Delirium in Survivors of Cardiac Arrest Treated With Mild Therapeutic Hypothermia

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Background Mild therapeutic hypothermia is recommended for comatose patients resuscitated from cardiac arrest. However, the prevalence of delirium and its associated risk factors have not been assessed in survivors of cardiac arrest treated with therapeutic hypothermia.
Objective To determine the prevalence of and risk factors for delirium among survivors of cardiac arrest who were treated with therapeutic hypothermia.
Methods A retrospective observational study of patients treated with therapeutic hypothermia after cardiac arrest from 2007 through 2014. Baseline demographic data and daily delirium assessments throughout the intensive care unit stay were obtained. The association between duration of delirium and various risk factors was assessed.
Results Of 251 patients, 107 (43%) awoke from coma. Among the 107 survivors, all had at least 1 day of delirium during their intensive care unit stay. Median number of days of delirium was 4.0 (interquartile range, 2.0-7.5). Multivariable analysis revealed that age (odds ratio, 1.72; 95% CI, 1.0-2.95; $P=.05$), time from cardiopulmonary resuscitation to return of spontaneous circulation (odds ratio 1.52; 95% CI, 1.11-2.07; $P=.01$), and total dose of prewarming propofol (odds ratio, 0.02; 95% CI, 0.00-0.48; $P=.02$) were associated with duration of delirium.
Conclusions All survivors of cardiac arrest treated with mild therapeutic hypothermia had at least 1 day of delirium. Age and time from initiation of cardiopulmonary resuscitation to return of spontaneous circulation were associated with prolonged delirium, whereas exposure to propofol was protective against delirium. These findings are limited to this unique cohort and may not be generalizable to different populations. (*American Journal of Critical Care.* 2016;25:e81-e89)

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Survival to discharge from the hospital after sudden cardiac arrest ranges from 5% to 40%, and mortality after resuscitation is determined by the extent of neurological injury.[1,2] Although recent evidence indicates that mild therapeutic hypothermia (33 °C) is not better than targeted-temperature management (36 °C), mild therapeutic hypothermia remains the standard of care after cardiac arrest because it is associated with improvement in neurological outcomes after ventricular fibrillation and ventricular tachycardic arrest.[3-7] However, outcomes remain poor, and identification of additional interventions and modifiable risk factors may lead to improvements in neurological outcomes.

Acute brain dysfunction (delirium) is the most common organ disorder in patients treated with mechanical ventilation in the intensive care unit (ICU).[8,9] Delirium is an independent predictor of poor outcomes, including long-term cognitive impairment and mortality.[10-14] Of note, a variety of ICU care processes influence delirium and have implications for patients after cardiac arrest. For example, use of benzodiazepines and physical restraints are common modifiable risk factors for delirium.[15-17] Currently, most therapeutic hypothermia protocols call for high doses of sedatives, usually midazolam, because of the use of paralytic agents to prevent shivering.[18]

Delirium is an independent predictor of poor outcomes.

Our primary aim was to determine the prevalence of delirium in survivors of cardiac arrest who had treatment with mild therapeutic hypothermia in the cardiovascular ICU. In addition, we sought to understand the relationship between potentially modifiable aspects of resuscitation and therapeutic hypothermia and duration of delirium among patients treated with therapeutic hypothermia.

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Methods

Study Design and Sample

We conducted a retrospective cohort study of patients admitted to the 27-bed cardiovascular ICU, a tertiary level critical care unit with an annual volume of 2800 patients, at Vanderbilt University Medical Center, Nashville, Tennessee. The study period began May 15, 2007, and ended January 1, 2014. Eligible patients included all patients admitted after cardiac arrest. We included the names of all patients treated with therapeutic hypothermia in a prospective registry (International Cardiac Arrest Registry). We then collected data retrospectively and input the information into a REDCap database (REDCap Consortium). We excluded patients if they were persistently comatose or died before awakening from coma.

Treating physicians determined the suitability of therapeutic hypothermia. Patients were considered for inclusion in the study if they had experienced a cardiac arrest with a primary cardiac etiology; therapeutic hypothermia could be started within 12 hours of return of spontaneous circulation (ROSC); and the patients were 18 years or older, remained unresponsive after experiencing ROSC, and had a time to ROSC less than 60 minutes.[19] Physicians cooled patients eligible for therapeutic hypothermia by using an active surface cooling device to maintain a core body temperature of 32 °C to 34 °C for a total of 24 hours after ROSC and then rewarmed the patients at a rate of 0.25 °C/h. Physicians also administered a neuromuscular blocker to all patients; cisatracurium and a sedative (midazolam or propofol) were used during active cooling. The appropriate institutional review board reviewed and approved the study.

