Emergency Department Interventions and Their Effect on Delirium’s Natural Course: The Folly May be in the Foley

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Background: Delirium frequently affects older emergency department (ED) patients and has been associated with accelerated cognitive and functional decline, increased length of stay (LOS), and higher in- and out-of-hospital mortality. Objectives: Care provided in the ED may have downstream effects on delirium duration during hospitalization. This study aimed to identify the modifiable factors of ED care associated with delirium duration in patients admitted to the hospital through the ED. Materials and Methods: This prospective cohort study enrolled ED patients who were 65 years and older and admitted to the hospital. Delirium was determined in the ED and during the first 7 days of hospitalization using the modified Brief Confusion Assessment Method. All delirious patients and a random selection (17%) of nondelirious patients were also enrolled. ED LOS, opioid administration, benzodiazepine administration, anticholinergic medication administration, and bladder catheter placement were obtained by medical record review. Multivariable proportional odds logistic regression was performed to determine if each of the factors was associated with delirium duration after adjusting for age, dementia, baseline function, comorbidity burden, severity of illness, nursing home residence, and central nervous system insult. Results: A total of 228 patients were enrolled. ED bladder catheter placement was significantly associated (adjusted proportional odds ratio = 3.1, 95% confidence interval: 1.3 to 7.4) with increased delirium duration after adjusting for confounders. ED LOS, opioid administration, benzodiazepine administration, and anticholinergic burden, however, were not. Conclusions: ED bladder catheter placement was significantly associated with delirium duration and may present an opportunity for intervention.

Keywords: Delirium, geriatrics, psychiatry

Introduction

Delirium frequently affects approximately 7%–12% older emergency department (ED) patients.[1-11] This form of acute brain dysfunction has been associated with accelerated cognitive and functional decline, increased length of stay (LOS), and higher in- and out-of-hospital mortality.[4,5,12-16] Delirium in the ED persists into hospitalization in 70% of cases, lasting for a median of 3 days.[4,16] For every day, a patient remains delirious, there is an incremental worsening in long-term function and cognition.[16] Delirium also causes the patient and their family’s significant emotional distress.[17] Interventions that reduce delirium duration and its negative sequelae are needed.

Unfortunately, there is no recommended treatment for delirium, especially in the ED setting.[18] Most interventions focus on modifying risk factors for delirium development but have not been shown to change the course of delirium once it has occurred.[19] With the goal of changing both the development and course of delirium, studies that identify modifiable risk factors for delirium duration are needed.

Furthermore, early treatment of delirium in the ED may further enhance the efficacy of any delirium intervention. The ED is the gateway for the majority of hospital admissions, and the care
provided in the ED often has downstream effects on patient care during hospitalization. Early intervention has been shown to improve outcomes in other syndromes, such as sepsis, acute coronary syndromes, and acute ischemic stroke.[20-22]

As the initial step of developing an ED intervention for delirium, we sought to identify the modifiable factors of ED care associated with delirium duration in patients admitted to the hospital through the ED.

Materials and Methods

This was a secondary analysis of a prospective cohort study entitled the Delirium in the ED and Its Extension into Hospitalization (DELINATE) study which enrolled older ED patients admitted to the hospital.[16] This study’s primary objectives were to describe the extent to which delirium in the ED persisted into hospitalization (ED delirium duration) and to determine how ED delirium duration was associated with 6-month functional status and cognition. The DELINATE study was conducted at a tertiary care, academic ED that evaluated approximately 67,000 patients annually. The Vanderbilt University Institutional Review Board (IRB) reviewed and approved this study (IRB # 111580).

Enrollment for the DELINATE study occurred between March 2012 and November 2014. Patients were included if they were 65 years or older, in the ED for <4 h at the time of enrollment, and unlikely to be discharged home according to the ED physician. Patients were excluded if they were non-English speaking, previously enrolled, deaf, comatose, nonverbal, or unable to follow simple commands before their current illness, they were considered unsuitable for enrollment by the treating physician or nurse, they were unavailable for enrollment with the 4-h time limit secondary to clinical care (e.g., resuscitations, procedures), or they were discharged home from the ED. Patients who were nonverbal or unable to follow simple commands before their acute illness were considered to have end-stage dementia and were excluded because the delirium assessment used in this study was not validated for this patient group. There were no additional eligibility criteria for this secondary analysis.

