The Circadian Temperature Trajectory Predicts the Severity and Prognosis in Critically Ill Patients

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Research

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Abstract

Background: Disrupted circadian temperature is commonly observed in patients in the intensive care unit (ICU). The aim of this study is to examine the association between body temperature (BT) circadian rhythm and mortality critically in patients receiving ICU admission for at least 24h.

Method: Adult patients with a complete record of temperature during the first 24 hours of ICU stay in the Multi-parameter Intelligent Monitoring in Intensive Care III (MIMIC-III) database were included in this retrospective cohort study. Body temperature circadian rhythm ratio (BTCRR) was calculated according to the value of mean nighttime divided by daytime mean temperature. All patients were divided into the nocturnal BT rising (NBTR) group (BTCRR >1) and the non-NBTR group (BTCRR≤1). Five subgroups were also built according to different quantile of BTCRR (5%, 10%, 30%, 50%). The associations of NBTR, subgroup, and BTCRR with 28-day mortality were assessed separately using Cox proportional hazards model.

Findings: The overall cohort comprised 32419 patients. The non-NBTR group (n=20148) had higher 28-day mortality than the NBTR group (n=12271). After adjusting for covariates, the analysis showed that NBTR was significantly associated with mortality at 28 days (hazard ratio: 0.923; 95% CI, 0.888–0.960, P<0.05). All results of subgroup analysis showed obvious statistical significance, and similar results persisted in the patients with different groups. The % BTCRR had a significant non-linear ($p < 0.05$) association with 28d-mortality after adjusting for other variables ($p < 0.05$). Increasing the percentage up to 101% resulted in a hazard ratio (HR) to reduced mortality (HR: 0.96; 95%, 0.941–0.972, P<0.001), while increases above 101 % didn't make a significant suggestion in mortality.

Conclusions: The findings of this study suggest that both low and high BTCRR indicates a poor outcome, such that having a BTCRR of 101% had a survival advantage. BTCRR may aid in the early identification of critically ill patients at high risk of 28-day mortality. These findings may provide a basis for future randomized controlled trials comparing temperature control of ICU patients.

Introduction

The condition of intensive care unit (ICU) patients is exposed to their own pathophysiological state as well as psychological, environmental, iatrogenic and other factors [1, 2]. Early physiological monitoring and systematic assessment can aid clinicians in making effective interventions to improve patient outcome [3]. However, existing severity scoring systems and prediction tools give rise to challenges in integrating a comprehensive panel of physiologic variables and presenting to clinicians interpretable models early in a hospital admission. In particular, most approaches to early prediction of the severity of patients in ICU rely on the first 24h, 48h or 72 h of a patient's ICU stay [4–6].

It is clear that the exposure factors of ICU patients induce disorders by affecting physiological homeostasis, including body temperature (BT), circadian rhythm, blood pressure, etc. [7]. To the best of our knowledge, this series of homeostasis imbalances is a major contributor to poor outcomes in ICU

patients, leading to emotional depression, delirium, immune disorders, and cognitive impairment [8]. It is generally recognized that homeostasis balances of BT typically reflected as approximately 0.5°C around a mean of 37.0°C in healthy individuals [9]. On the contrary, it's worth noting that abnormal circadian body temperature (CBT) is associated with worse Acute Physiology and Chronic Health Evaluation III scores (APCHE III), suggesting that CBT monitoring can be a good predictor of potential ICU patients or that adjusting their CBT may improve outcomes [7]. From this perspective, CBT in the intensive care unit may be a useful predictor of illness. However, there is still a lack of convincing evidence and forecasting strategies.

In this study, we extracted the BT records of the first 24 hours of ICU admission from the Multi-parameter Intelligent Monitoring in Intensive Care III (MIMIC-III) database [10]. We aimed to explore the associations of CBT characteristics with mortality to facilitate early risk stratification in the ICU.

Methods

Study Design

We conducted a retrospective cohort study of adult ICU admissions from the MIMIC-III database maintained by Beth Israel Deaconess Medical Center (BIDMC, Boston, MA) and the Massachusetts Institute of Technology (Cambridge, MA). MIMIC-III contains data from 61532 ICU admissions and includes demographic characteristics, vital signs, laboratory, physiologic information, medications, comorbidities, nursing notes, and survival outcomes in the adult ICUs of BIDMC from 2002 to 2011. Any researcher who agrees to the terms of the database must complete "Protection of Human Subjects" training before they can access the data.

Patient Population

The inclusion criteria were (1) age ≥ 16years at ICU admission and (2) day and night body temperature (BT) records during the first 24 hours in the ICU. The exclusion criteria were (1) multiple ICU admissions, (2) length of ICU stay < 1 day, (3) BT measured < 6 times on the day 1 of admission. All diseases in our study were classified using the International Classification of Diseases, Ninth Revision (ICD-9).

Given that all ICU admission records in the MIMIC-III database were anonymized, the requirement for individual ICU admission consent was waived by the institutional review board of Beth Israel Deaconess Medical Center.

