Length of Stay in the Emergency Department and Occurrence of Delirium in Older Medical Patients

LENGTH OF STAY IN THE EMERGENCY DEPARTMENT AND OCCURRENCE OF DELIRIUM AMONG OLDER MEDICAL PATIENTS

Bo Mario[1] MD, PhD; Bonetto Martina[2] MD; Bottignole Giuliana[1] MD; Porrino Paola[1] MD; Coppo Eleonora[1] MD; Tibaldi Michela[1] MD; Ceci Giacomo[1] MD; Raspo Silvio[2] MD; Cappa Giorgetta[2] MD; Bellelli Giuseppe[3] MD.

[1]SCDU Geriatria e Malattie Metaboliche dell'Osso; Città della Salute e della Scienza-Molinette. C.so Bramante 88, 10126 Torino Italia.

[2] S. C. Geriatria e Cure Intermedie - ASO S. Croce e Carle - Cuneo

[3]Dipartimento di Scienze della Salute, Università Milano-Bicocca, Milan and S. Gerardo Hospital, Acute Geriatric Unit, Monza, Italia

Corresponding author:

Paola Porrino

[1]SCDU Geriatria e Malattie Metaboliche dell'Osso; Città della Salute e della Scienza-Molinette.

postal address: C.so Bramante 88, 10126 Torino, Italy.

e-mail: paolapo1985@yahoo.it

Telephone number: 011-6336660

Fax number: 011- 6961045

Alternate corresponding author:

Giuliana Bottignole

[1]SCDU Geriatria e Malattie Metaboliche dell'Osso; Città della Salute e della Scienza-Molinette.

27 postal address: C.so Bramante 88, 10126 Torino, Italy.

28 e-mail: giulianabottignole@gmail.com

29 Telephone number: 011-6336660

30 Fax number: 011- 6961045

31

ABSTRACT

BACKGROUND: Intervention on modifiable risk factors for delirium is central to prevention and might translate into better prognosis, shorter hospital stays, higher rates of home discharge and reduced health costs for older inpatients.

OBJECTIVES: We aimed to evaluate whether Emergency Department (ED) length of stay before ward admission is associated with incident delirium among older patients.

DESIGN: Prospective cohort study

SETTING: Patients were evaluated for delirium in the ED and during the first three days in medical/geriatric wards.

PARTICIPANTS: 330 patients aged ≥75 year. Exclusion criteria: delirium at ED entry, coma, aphasia, stroke, language barrier, psychiatric disorder and alcohol abuse.

MEASUREMENTS: On ED admission, patients underwent standardized evaluation of comorbidity (Cumulative Illness Rating Scale, CIRS), cognitive impairment (Short Portable Mental Status Questionnaire, SPMSQ), functional independence (Activities of Daily Living, ADL, Instrumental Activities of Daily Living, IADL), pain (Numeric Rating Scale, NRS), and acute clinical conditions (Acute Physiology and Chronic Health Evaluation II, APACHE II score). During the first three days after ward admission, the presence of delirium (defined as at least one delirium episode within 72 hours) was daily assessed using the 4AT scale. ED length of stay was calculated as the time (hours) between ED registration and when the patient left the ED.

RESULTS: ED length of stay longer than 10 hours (OR 2.23, 95% C.I. 1.13 – 4.41), moderate-severe cognitive impairment (OR 5.47, 95% C.I. 2.76 – 10.85) and increasing age (OR 1.07, 95% C.I 1.01 – 1.13) were associated with delirium onset.

CONCLUSION: ED length of stay > 10 hours was associated with greater risk of delirium in hospitalized older patients, after adjusting for age and cognitive impairment.

INTRODUCTION

Older patients are frequently ill and, due to a greater severity of their illnesses, they require more exams and are hospitalized more often than the non-elderly (1). Moreover, the elderly have a greater level of urgency, longer average length of stay and greater risk of adverse events, including delirium, functional decline, readmission to the ED, and death (1 - 3).

According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition, (DSM-5) (4) delirium is a serious neuropsychiatric condition, characterized by acute and fluctuating disturbance in attention, orientation, and alteration in other cognitive domains and in the level of consciousness. Delirium represents a common disorder among older hospitalized patients, prevalence on admission ranging from 10% to 31% and incidence from 6% to 56% (5 - 8); it is related to increased short- and long-term mortality, long length of hospital stay, poor functional status, need for institutional care, and great national health expenditure (7, 9 -11). Therefore, the Assessing Care of Vulnerable Elders Project has ranked delirium among the top conditions for which the quality of care needs to be improved (9). The development of delirium involves the complex interrelationship between a vulnerable patient and exposure to precipitating factors or noxious insults (6, 12). Current evidence suggests that the most successful strategy to delirium prevention includes a multicomponent approach to modifiable risk factors (6, 13, 14). Since hospitals present several inherent risks for the development of delirium in elderly patients (15), identification of correctable hospitalization-related conditions predisposing to delirium might be extremely useful in daily clinical practice (16, 17). To the best of our knowledge the association between ED length of stay and delirium has not been investigated in older medical patients. Therefore, we aimed to evaluate whether ED length of stay is associated with incident delirium among older patients.