Consecutive enrollment occurred Monday through Friday at four randomly selected 4-h blocks per week (8A–12P, 10A–2P, 12P–4P, and 2P–6P) for a total of 16 h/week. Since 83%–92% of older enrolled ED patients would be nondelirious, all delirious and one out of six (~16.7%) randomly selected nondelirious older ED patients were enrolled to maximize the feasibility of our study.[1,11,13]

The specific ED interventions investigated were ED LOS, ED opioid administration, ED benzodiazepine administration, anticholinergic burden (ACB) of ED medication administration, and ED bladder (Foley) catheter placement.[23,24] We also recorded if the patient had an indwelling catheter that was placed before the ED arrival. ED opioid and benzodiazepine use was dichotomized for the purposes of this analysis. ED ACB was quantified using the ACB which assigned values of 0 (no cholinergic activity) to 3 (strong anticholinergic activity) to each medication.[23,24] The total ACB score is the sum of each medication’s cholinergic activity. These data were obtained by medical record review. We performed double data entry to verify the data entered were accurate. The primary outcome variable delirium duration was defined as the total number of days a patient being delirious in the ED and the first 7 days of hospitalization. Delirium was assessed in the ED at the time of enrollment (0 h) and at 3 h and once daily (usually in the mornings) during the hospitalization for 7 consecutive days after the ED visit or until hospital discharge, whichever came first. A patient was considered to be delirious in the ED if either the 0- or 3-h delirium assessment was positive. Patients who were never delirious in the ED or hospital were considered to have delirium duration of 0 days.

Delirium was determined by trained research assistants who received a 6–8-h training session which included didactic lectures, as well as simulated and live patient encounters. They were also involved in the validation of the delirium assessments used in this study.[25] In nonmechanically ventilated patients, delirium was ascertained using a modified Brief Confusion Assessment Method (bCAM), which is a brief (≤2 min) delirium assessment designed for use in the ED setting.[25] The bCAM uses the short-form CAM diagnostic algorithm.[26] In older ED patients, the modified bCAM is 82%–86% sensitive and 93%–96% specific for delirium as diagnosed by a psychiatrist, and its kappa is 0.87, indicating excellent interobserver reliability.[25] In mechanically ventilated patients, the CAM for the intensive care unit (CAM-ICU) was used to ascertain delirium.[27] The CAM-ICU is 93%–100% sensitive and 98%–100% specific for delirium in these patients, with a kappa of 0.96 indicating excellent interobserver reliability.[28] One hundred and ten (7.9%) out of 1399 bCAM or CAM-ICU assessments were missing because the patient was not available due to a prolonged procedure or diagnostic test or the patient refused. Because delirium status is highly correlated with the previous day, missing delirium assessments were imputed using last observation carried forward method.

Preillness function was determined in the ED using the Older American Resources and Services Activities of Daily Living questionnaire.[29] This scale was completed by the informant or patient and ranged from 0 (completely dependent) to 28 (completely independent). Medical record review was obtained to collect dementia status, comorbidity burden, severity of illness, and presence of a central nervous system (CNS) diagnosis. A patient was considered to have dementia if they had (i) documented dementia in the medical record, (ii) a premorbid short-form Informant Questionnaire on Cognitive Decline in the Elderly score (IQCODE) greater than a cutoff of 3.38, or (iii) prescribed cholinesterase inhibitors before admission.[30] The Charlson comorbidity index was used to quantify the patient’s comorbidity burden.[31] The IQCODE was completed by an informant who knew...
the patient well for >10 years. The Acute Physiology Score of the Acute Physiology and Chronic Health Evaluation II score was used to quantify severity of illness. The presence of a CNS diagnosis (meningitis, seizure, cerebrovascular accident, intraparenchymal hemorrhage, etc.,) was determined by two physician reviewers via medical record review. Any disagreement was adjudicated by a third physician reviewer.

This secondary analysis’ sample size was limited to 228 patients enrolled in the original DELINATE study. Measures of central tendency and dispersion for continuous variables were reported as medians and interquartile ranges; no transformation was performed for continuous variables. Categorical variables were reported as frequency (percentage). To determine if each ED-specific intervention was associated with delirium duration, proportional odds (or ordinal) logistic regression analyses were performed. Ordinal logistic regression was performed because delirium duration’s distribution was skewed [Figure 1]. Each model was adjusted for age, dementia, baseline function, comorbidity burden, severity of illness, nursing home residence, and CNS insult. For the bladder catheter model, we also adjusted for preexisting indwelling bladder catheter. For all models, the score Chi-square test was performed to determine if the proportionality odds assumption was met between the main effect and outcomes. A P > 0.05 indicated that the proportionality odds assumption was met. Unadjusted and adjusted proportional odds ratios (POR) with their 95% confidence intervals (95% CIs) were reported. All statistical analyses were performed with SAS version 9.4 (SAS Institute, Carey, NC, USA).