Data Extraction

The following ICU admission data were extracted from the MIMIC-III database: age, gender, ethnicity, BT, Sequential Organ Failure Assessment (SOFA), Acute Physiology Score III (APSIII), Renal Replacement Therapy (RRT), ventilation treatment, sepsis, cardiovascular disease, acute respiratory distress syndrome (ARDS), renal disease, type II diabetes, white blood cell (WBC), glucose, hematocrit, platelet, and survival outcomes (ICU, hospital, 28 days). Data were extracted using PostgreSQL v9.6.

Circadian Rhythm of BT

In this study, we focused on differences between average nighttime and daytime BT (℃). Consequently, the circadian rhythm of BT was described by body temperature circadian rhythm ratio (BTCRR) calculated as mean nighttime BT divided by mean daytime BT. Mean nighttime BT was calculated as all BT values during the night divided by the number of BT examinations, and the mean daytime BT was calculated as all BT values during the day divided by the number of BT examinations. Patients were divided into 2 groups according to the circadian rhythm of BT: the nocturnal BT rising (NBTR) group (> 1) and the non-NBTR group (≤ 1). 5 subgroups were also bult according to different quantile of BTCRR (5%, 10%, 30%, 50%): group A (≥ 50th percentile), group B (< 50th and ≥ 30th percentile), group C (< 30th and ≥ 10th percentile), group D (< 10th and ≥ 5th percentile), group E (< 5th percentile). The mean daytime BT value was computed as the average of all BT values from 6 AM to 10 PM, and mean nighttime MAP was from 10 PM to 6 AM the next day.

Outcomes

We reviewed the MIMIC-III database for information on therapy durations (admission time, discharge time, and death time). We obtained data on ICU stay, hospital stay and 28-d mortality by calculating relevant time points. The primary outcome measure in our study was 28-d mortality.

Statistical Analysis

Statistical analyses were performed using R software, version 3.6.2 (R Foundation for Statistical Computing). Continuous variables in the data were presented as mean value ± SD or median with interquartile range and categorical variables were presented as absolute numbers and percentage. Kolmogorov-Smirnov test was used to test the normality. The student t test or Mann-Whitney U test and Chi square or Fisher's exact tests were used to investigate the differences in quantitative and categorical variables, respectively between these groups. To assess the association of NBTR with 28-day mortality, we used univariate and multivariate Cox proportional hazards models for 28-day mortality and calculated Kaplan-Meier curves. In multivariate regression analyses, 5 models were built to show the modeling process, which could prove the stability of the association of NBTR with mortality. Model 1 was adjusted for age, gender, ethnicity. Model 2 was adjusted for model 1 plus an average of body temperature. Model 3 was adjusted for model 2 plus SOFA and APSIII. Model 4 was adjusted for model 3 plus primary diagnoses such as sepsis, cardiovascular disease, ARDS, renal disease, and type II diabetes. Model 5 was adjusted for model 4 plus laboratory analytical values such as WBC, glucose, hematocrit, and platelet.

To assess the association of BTCRR with 28-day mortality, we divided the population into five groups (A, B, C, D and E), and used univariate and multivariate Cox proportional hazards models for 28-day mortality. In multivariate regression analyses, 3 models were built. Model 1 was adjusted for age, gender, ethnicity, an average of body temperature. Model 2 was adjusted for model 1 plus WBC, glucose, hematocrit, and platelet. Model 3 was adjusted for model 2 plus SOFA, APSIII, sepsis, cardiovascular disease, ARDS, renal disease and type II diabetes. To show the relationships between BTCRR and 28-d

mortality, Kaplan-Meier curves were calculated, and cause-specific Cox proportional hazard models were implemented using restricted cubic splines, to predict the relative hazard of death in ICU with 95% confidence intervals.

Results

Data from a total of 61532 ICU admissions were accessed from the MIMIC-III database. We excluded 12821 admissions with ICU length of stay less than 24 hours, 3887 admissions with age less than 16 years and 3119 patients with multiple ICU admissions. Among the remaining patients, there were 39530 admissions with both day and night body temperature records during the first 24 hours in ICU. After 7111 patients with < 6 times BT measured on the day 1 of admission were excluded, 32419 patients were included in the analysis (Fig. 1).

Characteristics and Outcomes

Patients in the non-NBTR group had lower age ($P < 0.001$), higher SOFA ($P < 0.001$), and higher APSIII ($P < 0.001$). The proportion of patients with sepsis, cardiovascular disease, or renal disease in the non-NBTR group was higher ($P < 0.001$). On the first day of admission, there were more patients receiving ventilation therapy in the NBTR group ($P < 0.001$). Patients with ARDS or type II diabetes in the NBTR was more than the others ($P < 0.001$). Table 1 presents the characteristics across the classification of the circadian rhythm of BT. The patients in the non-NBTR group had higher ICU, hospital, and 28-day mortality than those in the NBTR group (8.0% versus 5.7%, 12.2% versus 8.9%, 11.6% versus 8.8%, respectively).

