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REPORTS OF ORIGINAL INVESTIGATIONS

# A retrospective observational study of daytime and nighttime transfers from the intensive care unit: through the lens of critical care response teams

# Une étude observationnelle rétrospective des transferts de jour et de nuit depuis l'unité de soins intensifs : selon la perspective des équipes d'intervention en soins intensifs

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## Abstract

**Purpose** *To evaluate the impact of nighttime compared with daytime transfers from the intensive care unit (ICU) on mortality in a hospital with a critical care response team (CCRT).*

**Methods** *We performed a retrospective observational study of ICU patients transferred between January 2011 and July 2013 who received CCRT follow-up. The transferred patients were divided into cohorts of daytime and nighttime transfers. A multivariable logistic regression model was used to identify independent predictors of mortality after ICU transfer.*

**Results** *There were 1,857 patients included in the study. With the exception of Multiple Organ Dysfunction Score on admission, transfers to a step-down unit, and lower urine output, there were no differences in the baseline characteristics, clinical events identified by CCRTs, and the number of CCRT interventions performed between daytime and nighttime transfers. Patients transferred at night were at higher risk of death in the univariate analysis but not in the multivariate analysis. Independent predictors of mortality included older age (odds ratio [OR], 1.02; 95% confidence interval [CI], 1.002 to 1.04), transfer to a medical service (OR, 1.96; 95% CI, 1.11 to 3.43), CCRT identification of hypoxemic respiratory failure (OR, 5.86; 95% CI, 3.11 to 11.04), decreased level of consciousness (OR, 3.14; 95% CI, 1.23 to 8.02), hypotension (OR, 3.69; 95% CI, 1.36 to 10.01), and longer CCRT duration of follow-up (OR, 1.02; 95% CI, 1.004 to 1.03).*

**Conclusions** *Nighttime transfer from the ICU was not an independent predictor of mortality. We identified unique predictors of mortality, including clinical events that CCRTs identified in patients immediately after ICU transfer. Future studies are required to validate these predictors of mortality in transferred ICU patients.*

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**Résumé**

**Objectif** *Évaluer l'impact sur la mortalité des transferts de nuit par rapport aux transferts de jour de l'unité de soins intensifs (USI) dans un hôpital disposant d'une équipe d'intervention en soins intensifs (EISI).*

**Méthode** *Nous avons réalisé une étude observationnelle rétrospective des patients de l'USI transférés entre janvier 2011 et juillet 2013 suivis par l'EISI. Les patients transférés ont été divisés en cohortes de transferts de jour et de nuit. Un modèle de régression logistique multivariée a été utilisé pour identifier les prédicteurs indépendants de mortalité après un transfert de l'USI.*

**Résultats** *L'étude a inclus 1857 patients. À l'exception du Score de défaillance multiviscérale, des transferts à une unité de soins intermédiaires et de la réduction du débit d'urine, aucune différence n'a été notée dans les caractéristiques de base, les événements cliniques identifiés par l'EISI et le nombre d'interventions de l'EISI effectuées entre les transferts de jour et de nuit. Les patients transférés la nuit étaient plus à risque de décès dans l'analyse univariée, mais pas dans l'analyse multivariée. Les prédicteurs indépendants de mortalité comprenaient un âge avancé (rapport de cotes [RC], 1,02; intervalle de confiance [IC] 95 %, 1,002 à 1,04), le transfert à un service médical (RC, 1,96; IC 95 %, 1,11 à 3,43), l'identification par l'EISI d'une insuffisance respiratoire hypoxémique (RC, 5,86; IC 95 %, 3,11 à 11,04), la diminution du niveau de conscience (RC, 3,14; IC 95%, 1,23 à 8,02), l'hypotension (RC, 3,69; IC 95%, 1,36 à 10,01), et une durée plus longue de suivi par l'EISI (RC, 1,02; IC 95 %, 1,004 à 1,03).*

