of timely documentation of the calling criteria? Was it due to poor staffing or heavy workload? Was it due to lack of communication among staff and during handover? Or, was it simply due to a fear of making a wrong call and lack of self-efficacy? The consistent finding in this study, and other similar studies, is that delayed calls occur more likely during the night shift which showed that some of the risk factors were possibly to be system related and its remedy may also be system orientated. Another area of investigation is risk factors at the patient level. What types of patients were more likely to

*See also p. 54.

Key Words: delayed calls; hospital mortality; medical emergency team; patient safety; rapid response system

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have a delayed call? What particular patient and disease factors may contribute to the increased likelihood of being called late? For example, would those patients who have a terminal illness and have a perceived poor prognosis be more likely to have a delayed activation of a RRT? To understand the reasons behind delayed calls, an audit of those calls and root-cause analyses of the reasons behind them are a good start. Such studies will enable further intervention to improve compliance. Repeated education on the importance of, and logistics of, a RRS which targets both nurse and medical staff may also need to be considered. The message is this: timely activation of a RRS does save patients' lives and willing is not enough, we must do.

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Fentanyl Pharmacokinetics in Critically Ill Patients: A Demonstration of Mixed Effects*

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The premise that dose-dependent drug concentrations in physiologic fluid or tissue (i.e., pharmacokinetics) are related to therapeutic or adverse drug effects (i.e., pharmacodynamics) is a cornerstone of pharmacology, drug development, and therapeutic drug monitoring. The conventional approach to human drug development involves determining the pharmacokinetic behavior of a drug (usually in healthy or stable volunteers) to guide subsequent dose-finding and formal comparative efficacy and safety studies aligning the proposed drug mechanism of action with physiologic response and patient outcomes in those with disease or illness. Unfortunately, this systematic progression is often forgone in critically ill patients leading to off-label drug use (1, 2) and use indicated for a particular derangement, illness, or disease (e.g., pneumonia, pain, arrhythmia, and hypertension), but without population-specific pharmacokinetic-pharmacodynamic data or commercially available drug assays to guide optimal dosing. Therefore, it is common when attempting to individualize dosing regimens in critically ill patients to work backward or borrow pharmacokinetic data from non–critically ill populations. However, extrapolating this information may under-represent complex physiologic changes and concomitant therapeutic interventions likely to affect drug pharmacokinetic-pharmacodynamic behavior.

With few exceptions, there is little evidence that empiric pharmacokinetic-pharmacodynamic qualities of a drug (e.g., where a drug goes; which receptors affected) should differ in critically ill populations. It is apparent, however, that physiologic changes related to critical illness are associated with quantitative differences in the pharmacokinetic behavior of many drugs (3, 4) that may affect precision of dose individualization. For example, changes in total body water and presence of systemic inflammation may increase the volume of distribution (Vd) of hydrophilic drugs, thus decrease plasma drug concentrations; hypothermia may decrease hepatic enzyme

***See also p. 64.**

Key Words: critical illness; drug dosing; pharmacodynamics; pharmacology; pharmacokinetics

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Delayed Rapid Response Team Activation Is Associated With Increased Hospital Mortality, Morbidity, and Length of Stay in a Tertiary Care Institution*

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Objective: To identify whether delays in rapid response team activation contributed to worse patient outcomes (mortality and morbidity).
Design: Retrospective observational cohort study including all rapid response team activations in 2012.
Setting: Tertiary academic medical center.
Patients: All those 18 years old or older who had a rapid response team call activated. Vital sign data were abstracted from individual patient electronic medical records for the 24 hours before the rapid response team activation took place. Patients were considered to have a delayed rapid response team activation if more than 1 hour passed between the first appearance in the record of an abnormal vital sign meeting rapid response team criteria and the activation of an rapid response team.
Interventions: None.
Measurements and Main Results: A total of 1,725 patients were included in the analysis. Data were compared between those who had a delayed rapid response team activation and those who did not. Fifty seven percent patients met the definition of delayed rapid response team activation. Patients in high-frequency physiologic monitored environments were more likely to experience delay than their floor counterparts. In the no-delay group, the most common reasons for rapid response team activation were tachycardia/bradycardia at 29% (217/748), respiratory distress/low Spo_2 at 28% (213/748), and altered level of consciousness at 23% (170/748) compared with respiratory distress/low Spo_2 at 43% (423/977), tachycardia/bradycardia at 33% (327/977), and hypotension at 27% (261/977) in the delayed group. The group with no delay had a higher proportion of rapid response team calls between 8:00 and 16:00, whereas those with delay had a higher proportion of calls between midnight and 08:00. The delayed group had higher hospital mortality (15% vs 8%; adjusted odds ratio, 1.6; $p = 0.005$); 30-day mortality (20% vs 13%; adjusted odds ratio, 1.4; $p = 0.02$); and hospital length of stay (7 vs 6 d; relative prolongation, 1.10; $p = 0.02$) compared with the no-delay group.
Conclusions: Delays in rapid response team activation occur frequently and are independently associated with worse patient mortality and morbidity outcomes. (*Crit Care Med* 2016; 44:54–63)
Key Words: delay; intensive care; morbidity; mortality; outcomes; rapid response team

In the United States, Canada, Europe, and Australia, the rate of adverse events in hospitalized patients has been estimated between 3% and 18% (1). Several studies have shown that if a patient has a cardiac arrest and requires cardiopulmonary resuscitation, survival to discharge is low at 7–26% (1). Other studies have confirmed that before adverse events such as cardiac arrest, patients exhibit physiologic deterioration (2–6). Initially the rapid response system (RRS) was designed to reduce serious adverse effects such as cardiac arrest on the floor by activating an "ICU without walls" (7) to the bedside when there was evidence of physiologic deterioration (4). The availability of a rapid response team (RRT) has face validity as a tool that can improve access to critical care resources and potentially rescue

*See also p. 239.