Association of NBTR with the 28-d mortality

The associations between NBTR and the 28-d mortality were further confirmed by COX regression (Table 2). After adjusted for age, gender, ethnicity, average of body temperature, SOFA, APSIII, sepsis, cardiovascular disease, ARDS, renal disease, type II diabetes, WBC, glucose, hematocrit, and platelet, the NBTR was independently associated with the 28-dmortality with a hazard ratio (HR) of 0.923 [95% confidence interval (CI) 0.888–0.960]. Kaplan-Meier survival curves revealed that the 28-d probability of survival was higher in the NBTR group than that in the NBTR group (Fig. 2).

Association of BTCRR with the 28-d mortality

In analyses in which the 28-d survival was the outcome, we classified BTCRR into 5 categories (Group A: ≥median, Group B: <50th and ≥ 30th percentile, Group C: <30th and ≥ 10th percentile, Group D: <10th and ≥ 5th percentile, Group E: <5th percentile). We conducted COX regression (Group A as Reference) for 5 categories as a predictor of the 28-d mortality and calculated Kaplan-Meier curves. Models were adjusted for age, gender, ethnicity, average of body temperature, SOFA, APSIII, sepsis, cardiovascular disease, ARDS, renal disease, type II diabetes, WBC, glucose, hematocrit, and platelet. In the group with low BTCRR (Group B and C), 28-d mortality had HRs of 1.053 (95% CI, 1.003–1.105) and 1.095 (95% CI, 1.043–1.149). In the group with very low BTCRR (Group D and E), 28-d mortality had HRs of 1.138 (95% CI, 1.048–1.234) and 1.115 (95% CI, 1.0126–1.213) (Table 3).

As observed in the Kaplan-Meier curves, Group E had the worst survival, whereas Group A survived the longest (log-rank $P < 0.05$) (Fig. 3). Figure 4 shows the Cox regression hazard ratios for BTCRR (HR value at 50% population with BTCRR as reference). The relationship between HR and BTCRR was U-shaped. It can be seen from the U-shaped figure that the population with a ratio of 1.01 has the highest survival advantage. Increasing the percentage up to 101% resulted in a hazard ratio (HR) to reduced mortality (HR: 0.96; 95%, 0.941–0.972, $P < 0.001$), while increases above 101 % didn't make a significant suggestion in mortality ($P = 0.44$).

Discussion

Circadian rhythm is a universal, built-in timing system that lasts nearly 24 hours and can be assessed through chronobiologic analysis of the time series of melatonin, cortisol and temperature [11]. This system was developed by the changes the human body respond to the external environment, specifically, the periodic changes in light and darkness caused by the Earth's revolution around the sun. Prior research generally confirms that circadian rhythms are controlled by a master clock in the suprachiasmatic nucleus (SCN) of the hypothalamus and regulated by the nerve hormone including the hypothalamo-pituitary-adrenal (HPA) axis and melatonin in the pineal gland [1, 12]. Patients hospitalized in the ICU are subject to changes in various zeitgebers due to light/dark cycles, social interactions, dietary patterns, medication, etc., which may cause changes in circadian rhythms such as core body temperature, leading to further adverse consequences [13, 14]. Our study explores the role of diurnal temperature trend in ICU patients in predicting illness and prognosis, and for the first time uses temperature models to distinguish the clinical trends of different groups.

Traditionally, temperature has been considered a dichotomous variable and patients are classified as febrile or nonfebrile based on absolute value. However, evidence suggests that temperature pattern analysis can convey meaningful clinical information whether or not patients meet the criteria for fever [15–17]. Varela et al. investigated the role of temperature change analysis in predicting survival in critically ill patients and found that temperature analysis was similar in its ability to predict mortality as the sequential organ failure assessment score [18]. Some scholars have reported that typical changes in temperature patterns include changes in amplitude, increases in frequency, or increases or decreases in baseline variability [19]. Therefore, it provides support for patients in intensive care units to explore effective diurnal temperature trend prediction models.

Published studies have reported the relationship between BT and biological rhythm or progression of disease or all-cause mortality in hospitalized, and ICU patients. Benjamin et al performed a cohort of severe trauma patients in France and reported that early exacerbation of the temperature rhythmicity is associated with the development of sepsis [20]. In another cohort of 6759 neurologic ICU patients from a 20-bed neurology ICU in the USA, elevated body temperature was found to predict higher mortality rate and worse outcome [21]. BT is one of the vital signs that can be used to evaluate APCHE III and mortality in critically ill patients [18]. However, no studies have reported circadian BT variation and its prognostic value in the ICU. In our study, we extracted complete BT records of patients' first 24 hours in the ICU from

a public database and investigated the circadian characteristics of BT to determine how to identify patients with a higher risk of mortality early in the hospital. We found that NBTR served as an important protective factor for higher survival in the 28-d mortality (HR: 0.923; 95% CI, 0.888–0.960) after adjusting for a series of covariates. To the best of our knowledge, this study is the first in which the relationship between the circadian rhythm of BT and ICU mortality has been evaluated.