**Conclusion** *Le transfert nocturne de l'USI n'est pas un prédicteur indépendant de mortalité. Nous avons identifié des prédicteurs particuliers de mortalité, notamment les événements cliniques identifiés par l'EISI chez les patients immédiatement après leur transfert de l'USI. Des études futures sont nécessaires pour valider ces prédicteurs de mortalité chez les patients transférés des soins intensifs.*

**Keywords** intensive care unit · patient transfer · after-hours care · critical care

Intensive care unit (ICU) patients transferred at night experience increased morbidity and mortality.[1-5] Although this phenomenon is not completely understood, possible reasons include patients' severity of illness both at time of admission and transfer, reduced patient-nursing ratios, hospital census forcing premature transfers, and transfer destination (step-down unit or ward).[6] What is not known is which patients are most susceptible to this phenomenon, and whether early intervention can prevent adverse outcomes that are associated with nighttime transfer. Many of the predictive factors identified have been static variables related to the patient's initial stay in the ICU, and the predictive power of these factors can be contextual to one hospital and not generalizable to others.[7,8] Not surprisingly, the evidence in support of these predictive factors remains heterogeneous.[9]

Critical care response teams (CCRTs) were founded on the notion that early identification of physiologic derangements (e.g., heart rate, blood pressure, respiratory rate, and oxygen saturation) in a patient can facilitate timely intervention. CCRTs are designed to identify the most vulnerable patients and bridge them to necessary critical care interventions.[10-12] Critical care response teams serve as an ICU outreach to reduce the incidence of cardiac arrests, postoperative complications, readmission to the ICU, and in-hospital mortality.[13-16] If CCRTs are sensitive to physiologic derangements occurring in ward patients, then they are well positioned to provide surveillance of ICU patients transferred to the ward as well. In some settings, CCRT perform routine follow-up of ICU patients transferred to the ward to ensure a stable transition. Whether this practice mitigates the previously reported risks associated with nighttime ICU transfer is not known.

Patients transferred from the ICU are at risk of developing adverse clinical events due to their complex care needs.[17] If CCRTs can identify dynamic clinical and physiologic variables arising during the post-ICU transfer follow-up that may predict adverse events, we expect that this will decrease mortality and readmission to the ICU. In our single-centre study, we describe the mortality of nighttime *vs* daytime transfers in an era of CCRT follow-up after ICU transfer; resource intensive outcomes pertaining to CCRT interventions; and predictive dynamic clinical and physiologic factors unfolding in the patient after their ICU transfer.

## Methods

### Study design and setting

This study was reviewed and approved by the Western University Research Ethics Board, (REB #102804). It was a single-centre, retrospective observational study conducted at the Critical Care Trauma Center (CCTC), London Health Sciences Center, Victoria Hospital. The CCTC is a 26-bed closed ICU that cares for patients with trauma and general medical/surgical issues. Victoria Hospital is a 588-bed, academic tertiary care centre located in London, Canada. We included all consecutive patients transferred from the ICU to the ward from January 2011 to July 2013. All patients transferred to the ward were

prescribed a mandatory minimum 24-hr CCRT follow-up, with any follow-up beyond 24 hr left to the discretion of the CCRT, based on the clinical status of the transferred patient. The CCRT comprises a critical care physician, a senior critical nurse, and a respiratory therapist. The CCRT evaluates the patient within several hours of their transfer from the ICU. We followed patients until hospital transfer or hospital death. Our inclusion criteria were all adult patients transferred from the ICU to the ward who received CCRT follow-up. Exclusion criteria included patients who were transferred to another hospital prior to completing their CCRT follow-up and patients who were previously included in the study. We grouped patients into two categories: daytime transfers (transferred between 07:00 and 20:59 hr) and nighttime transfers (transferred between 21:00 and 06:59 hr). The classification of daytime and nighttime transfers is based on previously published literature.[1]

We performed a sample size calculation using G*power version 3.1.6 (Faul, Erdfelder, Lang Buchner, 2007). The event rate and odds ratio (OR) for mortality associated with nighttime transfer was estimated using previous literature.[1,9] Using these estimates, a minimum sample size of 1,758 is required to identify a predictor variable with an OR of 1.25 in a population with an event rate of 10% with 80% power and a two-sided alpha level of 0.05. The sample size was inflated by 5% to adjust for the possibility of missing data.