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Dr. Barwise has a spouse who is a board member of Ambient Clinical Analytics (ACA) who has, and their institution has, patents with and stock in ACA. Dr. Gajic has disclosed work for hire. Dr. Herasevich consulted for and has stock in ACA. Mr. Pickering served as a board member for ACA. He and his institution have patents with, stock in, and received royalties from ACA. His institution received grant support from the Center for Medicare and Medicaid (Grant, Process AWARE). The remaining authors have disclosed that they do not have any potential conflicts of interest.

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patients who otherwise might suffer harm because of failure to escalate care. The presence of a RRS has been strongly advocated in the United States by organizations such as the Joint Commission (National Patient Safety Goal 16) (7, 8), and the Institute for Healthcare Improvement (9). Despite this, the literature is somewhat divided on the topic, with conflicting evidence about whether the RRS is effective or not (10–18). Several single-center observational studies have found improved outcomes with the introduction of the RRT; however, a major multicenter, cluster-randomized, controlled trial (10) and a systematic review and meta-analysis by Chan et al (4) did not find evidence to support the effectiveness of RRS. It has been suggested that the lack of RRS efficacy relates to ineffective activation of the RRT. This is a well-described phenomenon and a likely contributor to less than ideal RRS activation outcomes (19). Although mortality outcomes are commonly reported in RRS studies, there are fewer studies examining morbidity outcomes following delay (12).

The primary aim of this study was to examine the association between delayed RRT activation and hospital mortality. The secondary aim of the study was to determine the relationship between time to RRT activation and morbidity (ICU length of stay, hospital length of stay, invasive mechanical ventilator use, and vasopressor medication use). For the purpose of this study, delayed RRT activation was defined as a greater than 1-hour delay in RRT call from the first recorded, qualifying, abnormal vital sign (12).

METHODS

Setting and Study Design

A retrospective single-center cohort study was conducted in Mayo Clinic, Rochester, MN. The rapid response system database was used to identify all patients who had RRT activations from January 1st to December 31st, 2012. These patients were the subjects of the study. The study protocol was reviewed and approved as a minimal risk study by the institutional review board.

Mayo Clinic, Rochester, MN, is an academic tertiary referral center with just over 2,000 beds allocated between two hospital campuses, St. Marys Hospital and Methodist Hospital of which 213 are ICU beds (192 and 21, respectively). The hospital has approximately 135,000 admissions per year, with 15,500 ICU admissions in 2012.

Methodist Hospital has beds primarily for hematology/oncology, obstetrics/gynecology, and liver transplant patients. St. Marys Hospital has beds for medical, pediatric, psychiatric, rehabilitation, and surgical patients. The ICUs at this site are subspecialized but include 24 general medical and 16 medical cardiology beds, as well as subspecialized surgical beds. Accessibility to ICU beds is excellent; as such the lack of availability of an ICU bed does not arise as a reason for delay in transfer of an RRT patient to a higher level of care. There is a robust system for overflow between the subspecialty ICUs when needed with 24/7 attending staffing present in the accepting ICUs.

RRT Description

The rapid response system has been in place across the institution since March 2007. Each campus has its own RRT. The team is physician-led and is expected to respond within 15 minutes of being activated. The team consists of a critical care fellow, critical care respiratory therapist, and an ICU nurse. They are supervised by an in-house board-certified attending intensivist 24/7. All members of the team staff the ICU while providing RRT coverage. The team is available on site 24 hours daily, 7 days a week. During the study period, the frequency of RRT activations averaged between 40 and 60 activations per 1,000 discharges at St. Marys and Methodist campuses, respectively. Activation of the team can occur by any member of the healthcare team via a pager system.

The criteria for RRT activation (7) include staff concern, oxygen saturation < 90%, change in heart rate/pulse < 40 or > 130, change in systolic blood pressure < 90 mm Hg, change in respiratory rate < 10 and > 28/min, new-onset chest pain suggestive of ischemia, symptoms and signs of stroke, and change in conscious state. Changes are considered important if they are acute and persistent and unexpected (**Table 1**).

During the study period, there were 2,717 RRT calls across both hospital campuses. Patients were excluded for the following reasons: age younger than 18 years, no research authorization, outpatient status, and recurrent RRT calls. Those with recurrent RRT calls were excluded as it would have been very difficult to analyze whether the RRT call was associated with delay/no delay and what effect this had on their outcomes. We concluded that interpretation of delay in this context would be difficult. The final cohort consisted of 1,725 patients.

This included 605 patients who remained on the floor following RRT activation and the 1,120 that transferred to the ICU following RRT activation (**Fig. 1**).

Data Collection

Clinical characteristics and demographic information were collected using manual and automated retrieval from the institutional electronic medical record databases. The severity of illness at the time of RRT activation was evaluated using the Cardiac

TABLE 1. Rapid Response Team Activation Criteria

The criteria for rapid response team activation are as follows:
A staff member is worried about the patient
Acute and persistent declining oxygen saturation < 90%
Acute and persistent change in heart rate/pulse < 40 or > 130
Acute and persistent change in systolic blood pressure < 90 mm Hg
Acute and persistent change in respiratory rate < 10 and > 28/min
New-onset chest pain suggestive of ischemia
Acute and persistent change in conscious state (including agitated delirium)
Signs and symptoms suggestive of a stroke

Acute is defined as new and/or unexpected.