Covariates and Processes of Care After Cardiac Arrest

In addition to nonmodifiable baseline patient characteristics, we investigated potentially modifiable factors that we a priori hypothesized would have the

potential to affect the prevalence and duration of delirium in patients after cardiac arrest. We included factors related to severity of illness, initial resuscitation, and medication dose before a patient reached a temperature of 36°C. Patients' characteristics included age and comorbid illnesses. We obtained all baseline characteristics via retrospective chart review. We characterized severity of illness using the Acute Physiology and Chronic Health Evaluation II.[20] Initial resuscitation factors included occurrence of bystander cardiopulmonary resuscitation (CPR), initial rhythm (ventricular fibrillation or tachycardia, pulseless electrical activity or asystole), time in minutes from arrest to CPR by medical personnel, and time in minutes from CPR by medical personnel to ROSC (determined by review of emergency medical service records). Doses of medication during the therapeutic hypothermia from ICU admission to patient's arousal (score on the Richmond Agitation-Sedation Scale [RASS] > -4) included total micrograms of fentanyl, milligrams of midazolam, milligrams of propofol, and micrograms of cisatracurium.

Outcomes

We defined duration of delirium as the total number of days of delirium after initial arousal from coma. We assessed delirium status for each 24-hour interval, from the time the patient first reached an internal core temperature of 36°C until discharge from the ICU or death.

We assessed for coma and delirium daily by using the RASS and the Confusion Assessment Method for the ICU (CAM-ICU), respectively.[9,21-23] RASS and CAM-ICU are both previously validated tools with excellent interrater reliability and are suitable for determining the presence and type of delirium in broad populations of ICU patients.[9] Bedside nurses obtained RASS and CAM-ICU scores a minimum of twice daily for more than 90% of patient days. For the 52 of 772 days (6.7%) for which we had no usable assessments, we used the patient's status on the day before and the day after the missing day to compute the status for the missing day. Bedside nurses can reliably use the RASS and the CAM-ICU to detect delirious patients, and the RASS and CAM-ICU have been previously validated in the ICUs at Vanderbilt University Medical Center, including the cardiovascular ICU.[24]

Our team considered patients with RASS scores of -5 (unresponsive to physical and verbal stimulus) or -4 (responsive only to physical stimulus) for each 24 hours as comatose and therefore not eligible for evaluation of delirium. Each such day was classified as coma. During a 24-hour period, if a patient's RASS score reached or exceeded -3, we classified that day as delirious (CAM-ICU score positive at any time during a 24-hour period) or normal (CAM-ICU score negative during all assessments during a 24-hour period). We further categorized delirium, as assessed by the CAM-ICU, into hyperactive (RASS score +1 to +4) or hypoactive (RASS score 0 to -3). We classified a day as hypoactive if all CAM-ICU scores were positive during a 24-hour period with RASS scores from 0 to -3. We classified a day as hyperactive if all CAM-ICU scores were positive during a 24-hour period and the RASS scores were +1 to +4. We classified any day with all CAM-ICU scores positive during the 24-hour period with both hyperactive and hypoactive RASS scores as mixed.

Statistical Analysis

We used means and standard deviations and medians and interquartile ranges (IQRs) as appropriate to describe the patient characteristics of the overall population. The primary objective was to characterize the prevalence of delirium among cardiac arrest patients who were treated with therapeutic hypothermia and successfully warmed and aroused from coma. We report the proportion of patients with at least 1 day with positive CAM-ICU for the total included cohort.

The second aim of our study was to evaluate the potentially modifiable risk factors for delirium associated with resuscitation or therapeutic hypothermia protocols. For this step, we constructed a proportional odds logistic regression model to assess baseline risk factors for duration of delirium. Because of the highly skewed distribution, we used a proportional logistic model to analyze duration. The measure of association between predictors and outcomes in this model type is an odds ratio (OR). Because of the sample size, we could not include all factors collected; doing so would yield model overfitting. In addition to nonmodifiable baseline patient characteristics, we decided a priori to investigate potentially modifiable factors that we hypothesized could affect the prevalence and duration of delirium in patients after cardiac arrest. We included factors related to severity of illness, initial resuscitation, and medication dose before a patient reached a temperature of 36°C. Specific model variables included age, severity of illness, ventricular fibrillation or tachycardia vs pulseless electrical activity or asystole, time to CPR, time from CPR to ROSC, and total doses of fentanyl, midazolam, and propofol during therapeutic

Bedside nurses obtained RASS and CAM-ICU scores a minimum of twice daily.