## Data collection

We extracted data from the paper charts and the province-wide Critical Care Information System,[18] including age, sex, Multiple Organ Dysfunction Score (MODS) at time of admission, Nine Equivalents of Nursing Manpower Score (NEMS) on day of ICU transfer, ICU transfer dates and times, ICU admission source (ward, operating room, post-anesthesia care unit, emergency department, step-down unit, or external hospital), ICU admission diagnosis, referring physician service (team responsible for the patient prior to ICU admission), and transfer destination (step-down unit or ward).

We reviewed paper charts and collected relevant clinical events and laboratory data in the follow-up period post ICU transfer. We collected data on any concerns CCRTs documented in their clinical notes regarding clinical events that transpired during the mandatory post-ICU follow-up period. These clinical events include symptomatic lung secretions, decreased urine output, altered level of consciousness, hypoxemic and/or hypercapnic respiratory failure, hypotension, and abnormal lab values. We recorded data on interventions performed by CCRTs, such as intubation, institution of mechanical ventilation, nasogastric tube insertion, deep suctioning of secretions, intravenous (IV) fluid administration, obtaining IV access, electrolyte monitoring and replacement, antibiotic administration, goals of care discussions, and consultations to other specialty services. Data on diagnostic tests ordered by CCRTs such as blood gases, electrocardiography, and radiographic imaging were also collected.

We also collected data on the total number of CCRT visits during the mandatory ICU follow-up period and total follow-up duration. We distinguished between ICU readmissions and deaths that occurred during CCRT follow-up from those that occurred after CCRT follow-up was completed. We also distinguished total mortality (anticipated and unanticipated deaths) from unanticipated mortality. Patients with anticipated deaths had limitations on medical therapy established at the time of ICU transfer, precluding them from returning to the ICU or receiving aggressive CCRT intervention based on their prognosis and goals of care. These patients were still followed to ensure stable transition, support palliative therapy, or provide restricted medical management (e.g., antibiotics, IV fluid administration, non-invasive interventions).

## Data analysis

All analyses were performed using SPSS (IBM, Armonk, NY, USA). All tests presented are two-sided, and a $P$ value $< 0.05$ was considered statistically significant. Continuous variables with a normal distribution were expressed by means and standard deviations, while medians and interquartile ranges were used to describe variables without a normal distribution. Categorical variables are reported as counts and percentages. We compared the baseline characteristics, clinical events transpiring during the mandatory CCRT follow-up period, and interventions performed by CCRTs for daytime and nighttime transfers using the Student's t-test, Wilcoxon-rank sum test, or Chi squared statistic as appropriate. We also performed univariate analyses to identify associations between nighttime transfer and ICU readmissions and mortality.

Logistic regression was used to evaluate clinical factors predicting mortality (both total and unanticipated) after CCRT follow-up was completed. Our covariates for this model were selected *a priori* and based on previous studies showing an association between these variables and the outcome of interest.[1-5,9] Independent variables included in the regression models were age, daytime *vs* nighttime transfer from ICU, ICU length of stay, NEMS on day of ICU transfer, MODS, ICU admission diagnosis, patient category (medical or surgical patients), CCRT follow-up duration, and clinical events identified by CCRTs including lung secretions, decreased urine output, decreased level of

consciousness, hypoxemic and hypercapnic respiratory, hypotension, and abnormal lab values. Missing data were left as missing.