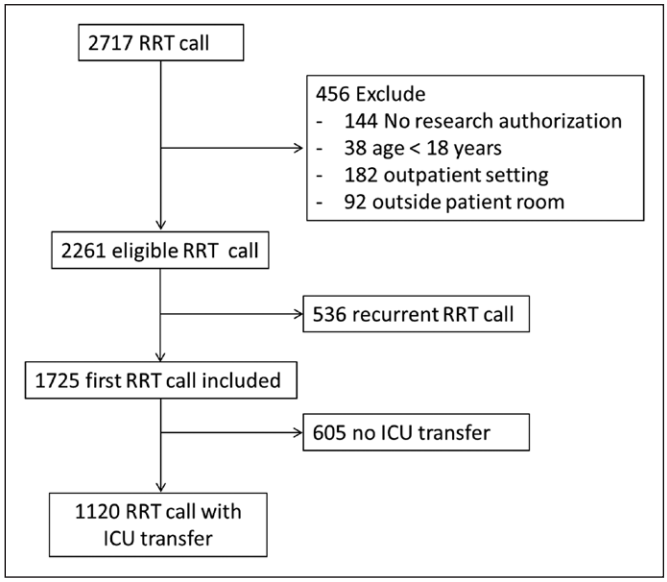

Figure 1. Study flow for rapid response team (RRT) cohort used in this retrospective study with inclusion and exclusion criteria.

Arrest Risk Triage (CART) score (20, 21). This score was chosen as it had the highest area under the curve when compared with VitalPAC Early Warning System, Modified Early Warning System, and Standardized Early Warning System for cardiac arrest, ICU transfer, and composite outcomes. It is based on respiratory rate, heart rate, diastolic blood pressure, and age (20). Comorbidities were evaluated using the Charlson Comorbidity Index score (6).

We reviewed vital signs including heart rate/pulse rate, systolic and diastolic blood pressure, respiratory rate, and oxygen saturation for each eligible patient for the 24 hours before the RRT was activated. Vital signs were categorized as either normal or abnormal based on the institutional RRT criteria described above. The time of the first abnormal vital sign meeting RRT criteria was noted.

The cohort was subdivided into two groups: 1) no delay: those that had an RRT activated within 1 hour of their first abnormal vital sign meeting RRT criteria were considered to have a timely, nondelayed activation (this included patients meeting RRT criteria that were nonvital sign based); 2) delay: those that had an RRT activated 1 hour after first abnormal vital sign meeting RRT criteria were considered to have a delay. The duration from the first abnormal vital sign meeting RRT criteria and the time of RRT activation was calculated. Those with delayed RRT activation were further subdivided depending on the length of the delay into 1- to 4-hour, 4- to 8-hour, and 8- to 24-hour delay (**Fig. 2**).

Outcome Measurements

The outcomes of interest included in-hospital mortality, all-cause mortality within 30 days following RRT activation, and hospital length of stay. We reviewed the patients' final status by retrieving the discharge status field of the administrative database and reviewing the electronic medical records. In patients whose final status was unknown, the Social Security Death Index was used.

We performed further analysis on the subgroup of patients who were transferred to the ICU following RRT activation. In the analysis of this cohort, we added vasopressor use, mechanical ventilation use, ICU mortality, and ICU length of stay to the outcome variables.

Statistics/Analysis

All continuous variables were reported as medians with interquartile range (IQR). All categorical variables were reported as counts with percentages. Student *t* test or analysis of variance was used to compare continuous variables between groups or multiple groups, respectively. CART and Charlson scores are nonnormal in distribution and were analyzed using Wilcoxon rank-sum test. Chi-square test was used to compare categorical variables. For binary outcomes including in-hospital mortality and 30-day mortality, we performed multivariate logistic regression analysis to assess the association between the delayed RRT activation and outcomes, adjusting for CART scores and baseline variables with p value of less than 0.05 in the univariate analysis. The adjusted odds ratio (OR) with 95% CI was reported. For continuous outcomes, including hospital and ICU length of stay, we performed multivariate negative binomial regression to assess the association between the delayed RRT activation and outcomes, adjusting for CART scores and baseline variables with p value of less than 0.05 in the univariate analysis. Accordingly, the relative prolongation with 95% CI was reported. A two-sided p value of less than 0.05 was considered statistically significant. SAS (version 9.3; SAS, Cary, NC) and JMP statistical software (version 9.0; SAS) were used for statistical analysis.

RESULTS

Full Cohort

Forty-three percent of the cohort (748/1,725) had a timely RRT activation and 57% (977/1,725) had a delayed RRT activation. The sex, age, and rates of do not resuscitate (DNR)/do not intubate (DNI) were not statistically different between the two groups. Median (IQR) Charlson scores were also the same in the no-delay and delay groups. CART scores differed, with those in the no-delay group having a median (IQR) CART score of 9 (4–17) versus a median CART score of 13 (8–24) for those with a delay.

The reasons for the RRT calls also differed between the two groups. In the group with no delay, the most common reasons for the RRT call as documented by the team were tachycardia/bradycardia at 29% (217/748). For those with delay, the most common reason for the RRT call was respiratory distress/low Spo_2 at 43% (423/977). A larger proportion of those in the no-delay group had chest pain 10% (75/748) versus 6% (61/977) in the delay group ($p = 0.004$).