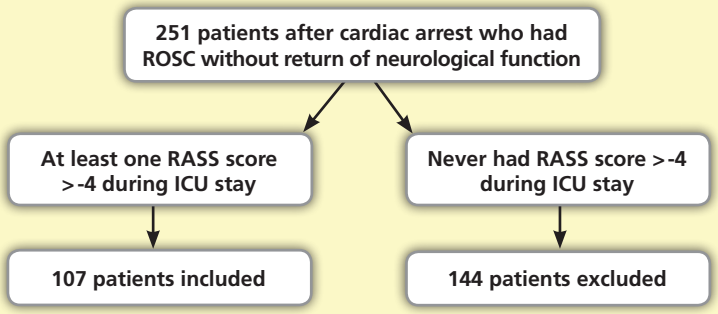

Figure 1 Flow diagram describing inclusion and exclusion criteria.

Abbreviations: ICU, intensive care unit; RASS, Richmond Agitation-Sedation Scale; ROSC, return of spontaneous circulation.

Table
Baseline characteristics of 107 survivors of cardiac arrest who were successfully warmed and wakened from coma

Characteristic	Value[a]
Age, median (IQR), y	57 (47-64)
Male sex	72 (67)
APACHE II score, median (IQR)	21 (18-24)
CPC score before cardiac arrest	
1	101 (95)
2	6 (5)
Cardiac arrest site	
Out of hospital	82 (77)
Witnessed cardiac arrest	92 (86)
Bystander cardiopulmonary resuscitation	73 (68)
Initial rhythm	
Ventricular tachycardia or fibrillation	85 (79)
STEMI	32 (30)
Intra-aortic balloon pump	17 (16)
Shock	46 (43)
Coronary angiography performed	83 (78)
Percutaneous coronary intervention	38 (36)
Temporary pacemaker	5 (5)
Fentanyl, total dose during ICU stay, median (IQR), mg (n=90)[b]	2700 (1569-4444)
Midazolam, total dose during ICU stay, median (IQR), mg (n=72)[b]	64 (40-108)
Propofol, total dose during ICU stay, median (IQR), µg (n=26)[b]	1198 (295-1663)

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; CPC, Cerebral Performance Categories Scale; ICU, intensive care unit; IQR, interquartile range; STEMI, ST-segment elevation myocardial infarction.
[a] Values are number (percentage) unless otherwise indicated in first column. Because of rounding, not all percentages total 100.
[b] Median for drug doses is only for those patients who received actual drug.

hypothermia. We used R statistical software (R Foundation for Statistical Computing) for all statistical analyses.

Sensitivity Analysis

To address whether or not delirium after warming was due to sedation alone, we divided the population across days between patients who received sedation (propofol, midazolam, or fentanyl) and those who did not. In addition, we analyzed patients given or not given a sedative, excluding fentanyl. Finally, we assessed for the prevalence of and subtypes for each of these subgroups.

Results

A total of 251 consecutive patients were treated with therapeutic hypothermia after cardiac arrest. The analysis includes 107 patients (43%) from the cohort who survived and awoke from coma and excludes the other 144 patients who died before ICU discharge or never had a RASS score greater than -3 that allowed assessment of delirium (Figure 1). Table 1 displays the demographic and baseline characteristics of the study cohort. The median age of survivors to first awakening was 57 (IQR, 47-64) years. The median score on the Acute Physiology and Chronic Health Evaluation II was 21.0 (IQR, 18.0-23.5), reflecting a high severity of illness. The majority of arrests had shockable rhythms (79%) and occurred out of the hospital (77%). Most patients received fentanyl for pain during therapeutic hypothermia (67%, n=72) and midazolam for sedation (84%, n=90).

Delirium occurred in 100% of survivors from the start of rewarming until the end of the ICU stay, for a median number of 4.0 days of delirium (IQR, 2.0-7.5). Figure 2 shows the distribution of cognitive status of patients each day after warming (coma, hypoactive delirium, mixed delirium, hyperactive delirium, and normal). Because the number of patients decreases over time, the relative percentage of patients is given for each patient day. Most of the episodes of delirium were hypoactive: 90% of patients had at least 1 hypoactive delirium day, 21% had at least 1 or more hyperactive delirium days, and 64% had at least 1 mixed delirium day. Normal mental status and coma were less common. In sensitivity analyses, the presence of sedation after warming did not affect the prevalence of delirium (Figure 3).