Wu's study showed that the prognosis for sepsis patients in ICU became worse with decreased temperature minimum (T min), as well as increased T max and T max–min [22]. Further analysis indicated that A36.5–37°C (A: the area under the temperature curve) was associated with a positive prognosis. Meanwhile, A38–38.5°C, A38.5–39°C, and A39–39.5°C could result in a poor prognosis. From that perspective, stratified comparison can better distinguish the survival conditions of different risk ratios. Therefore, it is necessary to scientifically distinguish the risk levels of different groups for accurate prediction of clinical outcomes of diseases. To exclude the effect of clinical indicators included in the analysis on the relationship between BTCRR and survival outcomes, we divided the participants into 5 groups according to various BTCRR proportion and then conducted interaction and subgroup analysis. Findings suggested that the higher the proportion, the higher the survival. The association between BTCRR and mortality remained significant in various subgroups. We have demonstrated a non-linear, significant association between the percent BTCRR and mortality by 28-d. The results suggest that increasing the BTCRR to approximately 100 % was associated with decreased mortality, while increases above that point were associated with increasing mortality. From the perspective of biorhythm, moderate elevation of body temperature at night in ICU patients may be a positive embodiment of immune protection. This is consistent with the normal body temperature regulation, indicating that the patient has better immune regulation function [23–27]. Therefore, BTCRR could be used as a reliable risk factor for ICU mortality.

An abnormal circadian status of BT is mainly caused by dysfunction of the thermoregulation center and day/night differences in physical activities [28]. Patients in the ICU usually experience tremendous acute stressors like infections, trauma, multiple organ dysfunctions, artificial light, noise, mechanical ventilation, enteral nutrition, and medications. These factors further lead to abnormal thermoregulation [29–31]. Previous studies showed that abnormal body temperature is determined by the outcome of energy metabolism [32]. In addition, abnormal BT variation observed in patients is associated with autonomic nervous system dysfunction and poor sleep quality, which is also common in ICU patients, unless they are sedated or unconscious [33, 34]. Nevertheless, there is still no definitive study of the mechanism behind the circadian changes in body temperature, which provides a train of thought for further exploration.

However, there are some limitations to our analysis. Firstly, MIMIC-III is a single-center database, and thus obvious selection bias cannot be ignored. On the positive side, the recruited patients were enrolled from various ICUs, in other words, their data may reflect real-world situations encountered by clinicians. Secondly, given the retrospective design, the data were previously collected. Therefore, some of the information is incomplete such as the frequency of BT monitoring, noise level, patient/nurse ratio.

Although we have adjusted for as many covariates as possible and conducted a series of sensitivity analysis, a multicenter prospective study with adequate covariates is needed to further confirm the association between BTCRR and prognostic outcomes in critically ill patients. Thirdly, our study is only an association between BTCRR and mortality, not a cause-and-effect relationship. Subsequently, a high-quality prospective research is urgently needed to evaluate causality between BTCRR and mortality.

Conclusions

The findings of this study suggest that both low and high BTCRR indicates a poor outcome, such that having a BTCRR of 101% had a survival advantage. BTCRR may aid in the early identification of critically ill patients at high risk of 28-day mortality. These findings may provide a basis for future randomized controlled trials comparing temperature control of ICU patients.

Declarations

- Ethics approval and consent to participate

Not applicable

- Consent for publication

All authors have agreed to publish this article

- Availability of data and material

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

- Competing interests

The authors declare that they have no competing interests

- Funding

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- Authors' contributions

H. Deng and X. Yu participated in the design of the study and performed the statistical analysis. J. Lin and Y. Liu contributed to the literature search and writing of the manuscript. Z. Tong conceived of the study, and participated in its design and coordination and helped to draft the manuscript. Y. Wei and W. Li had full access to all data in the study, and take full responsibility for the accuracy of the analyses and their interpretation. All authors read and approved the final manuscript.

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Not applicable

References

1. Chan MC, Spieth PM, Quinn K, Parotto M, Zhang H, Slutsky AS. Circadianrhythms: from basic mechanisms to the intensive care unit. Crit Care Med.2012;40:246–253.
2. Freedman NS, Gazendam J, Levan L, Pack AI, Schwab RJ. Abnormal sleep/wake cycles and the effect of environmental noise on sleep disruption in theintensive care unit. Am J Respir Crit Care Med. 2001;163:451–457.
3. Awad, A. and M. Bader-El-Den, et al. (2020). "Predicting hospital mortality for intensive care unit patients: Time-series analysis." Health Informatics J **26** (2): 1043-1059.
4. Pirracchio R, Petersen ML, Carone M, et al. Mortality prediction in intensive care units with the SuperICU Learner Algorithm (SICULA): a population-based study. Lancet Resp Med 2015; 3(1): 42–52.
5. Celi LA, Galvin S, Davidzon G, et al. A database-driven decision support system: customized mortalityprediction. J Pers Med 2012; 2(4): 138–148.
6. Kim S, Kim W and Park RW. A comparison of intensive care unit mortality prediction models throughthe use of data mining techniques. Healthc Inform Res 2011; 17(4): 232–243.
7. Gazendam JAC, Dongen HPAV, Grant DA, Freedman NS, Zwaveling JH, SchwabRJ. Altered circadian rhythmicity in patients in the ICU. Chest. 2013;144:483–489.
8. Li, J. and R. Li, et al. (2019). "Nocturnal Mean Arterial Pressure Rising Is Associated With Mortality in the Intensive Care Unit: A Retrospective Cohort Study." J Am Heart Assoc **8** (19): e012388.
9. Mackowiak PA: Concepts of fever. Arch Intern Med 1998, 158:1870-1881.
10. Johnson, A. E. and T. J. Pollard, et al. (2016). "MIMIC-III, a freely accessible critical care database." Sci Data **3**: 160035.
11. Shibata S, Yu T, Hirao A. The adjustment and manipulation of biologicalrhythms by light, nutrition, and abused drugs. Adv Drug Deliv Rev. 2010;62:918–927.
12. Telias I, Wilcox ME. Sleep and circadian rhythm in critical illness. Crit Care.2019;23:82.
13. Kiss K, F€oldesi I, K€oves B, Csernus V, Molnar Z. Circadian rhythm disruptionexists in ICU patients. Intensive Care Med Exp. 2015;3(Suppl 1):A428.
14. Telias, I. and M. E. Wilcox (2019). "Sleep and Circadian Rhythm in Critical Illness." Crit Care **23** (1): 82.
15. Cuesta D, Varela M, Miró P, Galdós P, Abásolo D, Hornero R, Aboy M:Predicting survival in critical patients by use of body temperature regularity measurement based on approximate entropy. Med Biol EngComput 2007, 45:671-678.
16. Mohr NM, Hotchkiss RS, Micek ST, Durrani S, Fuller BM: Change intemperature profile may precede fever and be an early indicator of sepsis: a case report. Shock 2011, 36:318-321.