Another notable difference between the two groups was the time of RRT activation. Those with no delay had 39% of the RRT activations (292/748) between the hours of 08:00 and 16:00. This is in contrast to the delay group in which only 33% of the activations (325/977) occurred during the same hours.

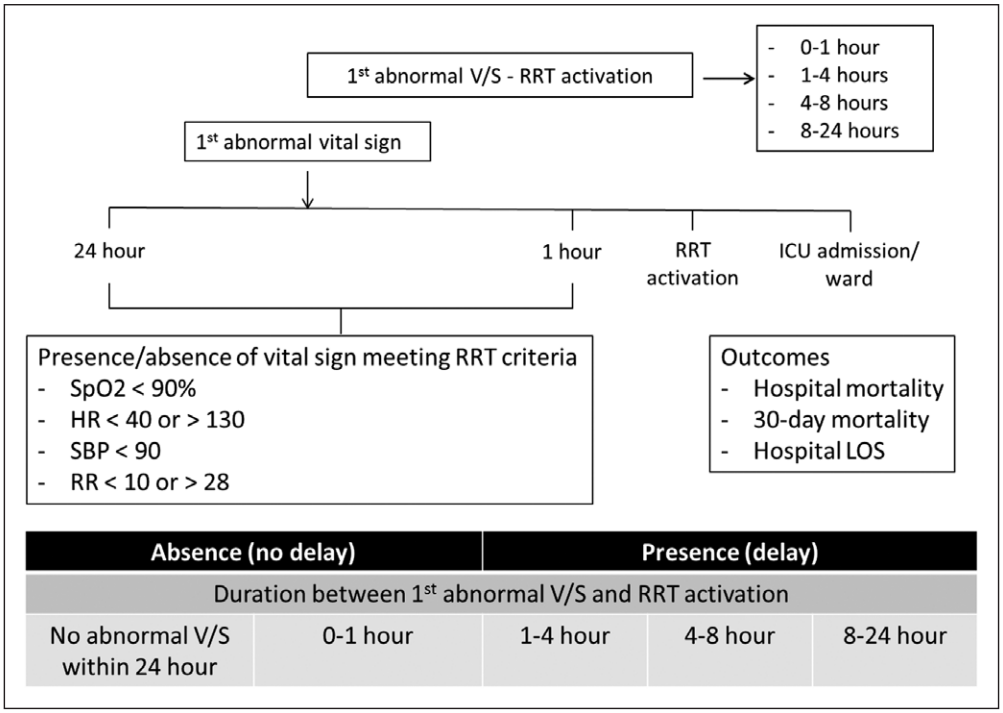

Figure 2. The cohort was subdivided into two groups: 1) No delay: those that had an rapid response team (RRT) activated within 1 hour of their first abnormal vital sign meeting RRT criteria. 2) Delay: those that had an RRT activated 1 hour or more after first abnormal vital sign meeting RRT criteria. Spo_2 = oxygen saturation, HR = heart rate, SBP = systolic blood pressure, RR = respiratory rate, LOS = length of stay.

Between the hours of 00:00 and 08:00, only 25% of the no-delay group (187/748) had RRT activations compared with 31% of the delay group (302/1,725). Sixty-two percent of those patients (381/610) who had an RRT called on a monitored floor had a delay. The odds of having a delay (for patients on monitored floors) were 1.45 (1.3–1.6) (**Table 2**).

During our review of the full cohort, we identified two groups of patients within the no-delay RRT activation cohort. One group included those who had a documented physiologic abnormality within 60 minutes of the RRT activation (327/748) and a second group who never had a recorded vital sign abnormality (421/748). Despite documentation of a valid physiologic reason for RRT activation, there was no recorded matching physiologic abnormality.

Full Cohort Outcomes: Delay Versus No Delay

Thirty-day mortality was 13% (98/748) in those with no delay versus 20% (196/977) in those with delay. Adjusted OR in the delayed group for 30-day mortality was 1.4 (1.07–1.88; $p = 0.02$). Hospital mortality was 8% (63/748) with no delay versus 15% (149/977) in those with delay. Adjusted OR in the delayed group for hospital mortality was 1.6 (1.15–2.23; $p = 0.005$) (**Table 3**).

Those in the no-delay group had a median hospital length of stay of 6 days (4–10) compared with a median of 7 days (4–13) for those with delay. Hospital length of stay demonstrated a relative prolongation, and when the data were stratified to exclude those who died, the relative prolongation of hospital stay remained statistically significant, 11% relative prolongation (1.02–1.2) following multivariate analysis.

Full Cohort Outcomes as Delay Increases

Patients with abnormal vital signs were then subdivided into subgroups 0- to 1-hour (no delay), 1- to 4-hour, 4- to 8-hour, and 8- to 24-hour delay as previously described to see whether there was an association between the duration of the delay from first abnormal vital sign and the outcomes. (Patients who never had an abnormal vital sign were excluded from this group.) The cohort consists of 1,304 patients. Hospital length of stay did not increase as delay increased. Adjusted OR showed progressive increases in 30 days and hospital mortality as length of delay increased. The adjusted OR for 30-day mortality for delay of 8–24 hours from first abnormal vital sign was 1.84 (1.27–2.69). Note that from delays of 1–4 to 4–8 hours, the OR increased from 1.07 (0.60–1.81) to 1.45 (0.84–2.46).The adjusted OR for hospital mortality increased to 2.14 (1.40–3.34) after 8-hour delay and was 1.96 (1.07–3.53) with 4-hour delay (**Table 4**).