We used a forward selection method of entry of covariates into the regression model to refine the precision of the estimated coefficients and determine the covariates with a mediator effect by scrutinizing each step in the equation. A $P = 0.1$ was used to permit entry into the model. Results are displayed as regression coefficients with 95% confidence intervals (CI) constructed for these coefficients. We evaluated our model's performance using the area under the receiver operating characteristics curve (AUC).

## Results

There were 2,015 ICU transfers to the ward or a step-down unit from January 2011 to July 2013. Of those, 158 transfers were excluded because they involved patients who had already been included in this study and had been re-admitted to the ICU. We included 1,857 ICU patients transferred to the ward. Of those, 1,316 (70.9%) were daytime transfers and 541 (29.1%) were nighttime transfers (Figure). There were no significant differences in any of the baseline demographics of patients transferred from the ICU during daytime and nighttime hours (Table 1), with the exception of the MODS score on admission, which was higher in the nighttime transfer group (5.2 *vs* 4.9, $P = 0.04$) and a higher proportion of patients transferred to a step-down unit during the day time compared with nighttime transfers (25.4% *vs* 20.1%, $P = 0.04$).

Abnormal lab values and hypoxemic respiratory failure were the most frequent causes of clinical concern identified by CCRTs, as shown in Table 1. Critical care response teams were more likely to be concerned about low urine output for patients transferred at night compared with those transferred during the day (3.0% *vs* 0.9%, $P = 0.001$). Lung secretions (5.2% *vs* 3.4%, $P = 0.08$) and hypercapnic respiratory failure (2.4% *vs* 1.2%, $P = 0.06$) were more frequently identified in nighttime transfers than in daytime transfers, but these findings were not statistically significant. For both groups, the most common interventions performed by CCRT was acquisition of radiographic studies, blood work monitoring, and/or electrolyte replacement, as shown in Table 1. There were no statistically significant differences in any intervention performed by CCRTs in the daytime and nighttime cohorts.

Unanticipated hospital mortality was higher for nighttime transfers (OR, 1.75; 95% CI, 1.04 to 2.95). There were no cases of unanticipated hospital mortality during the CCRT follow-up period after ICU transfer. In patients transferred to a medical service, nighttime transfers had increased odds of mortality compared with daytime transfers (OR, 1.96; 95% CI, 1.01 to 3.82), while there was no difference in mortality between daytime and nighttime transfers to a surgical service (OR, 1.37; 95% CI, 0.61 to 3.08). There was no difference in ICU readmission between daytime and nighttime transfers (Table 2).

We performed logistic regression analysis to identify predictors of unanticipated mortality (Table 3). Age in years, presence of hypoxemic respiratory failure, decreased level of consciousness, hypotension, and length of post-ICU CCRT follow-up duration were independent predictors of unanticipated mortality. Discriminatory performance for this model based on the AUC was 0.78 (95% CI, 0.72 to 0.84). We performed a sensitivity analysis and included deceased patients who were transferred out of the ICU with limitations on medical therapy. In addition to age, presence of hypoxemic respiratory failure, decreased level of consciousness, hypotension, and length of post-ICU CCRT follow-up duration, nighttime discharge was found to be an independent predictor of mortality (OR, 2.14; 95% CI, 1.30 to 3.53). Discriminatory performance for this model based on the AUC was 0.80 (95% CI,0.75 to 0.85).

Since nighttime transfers suffered higher unanticipated mortality but time of transfer did not independently predict this outcome, we performed a post hoc analysis and stratified our study population into daytime and nighttime transfers to identify differences in predictors of mortality within each cohort that explained these findings. The results of our logistic regression analysis stratified by time of transfer is seen in Table 4. For patients transferred during daytime hours, hypoxemic respiratory failure, decreased level of consciousness, and transfer destination predicted unanticipated mortality after CCRT follow-up was completed. This model's discriminatory performance showed an AUC of 0.73 (95% CI, 0.65 to 0.82). For the nighttime transfers, hypoxemic respiratory failure, hypotension, and CCRT follow-up duration predicted unanticipated mortality after CCRT follow-up was completed. Discriminatory performance for the nighttime group revealed the AUC to be 0.78 (95% CI, 0.67 to 0.90).