17. Papaioannou VE, Chouvarda IG, Maglaveras NK, Pneumatikos IA:Temperature variability analysis using wavelets and multiscale entropy in patients with systemic inflammatory response syndrome, sepsis, andseptic shock. Crit Care 2012, 16:R51.
18. Varela M, Churruca J, Gonzalez A, Martin A, Ode J, Galdos P: Temperaturecurve complexity predicts survival in critically ill patients. Am J Respir CritCare Med 2006, 174:290-298.
19. Drewry, A. M. and B. M. Fuller, et al. (2013). "Body temperature patterns as a predictor of hospital-acquired sepsis in afebrile adult intensive care unit patients: a case-control study." Crit Care **17** (5): R200.
20. Coiffard, B. and A. B. Diallo, et al. (2020). "Exacerbation of circadian rhythms of core body temperature and sepsis in trauma patients." J Crit Care **60**: 23-26.
21. Diringer, M. N. and N. L. Reaven, et al. (2004). "Elevated body temperature independently contributes to increased length of stay in neurologic intensive care unit patients." Crit Care Med **32** (7): 1489-95.
22. Wu, D. Y. and S. Q. Lu (2020). "The Effects of Abnormal Body Temperature on the Prognosis of Patients with Septic Shock." Ther Hypothermia Temp Manag **10** (3): 148-152.
23. Oster, H. and E. Challet, et al. (2017). "The Functional and Clinical Significance of the 24-Hour Rhythm of Circulating Glucocorticoids." Endocr Rev **38** (1): 3-45.
24. LaVoy, E. C. and C. A. Palmer, et al. (2020). "Bidirectional relationships between sleep and biomarkers of stress and immunity in youth." Int J Psychophysiol **158**: 331-339.
25. Irwin, M. and J. McClintick, et al. (1996). "Partial night sleep deprivation reduces natural killer and cellular immune responses in humans." FASEB J **10** (5): 643-53.
26. Shimba, A. and K. Ikuta (2020). "Glucocorticoids Regulate Circadian Rhythm of Innate and Adaptive Immunity." Front Immunol **11**: 2143.
27. Hand, L. E. and K. J. Gray, et al. (2020). "Regulatory T cells confer a circadian signature on inflammatory arthritis." Nat Commun **11** (1): 1658.
28. Laupland KB, Shahpori R, Kirkpatrick AW, Ross T, Gregson DB, Stelfox HT:Occurrence and outcome of fever in critically ill adults. Crit Care Med2008, 36:1531-1535.
29. Boldt J, Menges T, Kuhn D, Diridis C, Hempelmann G. Alterations in circulatingvasoactive substances in the critically ill—a comparison between survivorsand non-survivors. Intensive Care Med. 1995;21:218–225.
30. Van den Berghe G. Dynamic neuroendocrine responses to critical illness. Front Neuroendocrinol. 2002;23:370–391.
31. Muller B. Endocrine aspects of critical illness. Ann Endocrinol (Paris).2007;68:290–298.
32. Romanovsky AA, Sze ´kely M. Fever and hypothermia: two adaptive thermoregulatory responses to systemic inflammation. Med Hypotheses 1998;50:219–226.
33. Annane D. Body temperature in sepsis: a hot topic. Lancet Respir Med 2018;6:162–163.
34. Launey Y, Nesseler N, Malle ´dant Y, et al. Clinical review: fever in septic ICU patients—friend or foe. Crit Care 2011; 15:222.

Tables

Due to technical limitations, table 1 to 3 is only available as a download in the Supplemental Files section.