ICU Cohort

When the analysis was restricted to patients admitted to the ICU, the following was noted. Thirty-eight percent (422/1,120) of the ICU cohort had a nondelayed RRT activation, after meeting RRT criteria, and 62% of the ICU cohort (698/1,120) had a delayed activation. The sex, age, and rates of DNR/DNI were not statistically different between the two groups. The time to ICU admission was similar in both the delay and no-delay groups once the RRT had been activated. The median (IQR) Charlson scores were 3 in both groups. Notable baseline differences included median (IQR) CART scores of 9 (4–21) in the no-delay group versus median (IQR) CART scores of 17 (9–26) in the delay group. Within the no-delay group, the most common reason for RRT activation was heart rate abnormalities at 35% (149/422). As noted on the full cohort, we had a large number of patients in the no-delay group without recorded abnormal vital signs, these numbered 212 of 422 patients.

Within the delay group, the most common reason for RRT activation was respiratory distress or low Spo_2 making up 50% (350/698). Note some patients had primary and secondary reasons for the RRT call documented. A larger proportion of those with no delay had chest pain 9% (37/422) versus 4% (31/698) in the delay group ($p = 0.003$).

TABLE 2. Baseline Characteristics at Rapid Response Team Activation: Full Cohort

Characteristics	RRT Activation		p
	No Delay (*n* = 748)	Delay (*n* = 977)	
Age (yr)	66 (56–77)	65 (55–76)	0.95
Male sex	370 (49)	501 (51)	0.45
RRT call[a]			
Tachycardia/bradycardia	217 (29)	327 (33)	0.048
Altered level of consciousness	170 (23)	200 (20)	0.26
Hypotension	157 (21)	261 (27)	0.006
Respiratory distress or low Spo_2	213 (28)	423 (43)	< 0.001
Chest pain	75 (10)	61 (6)	0.004
RRT call time (hr)			0.01
0:00–8:00	187 (25)	302 (31)	
8:00–16:00	292 (39)	325 (33)	
16:00–24:00	269 (36)	350 (36)	
Weekend	187 (25)	277 (28)	0.12
Monitor floor	229 (31)	381 (39)	< 0.001
No. of HR/PR in 24 hr ≥ 12	160 (21)	575 (59)	< 0.001
No. of Spo_2 in 24 hr ≥ 12	142 (19)	598 (61)	< 0.001
DNR/DNI	103 (14)	138 (14)	0.83
Charlson score	3 (1–5)	3 (1–6)	0.35
Cardiac Arrest Risk Triage score	9 (4–17)	13 (8–24)	< 0.001

RRT = rapid response team, Spo_2 = oxygen saturation, DNR/DNI = do not resuscitate/do not intubate.
[a]Patients may have had more than one abnormality at the time of the RRT call.
Continuous variables are presented as median (interquartile range), and categorical variables are presented as *n* (%).

TABLE 3. Association Between Delayed Rapid Response Team Activation and Outcomes

Outcome, *n* (%)	No-Delay RRT Activation	Delay RRT Activation	Adjusted Odds Ratio (95% CI)[a]	p
30-d mortality	98 (13)	196 (20)	1.41 (1.07–1.88)	0.02
Hospital mortality	63 (8)	149 (15)	1.60 (1.15–2.23)	0.005
Outcome, Median, Interquartile Range)	**No-Delay RRT Activation**	**Delay RRT Activation**	**Relative Prolongation (95% CI)[a]**	*p*
Hospital length of stay (d)	6 (4–10)	7 (4–13)	1.10 (1.01–1.19)	0.03

RRT = rapid response team.
[a]Adjusted for RRT calling criteria (tachycardia/bradycardia, hypotension, respiratory distress or low oxygen saturation, chest pain), RRT call time, transfer from monitored floor, and Cardiac Arrest Risk Triage score at RRT activation.

Sixty-eight percent of those patients (268/394) who had an RRT called on a monitored floor had a delay. The odds of experiencing a delay on a monitored floor were 1.46 (1.1–1.9). Time of day was not statistically significant different between the group who had no delay and those who experienced a delay (**Table 5**).

ICU Cohort Outcomes: Delay Versus No Delay

Thirty-day mortality was 17% (71/422) in the group with no delay and 23% (158/698) in the group who experienced a delay. Hospital mortality was 11% (47/422) in those with no delay versus 18% (124/698) in the delay group. ICU mortality was 4% (17/422) for those who had no delay versus 9% (60/698) in patients who experienced delay. Hospital length of stay was 7 days (4–12) for those who had no delay versus 8 days (5–14) for those who experienced a delay. ICU length of stay was 1.3 days (0.8–2.6) in the no-delay group versus 1.7 days (1–3.2) in the delay group. Use of invasive mechanical ventilation was 16% (66/422) in the no-delay group versus 22% (152/698) in the delay group. Vasopressor use was 15% (63/422) in the no-delay group versus 24% (171/698) in the delay group.