METHODS

This prospective cohort study was conducted within two University teaching hospitals (Città della Salute e della Scienza, Molinette, Torino and Azienda Ospedaliera S. Croce e Carle, Cuneo, Piemonte, Northern Italy), between November and December 2014. The study protocol was in accordance with the recommendations of the World Medical Association for biomedical research involving human subjects, and approved by hospital Ethic Committee. Informed consent was obtained from the patients or, for those with cognitive impairment, from a proxy (closest relative or legal tutor).

All patients aged 75 years or older consecutively admitted to the ED were eligible to the study, if they were not delirious, had not coma, aphasia, stroke, language barrier and history of primary psychiatric disorder or alcohol abuse.

Delirium assessment

The presence of delirium was screened using the 4AT (18), a brief and easy to use tool (its administration requires no more than 2 min and does not require special training) which has been recently validated in older hospitalized patients (18). This scale comprises four items (18). Item 1 assesses level of alertness. The next two items are brief cognitive screening tests: the Abbreviated Mental Test—4 (AMT-4) and attention testing with Months Backwards. Item 4 assesses acute change or fluctuation in mental status. The 4AT is scored from 0 to 12, where 0 suggests that delirium and/or moderate to severe cognitive impairment is unlikely, scores 1 - 3 suggest possible moderate to severe general cognitive impairment (that is, corresponding to moderate to severe impairment on standalone dementia screening tools), and a score of 4 or above suggests possible delirium. A score of 4 or more can be generated by the positive level of alertness or change items, or un-testability on both cognitive items. Combinations of positive features may generate higher scores (for example, a drowsy, untestable patient who has a clear change in mental status would have a score of 12). In the

validation study, a score > 4/12 at the 4AT had a sensitivity of 89.7% and specificity 84.1% for delirium (83.3% and 91.3% among non-demented subjects, and 94.1% and 64.9% among demented patients, respectively). The areas under the receiver operating characteristic curves for delirium diagnosis were 0.93 in the whole population, 0.92 in patients without dementia and 0.89 in patients with dementia, suggesting good specificity to delirium in a dementia-free population, and good sensitivity to delirium in a dementia population (18).

In this study the 4AT was carried out as soon as possible in all patients after their ED arrival (3.3±1.1 hours since ED entry) by four geriatric postgraduate students, two for each hospital, trained over a 1-month period in using the 4AT scale to detect delirium within an acute geriatric ward. At the same time, two senior geriatricians, one at each hospital, supervised the administration of 4AT at ED arrival and diagnosed delirium, according to DSM-5 (4). This approach was undertaken because DSM-5 criteria represent the gold standard method for the diagnosis of delirium. The post-graduate students were not allowed to know the diagnosis made by the senior geriatricians and the senior geriatricians were not involved in the care of patients during their stay in ED. For those patients who were critically ill, proxy respondents were used as the primary source of information, using a hierarchy of proxies (8). Each proxy was specifically asked whether he or she could report on the patient's functional and mental abilities as evident before the patient's hospital admission. Patients who had not exclusion criteria, provided informed consent and were admitted to an acute medical or geriatric ward of the two hospitals, constituted the study sample.

Multidimensional geriatric assessment

On ED admission, demographic and relevant clinical data were collected. Standardized scales were used to evaluate comorbidity (Cumulative Illness Rating Scale, CIRS, the higher the score, the greater the number and severity of diseases) (19), cognitive impairment (Short Portable Mental Status Questionnaire, SPMSQ, the higher the score, the greater the

severity of cognitive impairment) (20), functional status (Activities of Daily Living, ADL, range: 0 – 6, higher scores indicate lower performance; Instrumental Activities of Daily Living, IADL, range: 0 –14, lower scores identify dependent subjects) (21, 22), pain (Numeric Rating Scale, NRS) (23) and illness severity (Acute Physiology and Chronic Health Evaluation II, APACHE II score) (24). ED length of stay was calculated as the time (hours) between ED registration and the time when the patient left the ED.

Outcome measures

The main outcome measure was the ascertainment of at least one delirium episode within 72 hours while the patient was admitted to the acute geriatric and medical wards. During this period patients were daily assessed for the presence of delirium using the same procedures described above for delirium assessment during ED stay.

Data analysis

Sample size for the variable time of stay in ED was calculated considering $\beta=0.9$ and $\alpha=0.05$, yielding a minimum sample size of 215 patients.