**RESULTS**

During the study period, 3383 older ED patients were screened. We enrolled 105 delirious ED patients and a random selection of 123 nondelirious ED patients, as detailed in Figure 2.

The description of our cohorts is summarized in Table 1. Delirious ED patients were more likely to be female, demented, having poorer preillness function, and a chief complaint of altered mental status. For all enrolled patients, the median (interquartile range(IQR)) total days with delirium were 1 (0, 3) days.

Table 2 lists the effect of each ED intervention on the total number of days delirious. ED bladder placement was the only ED intervention significantly associated with increased delirium duration.

**Table 1: Patient characteristics and demographics**

|                      | Nondelirious ED patients (n=123) | Delirious ED patients (n=105) |
|----------------------|-----------------------------------|-------------------------------|
| Age, median (IQR)    | 73 (69-80)                        | 75 (68-83)                    |
| Female gender, n (%) | 58 (47.2)                         | 68 (64.8)                     |
| Nonwhite race, n (%) | 12 (9.8)                          | 18 (17.1)                     |
| Nursing home residence, n (%) | 2 (1.6) | 5 (4.8) |
| Dementia, n (%)      | 31 (25.2)                         | 77 (73.3)                     |
| OARS ADL, median (IQR) | 26 (21-27)             | 16 (11-23)                    |
| IQCODE, median (IQR) | 3.19 (3.00-3.56)                  | 4.06 (3.28-4.69)              |
| Charlson, median (IQR) | 3 (2-5)                      | 3 (2-5)                       |
| APS, median (IQR)    | 4 (1-6)                           | 4 (2-6)                       |
| ED chief complaint, n (%) | 5 (4.1)                   | 7 (6.7)                       |
| Abdominal pain       | 4 (3.3)                           | 37 (35.2)                     |
| Chest pain           | 23 (18.7)                         | 0 (0.0)                       |
| Generalized weakness | 7 (5.7)                           | 11 (10.5)                     |
| Nausea/vomiting      | 8 (6.5)                           | 1 (1.0)                       |
| Shortness of breath  | 20 (16.3)                         | 5 (4.7)                       |
| Syncope              | 8 (7.3)                           | 0                             |
| *Incident delirium, n (%) | 12 (9.8)                  | 6 (5.7)                       |

*Incident delirium were delirium episodes that occurred after an episode of ED delirium resolved (2 consecutive days with negative delirium assessments) or new onset delirium that occurred in those who were not delirious in the ED. IQR: Interquartile range, APS: Acute physiology score, ED: Emergency department, OARS: Older American resources and services, ADL: Activities of daily living, IQCODE: Informant questionnaire on cognitive decline in the elderly.

**Figure 1:** Distribution of patients for each delirium duration day. Patients who were never delirious in the emergency department or hospitalization were assigned a delirium duration of 0 days.

**Figure 2:** Flow diagram of patients.
duration in both the unadjusted (POR = 3.7, 95% confidence interval [CI]: 1.6–8.2) and adjusted analyses (adjusted POR = 3.1, 1.3–7.4). In the unadjusted analysis, ED ACB was significantly associated with shorter delirium duration (POR = 0.6, 95% CI: 0.4–0.9), but this association was no longer significant after adjusting for age, dementia, baseline function, comorbidity burden, severity of illness, nursing home residence, and CNS insult (adjusted POR = 0.7, 95%CI: 0.4–1.2). ED LOS, ED opioid administration, ED benzodiazepine administration, and ED ACB were not significantly associated with the total number of days delirious. For all the models, the Chi-square test’s P values ranged from 0.0893 (ED benzodiazepine use) to 0.8855 (ED Foley catheter use), indicating that the proportionality assumption was met.

**Discussion**

Delirium frequently occurs in older ED patients and has negative consequences for the patient. Delirium interventions, especially for the ED, are lacking. As a first step to intervention development, we conducted this prospective cohort study of older ED patients being admitted to the hospital to identify the modifiable risk factors for delirium duration. In the adjusted analyses, we found that bladder catheter placement in the ED was associated with an increase in delirium duration, after adjusting for confounders. ED LOS and opioid, benzodiazepine, and anticholinergic medication administration were not observed to be associated with delirium duration. Because approximately 10% of our older ED patients had bladder catheters placed, this represents an opportunity for intervention and can potentially reduce the total number of days a patient is delirious.