TABLE 4. Association Between Length of Delay (From First Abnormal Vital Sign) to Rapid Response Team Activation and Outcomes

	First Abnormal Vital Sign–Rapid Response Team Activation			
Outcome	**0–1 Hr (*n* = 327)**	**1–4 Hr (*n* = 180)**	**4–8 Hr (*n* = 146)**	**8–24 Hr (*n* = 651)**
30-d mortality, *n* (%)	49 (15)	26 (14)	27 (18)	143 (22)
Adjusted OR (95% CI)[a]	1 (ref)	1.07 (0.62–1.81)	1.45 (0.84–2.46)	1.84 (1.27–2.69)
Hospital mortality, *n* (%)	33 (10)	15 (8)	23 (16)	111 (17)
Adjusted OR (95% CI)[a]	1 (ref)	0.90 (0.46–1.71)	1.96 (1.07–3.53)	2.14 (1.40–3.34)
Hospital length of stay, d, median (interquartile range)	7 (4–12)	8 (4–14)	7 (4–13)	7 (4–12)
Adjusted relative prolongation (95% CI)[a]	1 (ref)	1.10 (0.95–1.28)	1.02 (0.87–1.19)	1.02 (0.92–1.14)

OR = odds ratio, ref = reference group.
[a]Adjusted for rapid response team (RRT) calling criteria (tachycardia/bradycardia and respiratory distress), transfer from monitored floor, and Cardiac Arrest Risk Triage score at RRT activation.

When these results were adjusted, differences in vasopressor use and ICU mortality remained statistically significant. Adjusted OR for those experiencing delay requiring vasopressors in the ICU was 1.63 (1.17–2.28; $p = 0.003$). Following multivariate analysis, the OR for ICU mortality with delay was 1.75 (1.01–3.19; $p = 0.04$). We stratified the patients who were transferred to the ICU by excluding those who died, when calculating the length of ICU and hospital stay analysis. ICU length of stay demonstrated a relative prolongation of 16% (1.01–1.36) for those with delay. This may be of limited clinical

TABLE 5. Baseline Characteristics at Rapid Response Team Activation of Cohort Transferring to the ICU

	RRT Activation		
Characteristics	**No Delay (*n* = 422)**	**Delay (*n* = 698)**	***p***
Age (yr)	66 (56–76)	65 (55–76)	0.66
Male sex	221 (52)	362 (52)	0.87
RRT call[a]			
Tachycardia/bradycardia	149 (35)	248 (36)	0.94
Altered level of consciousness	93 (22)	153 (22)	0.96
Hypotension	89 (21)	178 (26)	0.09
Respiratory distress or low Spo_2	129 (31)	350 (50)	< 0.001
Chest pain	37 (9)	31 (4)	0.003
RRT call time (hr)			0.53
0:00–8:00	117 (28)	214 (31)	
8:00–16:00	156 (37)	240 (34)	
16:00–24:00	149 (35)	244 (35)	
Monitor floor	126 (30)	268 (38)	0.004
DNR/DNI	50 (12)	96 (14)	0.36
RRT call–ICU admission (hr)	0.57 (0.37–0.82)	0.55 (0.38–0.79)	0.87
Charlson score	3 (1–5)	3 (1–6)	0.36
Cardiac Arrest Risk Triage score	9 (4–21)	17 (9–26)	< 0.001

RRT = rapid response team, Spo_2 = oxygen saturation, DNR/DNI = do not resuscitate/do not intubate.
[a]Patients may have had more than one abnormality at the time of the RRT call.
Continuous variables are presented as median (interquartile range), and categorical variables are presented as *n* (%).

significance. Hospital length of stay was not prolonged in the delay group. Adjusted OR for hospital and 30-day mortality were not statistically significant (**Table 6**).

ICU Cohort Outcomes as Delay Increases

For the analysis, the cohort transferring to the ICU was then subdivided into subgroups 0- to 1-hour (no delay), 1- to 4-hour, 4- to 8-hour, and 8- to 24-hour delay, as previously described, to see whether there was an association between the duration of the delay and the outcomes. We excluded those with no abnormal vital signs, resulting in a total of 908 patients. ICU mortality and hospital mortality increased as length of delay increased. Adjusted ORs for ICU mortality and hospital mortality were statistically significant and demonstrated worse outcomes as delays increased. Patients who experienced a delay of 8–24 hours had a 2.85 (1.35–6.77) OR of dying in the ICU. Also notable was that the ICU mortality OR, following a 4-hour delay, was 2.73 (1.02–7.52). For hospital mortality, the OR was 2.17 (1.31–3.7) with delays of greater than 8 hours and 2.08 (1.06–4.09) following a 4-hour delay (Table 6). Thirty-day mortality was not statistically significant between the groups. Mechanical ventilation, vasopressor use, ICU length of stay, and hospital length of stay demonstrated no significant differences following adjustments (**Table 7**).

Sensitivity Analysis

Comparisons between the group that had no documented abnormal vital signs and group with abnormalities for just 1 hour (i.e., within the no delay) revealed no outcome differences following adjustments. This was true for the entire cohort and for the cohort that were admitted to the ICU following RRT activation (**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/B449).

Sensitivity analysis was also done on the full cohort excluding those who had no abnormal vital signs. Thirty-day mortality and hospital mortality remained significantly different between the delay and no-delay groups as previously noted. However, length of hospital stay was no longer significantly different between the two groups (**Supplemental Table 2**, Supplemental Digital Content 2, http://links.lww.com/CCM/B450).