Figure 4 shows the effects of modifiable risk factors for duration of delirium associated with resuscitation or therapeutic hypothermia protocols. In evaluation of baseline risk factors and number of delirium days, multivariable analysis indicated that age (OR, 1.72; 95% CI, 1.01-2.95; P=.05), and time from initiation of CPR to ROSC (OR, 1.52;

95% CI, 1.11-2.07; $P = .01$) correlated with more days of delirium. In contrast, use of propofol (OR, 0.02; 95% CI, 0.00-0.48; $P = .02$) correlated with shorter duration of delirium.

Discussion

Our results primarily indicate that all survivors of cardiac arrest treated with therapeutic hypothermia who awoke from coma experienced at least 1 day of delirium between rewarming and subsequent discharge from the ICU. Although the high prevalence of delirium may seem surprising, our cohort differs from typical ICU patients. The degree of injury that cardiac arrest induced, the tremendous swings in metabolism from therapeutic hypothermia, and the large doses of psychoactive medications all most likely contributed to the higher prevalence. Independent risk factors for longer duration of delirium included increased age and longer times from CPR to ROSC. Total propofol dose during therapeutic hypothermia and before warming correlated with fewer days of delirium, whereas total doses of fentanyl and midazolam did not correlate with the duration of delirium. The high prevalence of delirium in this population calls for a need to understand the relationship between delirium and long-term outcomes in these patients and then, if warranted, interventions that will decrease the prevalence of delirium in the time after resuscitation.

Delirium in ICUs varies depending on the specific population of patients. Reported prevalences vary from 25% in our mixed-population cardiovascular ICU[25] to 80% in medical ICUs.[9] Previous reports[26] have indicated that survivors of cardiac arrest who experienced a myocardial infarction have a higher prevalence of delirium than do ICU patients who did not experience a cardiac arrest. Compared with other ICU patients, survivors of cardiac arrest treated with therapeutic hypothermia have unique characteristics: they are older, have multiple comorbid conditions, have a high prevalence of coronary artery disease,[27] and experience an acute anoxic injury that typically results in multiorgan failure and a high in-hospital mortality. Although the percentage of subtypes of delirium in our cohort of patients was similar to that reported in previous studies,[8,9,13,21,25] the overall prevalence of delirium of 100% in our cohort (higher than that reported in other specific ICU populations) may reflect the unique nature of our population. Consistent with the findings of previous studies[25] in a general cardiovascular ICU population, the majority of our patients experienced hypoactive delirium. Physicians who care for patients after resuscitation from cardiac arrest should keep these data in mind, because the awareness may help focus care on decreasing the duration of delirium by developing and implementing evidence-based interventions.[28]