## Discussion

Transitions of care from the ICU to the ward can be tenuous for patients. Critical care response team follow-up after ICU transfer during this vulnerable period of transition might improve patient outcomes. In particular, ICU patients transferred to the ward at night are particularly vulnerable with higher mortality and morbidity.[1-5] In this study, we examined the effect of nighttime ICU transfer in the setting of routine CCRT

**TABLE 1** Characteristics of patients transferred from the ICU during daytime and nighttime hours

| | Daytime | Nighttime | *P* value |
|---|---|---|---|
| Total patients, *n* (%) | 1316 (70.9) | 541 (29.1) | |
| Age, yr, mean (SD) | 58.9 (17.8) | 60.6 (17.5) | 0.05 |
| Sex, female, *n* (%) | 561 (42.6) | 238 (44.0) | 0.61 |
| MODS, (SD) | 4.9 (3.0) | 5.2 (3.0) | 0.04 |
| NEMS on day of ICU discharge, median [IQR] | 15 [6-18] | 15 [6-18] | 0.95 |
| ICU LOS, days, median [IQR] | 4.0 [2.1-8.0] | 4.2 [2.3-8.9] | 0.06 |
| CCRT follow-up duration after ICU discharge, hr, mean (SD) | 26.3 (15.4) | 26.0 (18.1) | 0.75 |
| Admission source, *n* (%) | | | 0.37 |
| Emergency department | 399 (30.3) | 175 (32.3) | |
| OR/PACU | 408 (31.0) | 165 (30.5) | |
| Ward | 273 (20.7) | 113 (20.9) | |
| Other hospital | 170 (12.9) | 71 (13.1) | |
| Step-down unit | 55 (4.2) | 13 (2.4) | |
| Other | 11 (0.8) | 4 (0.7) | |
| Admission diagnosis, *n* (%) | | | 0.05 |
| Respiratory | 434 (33.0) | 209 (38.6) | |
| Trauma | 202 (15.3) | 55 (10.2) | |
| Cardiovascular | 172 (13.1) | 69 (12.8) | |
| Gastrointestinal | 89 (6.8) | 29 (5.4) | |
| Neurologic | 37 (2.8) | 21 (3.9) | |
| Metabolic/endocrine | 40 (3.0) | 17 (3.1) | |
| Oncology/hematology | 31 (2.4) | 9 (1.7) | |
| Genitourinary | 4 (0.3) | 1 (0.2) | |
| Musculoskeletal/skin | 5 (0.4) | 5 (0.9) | |
| Other | 302 (22.9) | 126 (23.3) | |
| Transfer destination, step-down unit, *n* (%) | 334 (25.4) | 113 (20.1) | 0.04 |
| Clinical events identified by CCRTs, *n* (%) | | | |
| Abnormal lab value | 113 (8.6) | 43 (7.9) | 0.65 |
| Decreased urine output | 12 (0.9) | 16 (3.0) | 0.001 |
| Hypotension | 26 (2.0) | 11 (2) | 0.94 |
| Decreased level of consciousness | 34 (2.6) | 17 (3.1) | 0.51 |
| Increased lung secretions | 45 (3.4) | 28 (5.2) | 0.08 |
| Hypoxemic respiratory failure | 92 (7.0) | 35 (6.5) | 0.68 |
| Hypercapnic respiratory failure | 16 (1.2) | 13 (2.4) | 0.06 |
| Interventions performed by CCRTs, *n* (%) | | | |
| Radiographic studies | 69 (5.3) | 23 (4.3) | 0.37 |
| Bloodwork monitoring | 63 (4.8) | 23 (4.3) | 0.61 |
| Blood gas acquisition | 35 (2.7) | 17 (3.2) | 0.57 |
| IV fluid administration | 29 (2.2) | 18 (3.4) | 0.16 |
| Antibiotic administration | 34 (2.6) | 13 (2.4) | 0.82 |
| Suctioning of secretions | 29 (2.2) | 15 (2.8) | 0.47 |
| Goals of care discussion | 13 (1.0) | 8 (1.5) | 0.36 |
| Consultation of another service | 31 (2.4) | 7 (1.3) | 0.14 |
| Request for ECG | 26 (2.0) | 7 (1.3) | 0.31 |
| Non-invasive positive-pressure ventilation administration | 9 (0.7) | 9 (1.7) | 0.05 |
| Intubation | 6 (0.5) | 7 (1.3) | 0.07 |
| Central or peripheral IV insertion | 7 (0.5) | 5 (0.9) | 0.35 |