DISCUSSION

This retrospective study demonstrates that activation of the RRT at greater than 1 hour after meeting RRT criteria is common (57% of RRT calls), even in a mature RRS environment, and is independently associated with increased 30-day mortality, hospital mortality, and hospital length of stay in all patients. Additionally, an increased ICU mortality, vasopressor use, and a trend toward increased ICU length of stay for those transferring to the ICU were identified. As delay increased, 30-day mortality, hospital mortality, and ICU mortality outcomes worsened and the need for vasopressors increased. For a delay of 4 hours or more, the ORs for these outcomes significantly increased, which suggest that a 4-hour delay may be a more critical timeframe than a 1-hour delay. Additionally, delay in RRT activation was also noted as more frequent in those patients in a monitored environment compared with those who were not on monitored floors. More than 60% of those who had a RRT on a monitored floor had a delayed RRT in both the full cohort and the ICU cohort. Delays were also more common between the hours of midnight and 8 AM.

Several studies have shown that a delay in RRT activation is associated with increased mortality (22). Chen et al (15) concluded that as the proportion of early emergency team calls increases, the rate of cardiac arrests and unexpected deaths decreases. This inverse relationship provides support for the notion that early review of acutely ill patients by a team knowledgeable in critical care is desirable (23). This study confirms that delay is associated with increased mortality. This study also shows that delay is associated with worse morbidity outcomes, and this has not been studied so rigorously. The effect of increasing delay from 1 to 24 hours after vital signs meeting RRT criteria has not been widely documented and raises

TABLE 6. Association Between Delayed Rapid Response Team Activation and Outcomes in Patients Transferring to the ICU

Outcome, *n* (%)	No-Delay RRT Activation	Delay RRT Activation	Adjusted Odds Ratio (95% CI)[a]	*p*
Mechanical ventilator use	66 (16)	152 (22)	1.23 (0.88–1.71)	0.23
Vasopressor	63 (15)	171 (24)	1.63 (1.17–2.28)	0.003
ICU mortality	17 (4)	60 (9)	1.75 (1.01–3.19)	0.04
Hospital mortality	47 (11)	124 (18)	1.41 (0.97–2.07)	0.07
30-d mortality	71 (16.8)	158 (22.6)	1.20 (0.86–1.67)	0.28
Outcome, Median, Interquartile Range)	**No-Delay RRT Activation**	**Delay RRT Activation**	**Relative Prolongation (95% CI)[a]**	***p***
ICU LOS (d)	1.3 (0.8–2.6)	1.7 (1.0–3.2)	1.16 (1.03–1.32)	0.02
Hospital LOS (d)	7 (4–12)	8 (5–14)	1.09 (0.99–1.21)	0.09

RRT = rapid response team, LOS = length of stay.

[a]Adjusted for RRT calling criteria (respiratory distress or low oxygen saturation, chest pain), transfer from monitored floor, and Cardiac Arrest Risk Triage score at RRT activation.

TABLE 7. Association Between Length of Delay (From First Abnormal Vital Sign) to Rapid Response Team Activation and Outcomes in Patients Transferring to the ICU

Outcome	First Abnormal Vital Sign–Rapid Response Team Activation			
	0–1 Hr (*n* = 209)	1–4 Hr (*n* = 129)	4–8 Hr (*n* = 105)	8–24 Hr (*n* = 465)
Mechanical ventilator use, *n* (%)	32 (15)	27 (21)	21 (20)	105 (23)
Adjusted OR (95% CI)	1 (ref)	1.44 (0.80–2.56)	1.32 (0.70–2.44)	1.55 (1.00–2.45)
Vasopressor, *n* (%)	35 (17)	35 (27)	27 (26)	109 (23)
Adjusted OR (95% CI)	1 (ref)	1.92 (1.11–3.30)	1.67 (0.93–2.98)	1.61 (1.05–2.51)
ICU LOS, d, median (IQR)	1.5 (1.0–2.9)	1.5 (0.9–3.3)	1.7 (0.9–3.1)	1.7 (1.0–3.2)
Adjusted relative prolongation (95% CI)	1 (ref)	1.10 (0.90–1.34)	1.05 (0.85–1.30)	1.11 (0.95–1.29)
ICU mortality, *n* (%)	8 (4)	5 (4)	10 (10)	45 (10)
Adjusted OR (95% CI)	1 (ref)	1.08 (0.32–3.37)	2.73 (1.02–7.52)	2.85 (1.35–6.77)
Hospital LOS, d, median (IQR)	8 (5–13)	8 (5–17)	7 (4–16)	8 (5–13)
Adjusted relative prolongation (95% CI)	1 (ref)	1.15 (0.97–1.38)	1.08 (0.91–1.31)	0.99 (0.87–1.14)
Hospital mortality, *n* (%)	23 (11)	10 (8)	21 (20)	93 (20)
Adjusted OR (95% CI)	1 (ref)	0.71 (0.31–1.54)	2.08 (1.06–4.09)	2.17 (1.31–3.70)
30-d mortality, *n* (%)	37 (18)	20 (16)	23 (22)	115 (25)
Adjusted OR (95% CI)	1 (ref)	0.86 (0.46–1.58)	1.28 (0.69–2.33)	1.53 (0.99–2.38)

OR = odds ratio, ref = reference group, LOS = length of stay, IQR = interquartile range.

Adjusted for rapid response team (RRT) calling criteria (tachycardia/bradycardia and respiratory distress), transfer from monitored floor, and Cardiac Arrest Risk Triage score at RRT activation.

questions about why persistent critical physiologic abnormalities do not cause concern and activation of an RRT. Most notably, when assessing outcomes with increasing delay in the full cohort, as delay extended from the 1- to 4-hour to 4- to 8-hour subgroup, hospital mortality more than doubled from 0.71 to 2.08. Within the ICU cohort, as delay increased from the 1- to 4-hour to 4- to 8-hour delay subgroups, the OR for ICU mortality also more than doubled from 1.08 to 2.73.