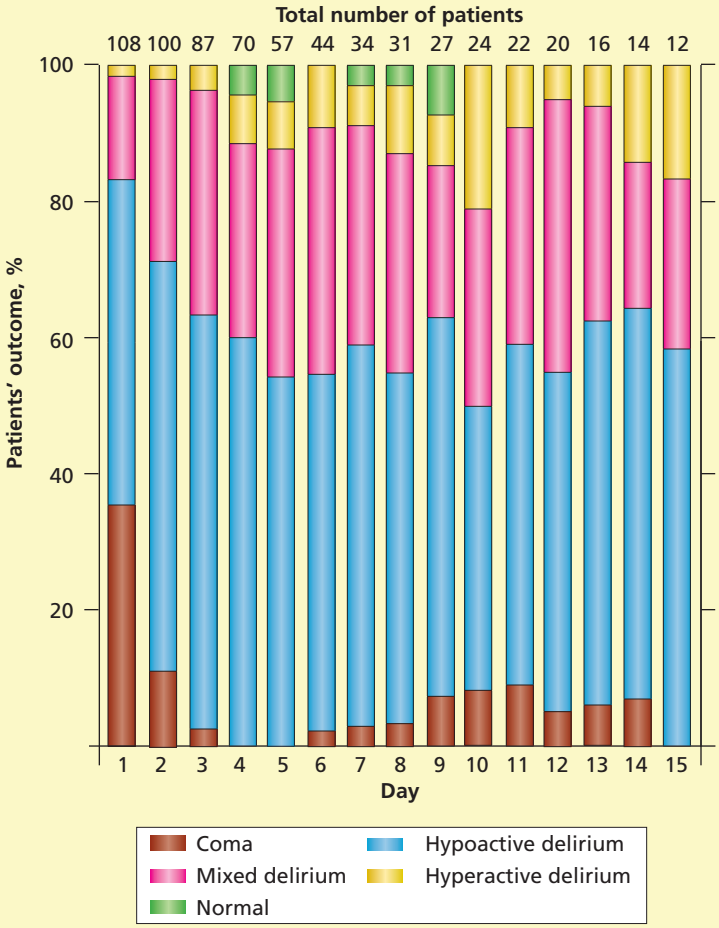

Figure 2 Percentage of delirium subtypes each day after rewarming.

We examined risk factors both before and after resuscitation that we hypothesized could influence the duration of delirium. Among prehospital risk factors, age and longer times from initiation of CPR to ROSC correlated with increased duration of delirium. Age has previously been included as a known risk factor for delirium.[16] Longer times from initiation of CPR to ROSC might reflect the detrimental effect that hypoxia has on brain function after therapeutic hypothermia. This finding supports the need for continued training of medical personnel in high-quality CPR that includes timely direct cardioversion to reestablish a perfusing rhythm.

> Delirium occurred in 100% of cardiac arrest survivors treated with mild hypothermia.

Our protocol for therapeutic hypothermia, similar to the protocol of many other institutions, calls for high doses of sedatives before warming because of the need for paralytics to prevent shivering. We hypothesized that the use of sedation after