Figures

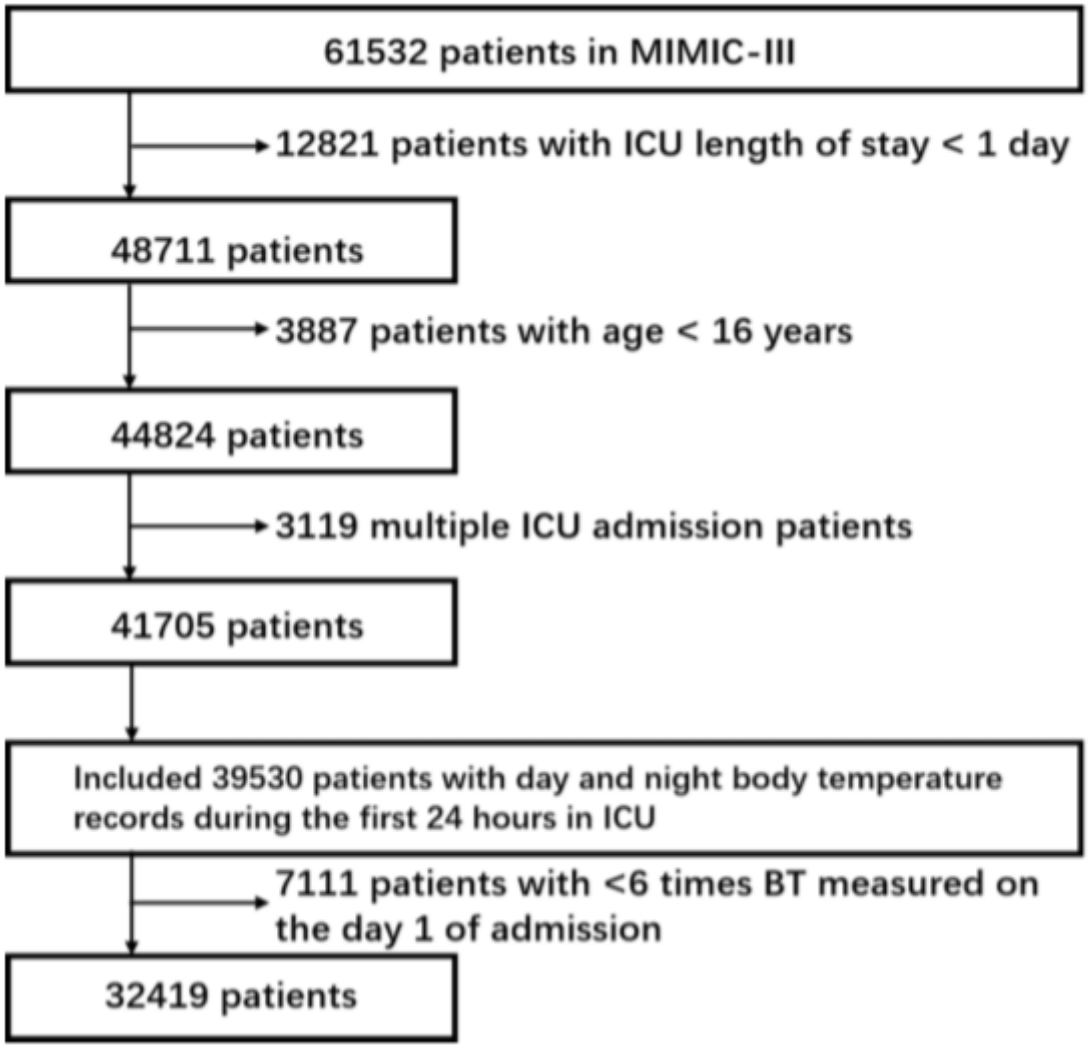

Figure 1

Flowchart of participants selection. A total of 32419 patients were included in the analysis. ICU: intensive care unit; BT: Body temperature; MIMIC-III: Multiparameter Intelligent Monitoring in Intensive Care III.