**TABLE 1** continued

| | Daytime | Nighttime | *P* value |
|---|---|---|---|
| NG/OG tube placement | 2 (0.2) | 1 (0.2) | 1.00 |

Data are presented as *n* (%), mean (SD), or median [IQR].

CCRT = critical care response team; ECG = electrocardiogram; IV = intravenous; IQR = interquartile range; LOS = length of stay; MODS = Multiple Organ Dysfunction Score; NEMS = Nine Equivalents of Nursing Manpower User Score; NG = nasogastric; OG = orogastric; OR = operating room; PACU = postanesthesia care unit; SD = standard deviation.

**TABLE 2** Univariate analysis of ICU readmission and mortality in patients transferred during daytime hours and nighttime hours

| Outcome, *n* (%) | Daytime (*n*=1316) | Nighttime (*n*=541) | Odds ratio (95% CI) | *P* value |
|---|---|---|---|---|
| Unanticipated in-hospital mortality during CCRT follow-up | 0 (0) | 0 (0) | - | - |
| ICU readmission during CCRT follow-up only | 32 (2.4) | 17 (3.14) | 1.30 (0.72 to 2.32) | 0.39 |
| Total ICU readmission | 81 (6.2) | 42 (7.8) | 1.28 (0.87 to 1.89) | 0.21 |
| Unanticipated in-hospital mortality | 36 (2.7) | 25 (4.6) | 1.75 (1.04 to 2.95) | 0.03 |
| Medical patients | 17 (1.3) | 16 (3.0) | 1.96 (1.01 to 3.82) | 0.05 |
| Surgical patients | 19 (1.4) | 9 (1.7) | 1.37 (0.61 to 3.08) | 0.44 |

CI = confidence interval; CRRT = critical care response team; ICU = intensive care unit.

**TABLE 3** Univariate and multivariate analysis: odds ratios of factors predicting total and unanticipated mortality

| | Univariate (95% CI) | Multivariate (95% CI) |
|---|---|---|
| **Unanticipated mortality** | | |
| Age | 1.79 (1.07 to 3.00) | 1.02 (1.002 to 1.04) |
| Hypoxemic respiratory failure | 8.95 (5.07 to 15.79) | 5.86 (3.11 to 11.04) |
| Medical patient | 1.46 (0.87 to 2.43) | 1.96 (1.11 to 3.43) |
| Decreased level of consciousness | 5.41 (2.32 to 12.60) | 3.14 (1.23 to 8.02) |
| Hypotension | 8.18 (3.42 to 19.57) | 3.69 (1.36 to 10.01) |
| CCRT follow-up duration | 2.07 (1.19 to 3.60) | 1.02 (1.004 to 1.03) |
| **Total mortality*** | | |
| Age | 2.12 (1.28 to 3.50) | 1.03 (1.01 to 1.05) |
| Hypoxemic respiratory failure | 8.98 (5.39 to 14.94) | 6.02 (3.36 to 10.76) |
| Medical patient | 1.98 (1.24 to 3.15) | 2.58 (1.54 to 4.33) |
| Nighttime discharge | 2.16 (1.37 to 3.42) | 2.14 (1.30 to 3.53) |
| Decreased level of consciousness | 5.42 (2.54 to 11.59) | 3.48 (1.48 to 8.16) |
| Hypotension | 8.20 (3.72 to 18.04) | 3.35 (1.30 to 8.65) |
| CCRT follow-up duration | 1.89 (1.16 to 3.06) | 1.01 (1.003 to 1.02) |