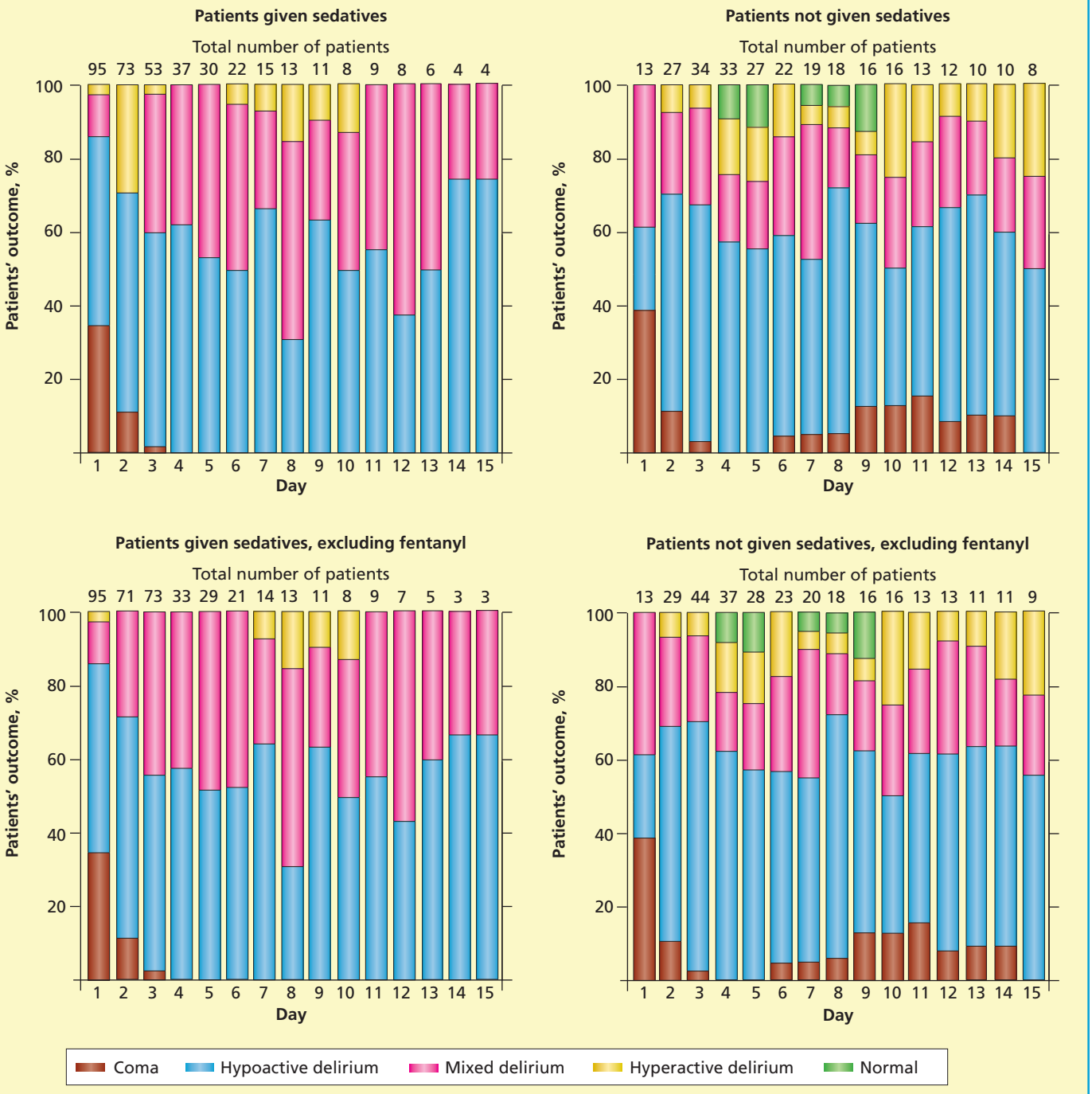

Figure 3 Comparison of prevalence of delirium between patients receiving and patients not receiving sedatives.

resuscitation but before rewarming (ie, sedation used during therapeutic hypothermia and before rewarming) could represent a modifiable risk factor that might increase the prevalence of delirium in our patients. Surprisingly, in our investigation of modifiable risk factors after resuscitation, higher doses of propofol during therapeutic hypothermia protected patients and correlated with decreases in the duration of delirium, and total doses of midazolam during therapeutic hypothermia did not correlate with increases in the duration of delirium. To our knowledge, no previous study has indicated an association between total propofol dose and a reduced number of days of delirium. Although previous reports[8,16] indicated an association between benzodiazepines and delirium in several different populations of ICU patients, the patients in our study clearly are a unique group

who responded differently to sedatives than did other critically ill patients in previous reports. Type I error may explain these findings related to propofol. Alternatively, our data on benzodiazepines may be underpowered for determining truth.

A consideration of some additional hypotheses of why total propofol dose before warming and not midazolam correlated with duration of delirium is worthwhile. First, we evaluated the total dose of sedatives used during therapeutic hypothermia and did not analyze the effect of sedative use after rewarming. Therefore, we limited our ability to assess the effect of sedatives after warming. Second, we provided propofol more frequently to patients closer to the end of the study period, and therefore the results may reflect changes in practice that may have occurred in later years. Alternatively, the use of propofol may represent confounding by indication, because we preferentially provided propofol during therapeutic hypothermia to patients who were at lower risk of delirium.

To determine whether or not sedation after warming was the cause of the high prevalence of delirium in the study, we split the sample population into patients who were or were not given sedatives. Figure 3 shows that by day 4, the prevalence of delirium in the patients receiving sedatives was approximately equivalent to the prevalence in the patients not receiving sedatives. In addition, in the smaller group who received no sedatives in the first few days after warming, the prevalence of delirium remained high. This finding indicates that the high prevalence of delirium, especially at later time points, is not all due to sedation. Of note, to our knowledge, no data exist to suggest differences between "sedative delirium" and "nonsedative delirium" in patients treated with mild therapeutic hypothermia after cardiac arrest. Further study is needed to understand whether or not outcomes differ if delirium occurs with or without sedation.

Our study has several limitations. First, in 2013, Nielsen et al[7] published results indicating that mild therapeutic hypothermia is not superior to targeted temperature management for care after resuscitation from cardiac arrest. The design used in that study differed from our study design, and therefore we cannot directly compare the findings of Nielsen et al with the findings of the landmark trials[3,4] from 2002 that established mild therapeutic hypothermia as the standard of care. Ongoing trials of the effect of different doses of therapeutic hypothermia may yield better guidelines in the future. Despite the results from the targeted temperature management trial,[7] the results of our study still apply to current practice, because mild therapeutic hypothermia remains guideline-based therapy for care after resuscitation from cardiac arrest.