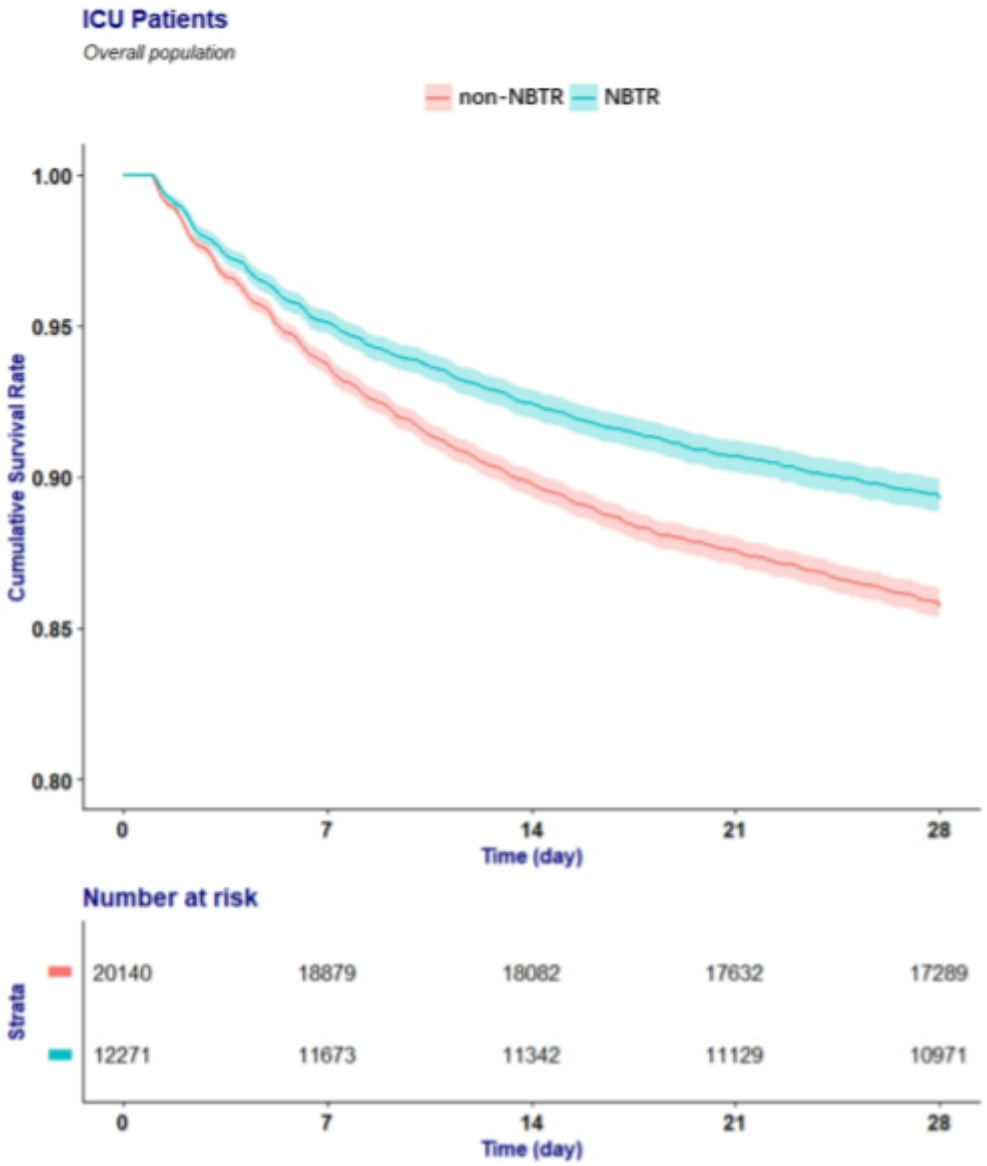

Figure 2

Kaplan–Meier survival analysis plot for 28-day mortality with NBTR. The curves show that patients with non-NBTR in the ICU had lower rates of 28-day survival. NBTR: nocturnal body temperature rising.