* Includes patients who had limitations on medical therapy at the time of intensive care unit admission.

CI = confidence interval; CCRT = critical care response team.

follow-up and whether CCRTs can identify predictors of mortality and morbidity. We observed that the adjusted risk of unanticipated death is not different between patients transferred from the ICU during nighttime hours compared with those transferred during daytime hours. To our knowledge, this is the first study to identify clinical and

**TABLE 4** Univariate and multivariate analysis: odds ratios of factors predicting unanticipated mortality stratified by time of transfer

| | Univariate (95% CI) | Multivariate (95% CI) |
|---|---|---|
| **Daytime discharges** | | |
| Hypoxemic respiratory failure | 8.03 (3.85 to 16.75) | 7.07 (3.30 to 15.12) |
| Decreased level of consciousness | 7.09 (2.57 to 19.57) | 5.92 (1.95 to 17.98) |
| Discharge to step-down unit | 0.17 (0.04 to 0.70) | 0.18 (0.04 to 0.77) |
| **Nighttime discharges** | | |
| Hypoxemic respiratory failure | 11.67 (4.66 to 29.20) | 9.46 (3.39 26.39) |
| Hypotension | 15.68 (4.11 to 59.80) | 15.97 (3.05 to 83.74) |
| CCRT follow-up duration | 2.28 (0.93 to 5.59) | 1.02 (1.003 to 1.03) |

CCRT = critical care response team; CI = confidence interval.

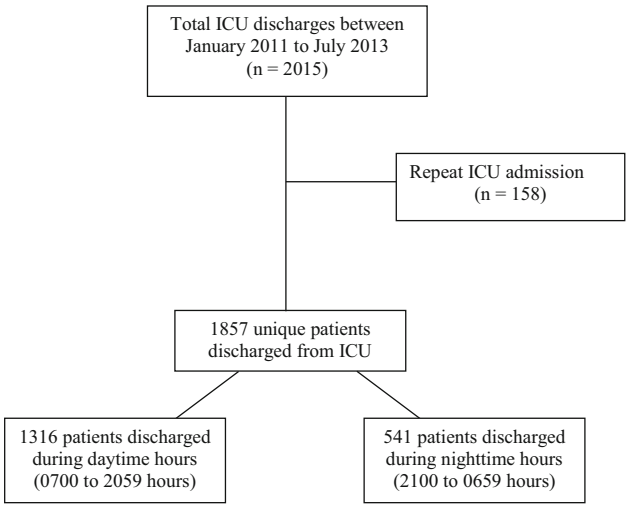


**FIGURE** Consort flow diagram of all intensive care unit transfers during the study period.

physiologic variables transpiring immediately after ICU transfer that predicted mortality later in the clinical course of the patient.

In prior studies, increased mortality with nighttime ICU transfers has been ascribed to both patient-related factors and system-related factors. These predictors of mortality after nighttime ICU transfer include age, comorbidities, disease severity at the time of ICU admission, and reduced nurse-to-patient ratios.[7,8] Despite controlling for known predictor variables, clinical events identified by CCRTs in the follow-up immediately after ICU transfer predicted mortality, even after CCRT follow-up was concluded. We hypothesize that CCRTs are attuned to subtle hemodynamic and physiologic derangements in a patient that may threaten their wellbeing downstream in their hospital stay. In support of this hypothesis, CCRTs electing to follow transferred patients for longer than the mandatory follow-up time independently predicted downstream readmission and mortality. Future prediction models for mortality in patients transferred at night should give attention to the dynamic clinical evolution of these patients on the ward. Patients in whom CCRTs identified new clinical processes including hypoxemic respiratory failure, hypotension, or altered level of consciousness may merit more intensive and longer follow-up, or be considered for early semi-elective readmission to a step-down monitored unit.