The presence of monitoring should alert providers to abnormal vital signs and physiologic deterioration leading to earlier activation of the RRS. Contrary to this notion and what others have demonstrated, we noted that the ability to monitor patients contributed to a delay in activation. We suggest that monitoring may be empowering floor clinicians to adopt a watch and wait approach. The frequent access to vital sign measurements appears to give floor providers a tool whereby they can effectively give and measure a response to a treatment. The patient may be receiving appropriate interventions from the primary team in response to abnormal vital signs prior to the RRT call, so their physiologic deterioration may have been noted and being treated and therefore the RRT call is delayed. This finding has not been shown before and does not support the notion that continuous monitoring might improve afferent limb effectiveness (14).When we excluded patients who had no abnormal vital signs recorded with an RRT activated on a monitored floor, the OR for experiencing a delay in RRT activation increased to 1.71 (1.3–2.25). This gives further evidence that when monitoring, even in the presence of abnormal vital signs meeting RRT criteria, there is a higher likelihood of delay in RRT activation.

The study results indicate that certain symptoms and signs are more likely to trigger an immediate RRT activation (e.g., chest pain with concern about ischemia) and other vital signs and symptoms may not be as concerning to staff (e.g., respiratory distress/low SpO_2). It is difficult to make comparisons with other studies as calling criteria in other institutions vary considerable and do not always include chest pain.

The group with delay had more RRT calls between midnight and 08:00, while those with no delay had a larger proportion of RRTs between 8:00 and 16:00. This may be due to several factors including improved ratio of staff during the day, different vital sign routines during the day compared with the night, concern about disturbing patients at night, as well as the availability of the primary teams who are familiar with the patient's baseline status, and therefore recognize deterioration. Several other studies have also noted a similar circadian pattern of RRT activation, with fewer calls between midnight and 6 AM (24, 25).

Limitations: This is a single-center study with system and organizational structures that may make the study findings difficult to apply to other institutions. The patient cohort was limited to those patients who had an RRT activation, and it does not address those who never had an RRT activated despite the presence of abnormal vital signs meeting RRT criteria. In addition, the patient cohort reviewed reflects 1 year of RRT activations. This study did not determine whether any interventions

were performed by the primary care team during physiologic deterioration and prior to RRT activation. It is possible that vital sign abnormalities were noted and treatments were initiated in response to the abnormalities. RRT activation may then have been delayed despite recognition of patient's deterioration.

Given the retrospective and observational nature of the data, it is not possible to attribute causality to the delay in activation of RRT and the reported outcomes. Thus, it is difficult to definitively identify those patients who might benefit most from earlier activation of RRT or alternatives to the current RRS in place in the institution. A large part of the initial cohort (536/2,261) needed to be excluded as they had recurrent RRT calls making it difficult to measure delay of activation and results difficult to interpret. Further analysis of these patients was not within the scope of this study.

The study also identified a large subgroup of patients without abnormal vital signs documented, grouped in our initial analysis as the "no-delay" group (Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/CCM/B449). These patients had valid reasons for RRT recorded in their charts and a significant proportion of patients required ICU admission. The lack of documented vital signs reflects either infrequent measurements on the floor that were inadequate for detection of physiologic abnormalities or poor documentation either ongoing or at the time of acute deterioration. It is also possible that the nonexistence of a recorded vital sign abnormality reflected the acute clinical change in stability resulting in the RRT activation.

It is difficult to interpret our findings based on RRT physiologic criteria in this group. However, when compared with those with no delay and with documented vital sign abnormalities, there were no differences in adjusted outcomes using multivariate analysis. This was true within the full cohort of RRT activations and the cohort who transferred to the ICU following RRT activation. When we excluded the group with no abnormal signs in the analysis, the results remained largely the same except for hospital length of stay which lost statistical significance.

This study used 1 hour after vital sign abnormalities as the cutoff for delayed activation. This time limit was picked based on two other studies: one of which used 30 minutes (22) and one of which used 60 minutes (12). The study team chose the more conservative timeframe based on workable feasibility. As noted above, the study findings suggest that for many physiologic abnormalities, 4 hours may be a more critical time when delay starts to affect outcomes.

Further studies are needed using propensity scores to confirm the association between delay and worse outcomes. Matching patients with delayed and nondelayed RRT activation with the same calling criteria would be helpful to confirm the findings of the study. Development of algorithms with risk stratification to help identify patients at risk of deterioration would be a useful future area of research.

CONCLUSIONS

This retrospective study demonstrates that activation of the RRT at greater than 1 hour after meeting RRT criteria is common and is independently associated with increased 30-day mortality, increased hospital mortality, and increased hospital length of stay. This study also suggests that as time from first abnormal vital sign to RRT activation increases, this association becomes stronger for 30-day mortality and hospital mortality. For those patients transferring to the ICU, delay is also associated with increased ICU mortality, increased vasopressor use, and increased length of ICU stay. The association between ICU mortality and hospital mortality increases as delay increases. Monitoring of patients on the floor is often associated with a delay, and delays are more likely between 00:00 and 08:00. The study suggests that 4-hour delay may be a significant time cut-off in which outcome differences are most notable.

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