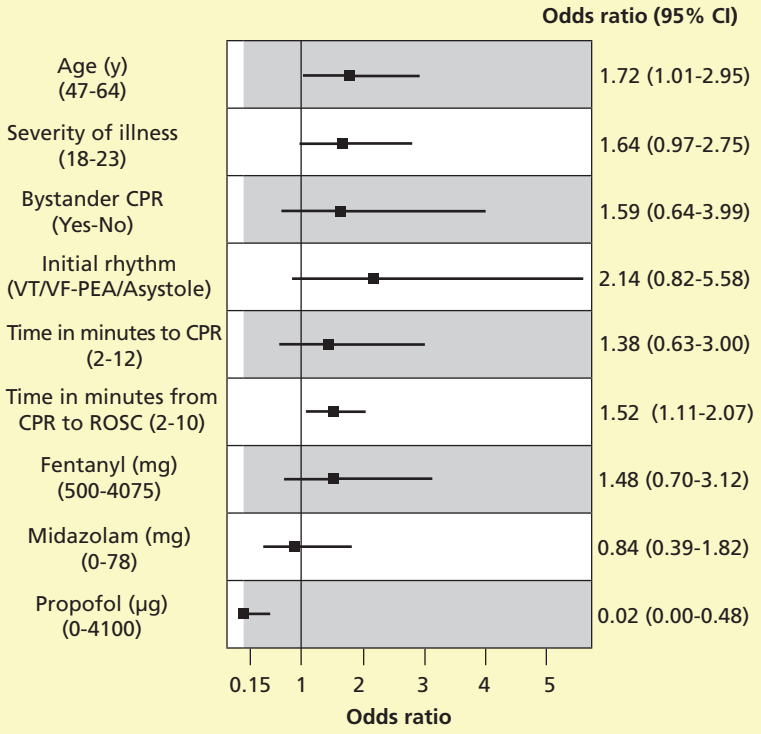

Figure 4 Effect of modifiable risk factors on duration of delirium associated with resuscitation or therapeutic hypothermia protocols.

Abbreviations: CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.

Second, we wished to examine factors exclusive to patients treated with therapeutic hypothermia, and we have no data on patients not treated with therapeutic hypothermia. Third, our institution limits us to a specific protocol for therapeutic hypothermia, which may limit the generalizability of our data. Fourth, our model included variables that were determined a priori. In order to prevent overfitting of our models, the list of confounders did not include all options, and unmeasured variables may exist that could alter our results.

> Older age and longer times from initiation of CPR to ROSC correlated with increased duration of delirium.

Fifth, the prevalence and duration of delirium in our results may exceed those in previous reports because we do not have differential measurements of CAM-ICU scores before and after a spontaneous awakening trial, and our results may include patients with rapidly reversible delirium due to sedation.[29] This effect most likely is small because of the high prevalence of delirium among patients without

exposure to sedatives in sensitivity analyses. Finally, we did not structure this study to assess the role of delirium in adverse outcomes, such as mortality or long-term cognitive impairment; this role remains unknown in patients treated with mild hypothermia after resuscitation from cardiac arrest.

Conclusion

The results of this retrospective observational study indicate a remarkably high prevalence of delirium during the ICU stay in patients treated with therapeutic hypothermia after cardiac arrest. Older ages and longer times from initiation of CPR to ROSC were associated with increased duration of delirium, and higher total propofol dose used during therapeutic hypothermia. Because of the marked effect of delirium on outcomes indicated in numerous other investigations, further prospective research is needed to understand the relationship between sedative and paralytic choice during therapeutic hypothermia and prevalence and duration of delirium, as well as the relationship between delirium and long-term outcomes in patients treated with therapeutic hypothermia after cardiac arrest.

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For more about delirium visit the *Critical Care Nurse* website, **www.ccnnonline.org**, and read the article by Rivosecchi, et al, "Nonpharmacological Interventions to Prevent Delirium: An Evidence-Based Systematic Review" (February 2015).