Even with implementation of CCRT, nighttime ICU transfers were still associated with an increased risk of unanticipated mortality in the crude analysis but not the adjusted analysis. Time of transfer was no longer a predictor of mortality in patients transferred at night when accounting for limitations on medical therapy. Although our conclusion is in contrast with previously published reports, prior studies did not comment on limitations of medical therapy at the time of ICU transfer.[4,5,19-23] The results of our study highlight how crucial it is for future studies to adjust for patients transferred to the ward with limitations on medical therapy.

We hypothesize that time of transfer from the ICU may be acting as a moderator variable for clinical events occurring during the CCRT follow-up period. For example, the odds of death due to clinical events like hypoxemic respiratory failure and decreased level of consciousness that developed after ICU transfer is higher in nighttime transfers than daytime transfers. The strength of the association between clinical and physiologic predictors such as hypoxemic respiratory failure and hypotension is greater in patients transferred at night than those transferred during daytime hours.

Are nighttime transfers a distinctly different and more vulnerable cohort of patients? In our single-centre cohort study, daytime and nighttime transfers had similar patient demographics and baseline characteristics. Nevertheless, some interesting trends have emerged. Only concern

regarding low urine output was identified by CCRTs more frequently in the nighttime ICU transferred patients when compared with their daytime counterparts. In the nighttime transfer group, there was a higher incidence of CCRTs identifying lung secretions, hypercapnic respiratory failure, and subsequently a higher incidence of intubation and implementation of non-invasive positive-pressure ventilation, but these findings were not statistically significant. Since the incidence of these clinical entities and interventions are low, our cohort may have been underpowered to detect a difference.

Our study has several strengths and limitations. We recruited a large cohort of patients and were powered to detect small effect sizes in our predictor variables. We also collected information on limitations on medical therapy at the time of ICU transfer in deceased patients, an important yet often neglected variable in prior studies. To our knowledge, this is the first study to identify clinical and physiologic events occurring in the post-ICU transfer period as predictors of mortality. Our study, however, lacks a control group that did not receive CCRT follow-up post ICU transfer, so we cannot comment on the effect of CCRT as an intervention. Nevertheless, many determinants of nighttime mortality are influenced by system factors such as hospital infrastructure and staffing. Therefore, our findings would require multicentre validation in a larger cohort. Prospective studies that focus on the immediate ICU transfer period are needed to validate our findings. Future research in this area should focus on characterizing the phenotype of ICU patients transferred at night and developing clinical prediction models for transferred ICU patients that use clinical events identified by CCRTs on the ward. Clinical events identified by CCRT that are predictive of adverse events can serve as points of intervention in future clinical trials.

## Conclusion

In summary, our study has shown that patients transferred from the ICU at night did not have a higher adjusted risk of unanticipated mortality. Based on the results of our sensitivity analysis, the association between nighttime transfer and mortality may be a result of limitations on medical therapy at the time of transfer. We also show that during the mandatory follow-up conducted by CCRTs after ICU transfer, the identification of dynamic physiologic and clinical derangements, such as hypoxemic respiratory failure, decreased level of consciousness, or hypotension predicted mortality later in the patients' care, after CCRT follow-up was completed and those issues were addressed. Critical care response teams have the potential to identify these vulnerable patients who develop clinical derangements and who are at higher risk of death. Future studies should validate these findings and evaluate interventions, including longer CCRT follow-up for these at-risk patients.

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