We observed that urinary bladder catheterization was associated with an increase in the total number of days delirious, consistent with previous studies in older ED patients. This finding adds to the existing literature being reported that older hospitalized patients who receive urinary bladder catheterization are at increased risk to develop delirium (incident delirium) by twofold. In addition to delirium, urinary bladder catheterization has other negative sequelae associated with it. It is the leading cause of healthcare-acquired urinary tract infections, and it also increased hospital length of days and higher risk of death during hospitalization and 90 days. Consequently, placing urinary bladder catheters in the ED or any setting should be avoided unless absolutely clinically indicated. Because we observed that 10% of our cohort had a urinary bladder catheter placed in the ED, this presents an opportunity for intervention to reduce delirium duration.

In contrast to urinary bladder catheter placement, our data suggest that reducing ED opioid, anticholinergic, and benzodiazepine medication may not improve delirium duration. While previous studies have suggested that these medication classes are associated with delirium, most were conducted postoperative and inpatient settings and may have limited generalizability to the older ED patient population.

There are several potential reasons for these discordant findings. Many of these studies evaluated how these drug classes increased the risk of the development of delirium, whereas a substantial proportion of our patients were delirious at enrollment. In addition, only 3% of our patients received benzodiazepines, so the ability to detect an association with benzodiazepines and delirium duration may have been limited. Finally, pain itself has been associated with increased delirium, so ED administration of opioid medications may be protective in some cases.

We did not find an association between ED LOS and delirium duration. Previous studies have observed that prolonged ED LOS increases the risk or odds of incident delirium. Inouye et al. observed that ED LOS >12 h was associated with a twofold increased odds of developing delirium during hospitalization. More recently, Bo et al. observed that ED LOSs >10 h similarly increased the odds of delirium. This suggests that reducing ED LOS may be more useful in preventing delirium rather than treating delirium after it occurs.

Our study has several notable limitations. First, it was a single-center study performed at an academic hospital, so its results may not be generalizable to other settings. Second, this was a secondary analysis and it is possible that type 1 error (false positive) may have occurred. Conversely, there were low numbers of some of the ED interventions such as benzodiazepine administration. It is possible that type 2 error (false negative) may have occurred. Our study should be confirmed in other settings. Third, we did not evaluate how these interventions impact long-term outcomes such as cognition, function, or mortality due to the limited number of delirious patients enrolled. Future studies should investigate how these risk factors impact such outcomes in delirious

### Table 2: Multivariable proportional odds logistic regression models to identify emergency department-specific modifiable factors for delirium duration

| Independent variable | Nondelirious ED patients (n=123) | Delirious ED patients (n=105) | Unadjusted POR (95% CI) | Adjusted POR (95% CI) | C-statistic for adjusted model |
|----------------------|---------------------------------|-------------------------------|-------------------------|------------------------|-------------------------------|
| ED LOS (h)           | 8.7 (7.0-12.4)                  | 9.1 (6.6-11.9)                | 1.0 (1.0-1.0)           | 1.0 (1.0-1.0)           | 0.773                         |
| ED opioid administration | 34 (27.6)                     | 18 (17.1)                     | 0.6 (0.3-1.1)           | 0.8 (0.4-1.6)           | 0.774                         |
| ED benzodiazepine administration, % | 4 (3.3)                     | 3 (2.9)                       | 0.7 (0.2-3.0)           | 1.6 (0.4-6.8)           | 0.772                         |
| ED medication anticholinergic burden | 0 (0-1)                     | 0 (0-1)                       | 0.6 (0-4-9)             | 0.7 (0.4-1.2)           | 0.774                         |
| ED Foley placement, % | 5 (4.1)                        | 16 (5.2)                      | 3.7 (1.6-8.2)           | 3.1 (1.3-7.4)           | 0.783                         |

*P value provided for adjusted POR. POR: Proportional odds ratio, 95% CI: 95% confidence interval, LOS: Length of stay, ED: Emergency department
patients. Fourth, the modified bCAM is 82%–86% sensitive and misclassification may have occurred, and this may have over- or under-estimated our estimates. However, we used modified bCAM because it could be reliably performed by nonclinical research personnel and it has been validated in older ED patients. Fifth, we did not adjust for care provided beyond the ED, which may have led to residual confounding, such as duration of bladder catheter use.

Conclusions
We observed that urinary bladder catheter placement was associated with prolonged delirium duration and may present an opportunity for intervention. ED opioid, benzodiazepine, and anticholinergic medication use and ED LOS were not associated with prolonged delirium duration.

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Conflicts of interest
There are no conflicts of interest.

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