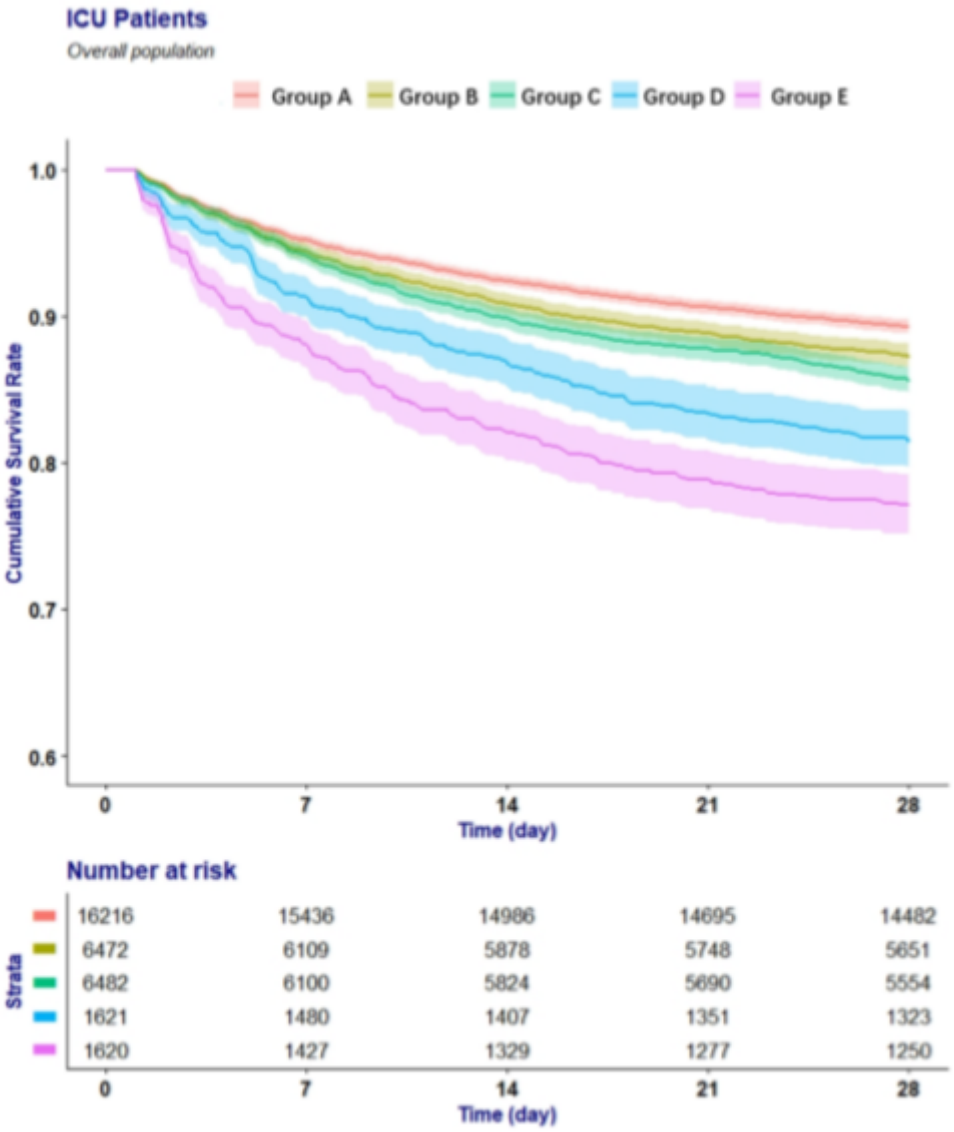

Figure 3

Kaplan–Meier survival analysis plot for 28-day mortality with subgroups. The curves show that patients with lower subgroup level in the ICU had lower rates of 28-day survival. Group A (≥50th percentile), Group B (<50th and ≥30th percentile), Group C (<30th and ≥10th percentile), Group D (<10th and ≥5th percentile), Group E (< 5th percentile).

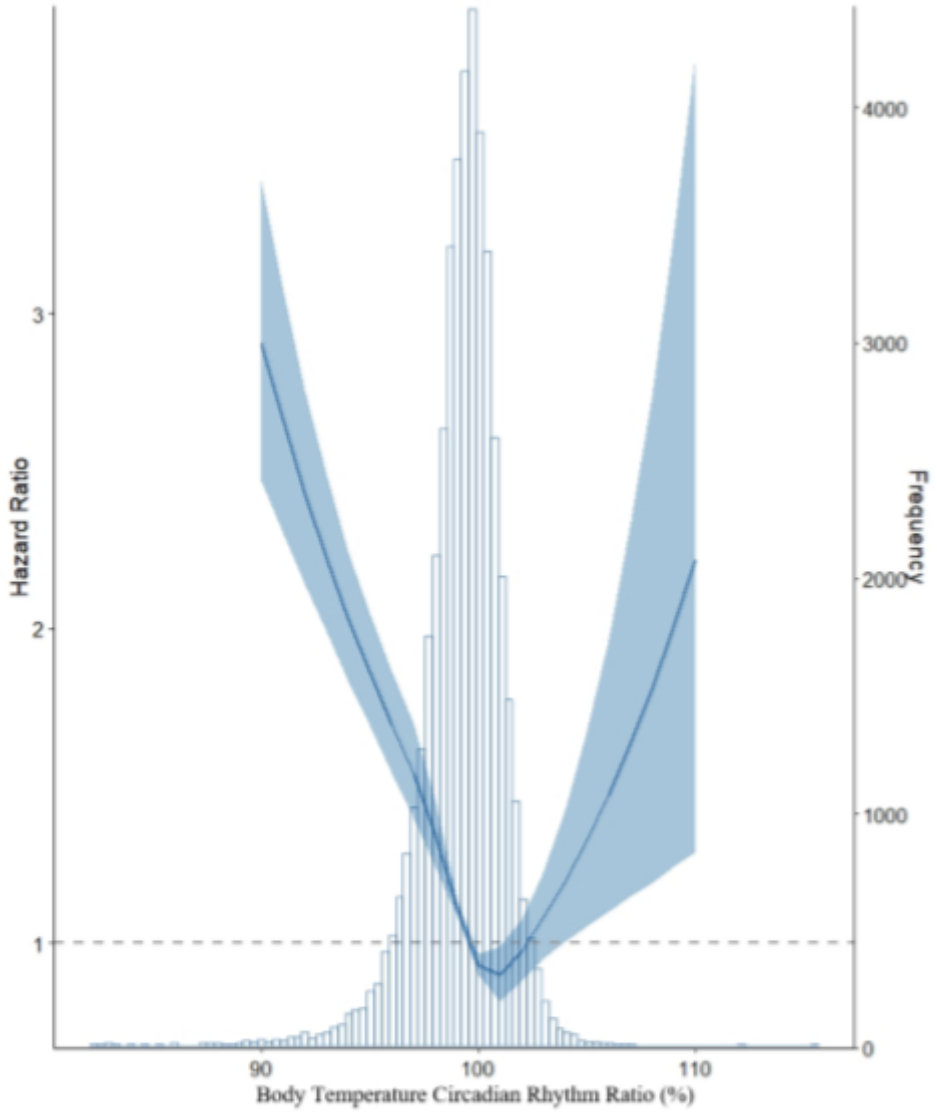

Figure 4

Association of body temperature circadian rhythm ratio percent with 28-day mortality.

Supplementary Files

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- Table.pdf