REFERENCES

1. Peberdy MA, Kaye W, Ornato JP, et al. Cardiopulmonary resuscitation of adults in the hospital: a report of 14 720 cardiac arrests from the National Registry of Cardiopulmonary Resuscitation. *Resuscitation.* 2003;58(3):297-308.
2. Stiell IG, Wells GA, Field B, et al; Ontario Prehospital Advanced Life Support Study Group. Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med.* 2004;351(7):647-656.
3. Hypothermia After Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest [published correction appears in *N Engl J Med.* 2002;346(22):1756]. *N Engl J Med.* 2002;346(8):549-556.
4. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med.* 2002;346(8):557-563.
5. Hazinski MF, Nolan JP, Billi JE, et al. Part 1: executive summary: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with treatment recommendations. *Circulation.* 2010;122(16)(suppl 2):S250-S275.
6. Nolan JP, Morley PT, Vanden Hoek TL, et al; International Liaison Committee on Resuscitation. Therapeutic hypothermia after cardiac arrest: an advisory statement by the advanced life support task force of the International Liaison Committee on Resuscitation. *Circulation.* 2003;108(1):118-121.
7. Nielsen N, Wetterslev J, Cronberg T, et al; TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. *N Engl J Med.* 2013;369(23):2197-2206.
8. Pandharipande P, Cotton BA, Shintani A, et al. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. *J Trauma.* 2008;65(1):34-41.
9. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *JAMA.* 2001;286(21):2703-2710.
10. Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med.* 2004;32(4):955-962.
11. Girard TD, Jackson JC, Pandharipande PP, et al. Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Crit Care Med.* 2010;38(7):1513-1520.
12. Pisani MA, Kong SY, Kasl SV, Murphy TE, Araujo KL, Van Ness PH. Days of delirium are associated with 1-year mortality in an older intensive care unit population. *Am J Respir Crit Care Med.* 2009;180(11):1092-1097.
13. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA.* 2004;91(14):1753-1762.
14. Ely EW, Gautam S, Margolin R, et al. The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med.* 2001;27(12):1892-1900.
15. Pisani MA, Murphy TE, Araujo KL, Van Ness PH. Factors associated with persistent delirium after intensive care unit admission in an older medical patient population. *J Crit Care.* 2010;25(3):540 e1-540.e7.
16. Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology.* 2006;104(1):21-26.
17. Lat I, McMillian W, Taylor S, et al. The impact of delirium on clinical outcomes in mechanically ventilated surgical and trauma patients. *Crit Care Med.* 2009;37(6):1898-1905.
18. Chamorro C, Borrallo JM, Romera MA, Silva JA, Balandin B. Anesthesia and analgesia protocol during therapeutic hypothermia after cardiac arrest: a systematic review. *Anesth Analg.* 2010;110(5):1328-1335.
19. Hollenbeck RD, Wells Q, Pollock J, et al. Implementation of a standardized pathway for the treatment of cardiac arrest patients using therapeutic hypothermia: "CODE ICE." *Crit Pathw Cardiol.* 2012;11(3):91-98.
20. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985;13(10):818-829.
21. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med.* 2001;29(7):1370-1379.
22. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med.* 2002;166(10):1338-1344.
23. Ely EW, Truman B, Shintani A, et al. Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). *JAMA.* 2003;289(22):2983-2991.
24. Vasilevskis EE, Morandi A, Boehm L, et al. Delirium and sedation recognition using validated instruments: reliability of bedside intensive care unit nursing assessments from 2007 to 2010. *J Am Geriatr Soc.* 2011;59(suppl 2):S249-S255.
25. McPherson JA, Wagner CE, Boehm LM, et al. Delirium in the cardiovascular ICU: exploring modifiable risk factors. *Crit Care Med.* 2013;41(2):405-413.
26. Uguz F, Kayrak M, Cíçek E, Kayhan F, Ari H, Altunbas G. Delirium following acute myocardial infarction: incidence,

clinical profiles, and predictors. *Perspect Psychiatr Care.* 2010;46(2):135-142.
27. Dumas F, Cariou A, Manzo-Silberman S, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. *Circ Cardiovasc Interv.* 2010;3(3):200-207.
28. Balas MC, Vasilevskis EE, Burke WJ, et al. Critical care nurses' role in implementing the "ABCDE bundle" into practice. *Crit Care Nurse.* 2012;32(2):35-38, 40-47.
29. Patel SB, Poston JT, Pohlman A, Hall JB, Kress JP. Rapidly reversible, sedation-related delirium versus persistent delirium in the intensive care unit. *Am J Respir Crit Care Med.* 2014;189(6):658-665.

CE 1.0 Hour

Notice to CE enrollees:

This article has been designated for CE contact hour(s). The evaluation tests your knowledge of the following objectives:

1. Describe the prevalence of delirium in patients treated with mild therapeutic hypothermia after cardiac arrest.
2. Evaluate for risk factors associated with prolonged duration of delirium after mild therapeutic hypothermia.
3. Consider factors that can be protective against delirium after mild therapeutic hypothermia.

To complete evaluation for CE contact hour(s) for test #A1625042, visit www.ajcconline.org and click the "CE Articles" button. No CE test fee for AACN members. This test expires on January 1, 2019.

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