Continuous variables are presented as median (interquartile), while categorical data are presented as number and proportions. The normal distribution of the quantitative variables, after a pre-test for homogeneity of variances, was evaluated using a graphical method and the Kolmogorov-Smirnov test. If abnormal distribution was present, a nonparametric test was used (Mann-Whitney U test). Categorical variables were analyzed by the chi-square test.

Covariates were selected as categorical variables according to a recent review by Ahmed et al (25) on delirium among older hospitalized patients, and included severe cognitive impairment (SPMSQ $\geq$ 6), severe comorbidity (CIRS $\geq$ 5), severe acute clinical conditions (APACHE > 15), functional dependence (ADL $\geq$ 3), polypharmacy (daily drugs taken $\geq$ 11), one or more hospital admissions during last year, presence of urinary catheter, low albumin levels (< 3.4 g/dl), dehydration/renal failure (blood urea/creatinine ratio >18), low sodium

157 levels (< 133 mEq/l), anemia (hematocrit < 30% and/or hemoglobin levels < 10 g/dl), high
158 glucose levels (> 140 mg/dl), and severe pain (NRS ≥ 2).
159 Univariate analysis was performed using Mann-Whitney U test for continuous variables and
160 χ^2 test for categorical variables. Variables associated with delirium occurring during
161 admission to medical and geriatric wards were then introduced in a logistic regression for
162 multivariate modeling (forward stepwise method) to identify variables independently
163 associated with delirium incidence in the whole sample of patients. The variable ED length of
164 stay was measured in hours and divided into quartiles; the 75° percentile identified those who
165 had a ED length of stay greater than 10 hours.
166

RESULTS

During the study period 1112 patients aged 75 years or older were admitted to the ED of the two hospitals, and 691 patients were discharged directly from the ED or admitted to surgical or specialty units. Among the 421 eligible patients, 54 patients or proxies did not give consent to participation and exclusion criteria were identified in 37 patients (13 patients had delirium at entry, 15 patients had stroke, 5 were in coma, and 4 had psychiatric disorders), leaving an overall sample of 330 patients (mean age 83.2 ± 5.4 years, 51.8% males) for analysis. Main demographic and clinical variables are reported in Table 1. Most of patients were community-dwellers living alone or with relatives, and had not hospital admissions during last years; functional dependence and at least moderate cognitive impairment were observed in roughly half and one-third of them, respectively. Median length of ED stay was 5 hours (interquartile range 3.0-10.0 hours), and median length of stay in hospital was 10 days, with more than 90% of patients discharged at home.

During the first three days from ward admission, delirium was diagnosed in 52 patients (15.8%): 16 (4.8%) cases occurred in the first day, 20 (6.2%) during the second day and 16 (4.8%) during the third day. Increasing age, moderate-severe cognitive impairment, urinary catheter placement and ED length of stay longer than 10 hours were associated with delirium occurrence at univariate analysis (Table 2). All of these variables, with the exception of urinary catheter placement in ED, were found to be independently associated with delirium occurrence (Table 3).

In the overall sample, several variables (increasing age, functional dependence, comorbidity, severity of pain and illness severity at entry, dehydration/renal failure and high glucose levels at entry) were found to be associated with ED length of stay >10 hours, but only greater severity of acute pathophysiological state (APACHE score >15) and greater burden of comorbidity (CIRS score ≥ 5) were independently associated with longer ED permanence.

Among patients who had a ED length of stay greater than 10 hours, increasing age, moderate-severe cognitive impairment and placement of urinary catheter were independently associated with higher incidence of delirium, the latter two being associated with a fivefold and fourfold increased risk of delirium occurrence, respectively.

DISCUSSION

In a cohort of older in-patients we observed that ED stay longer than 10 hours was associated with a more than twofold increased risk of developing delirium in the following 72 hours. Increasing age and moderate-severe cognitive impairment were also associated with higher risk of incident delirium. Illness severity and burden of comorbidity were associated with longer ED permanence. Among patients who remained in ED more than 10 hours, in addition to age, moderate-severe cognitive impairment and urinary catheter placement were predictors of developing delirium in acute wards, with a risk that increased by more than fivefold and fourfold, respectively.

Dementia and cognitive impairment (7, 8), as well as urinary catheter placement (26), are well-recognized risk factors for in-hospital delirium occurrence. In keeping with the vulnerability model postulated by Inouye and Charpentier (27), our findings suggest that prolonged ED length of stay might be a crucial environmental variable contributing to the risk of developing delirium, particularly among the most prone patients, that is those at older age and cognitively impaired. Several factors associated with longer ED permanence – such as the stress of being in an unfamiliar overcrowded and noisy environment, delayed boarding of admitted patients, bed rest, iatrogenic harm from procedures or medication administration - might predispose to delirium onset (2, 3, 7, 15 – 17, 28).

Another plausible although unlikely explanation is that delirium occurred in those patients with more severe predisposing and precipitating factors, as indirectly supported by the finding that APACHE II score and comorbidity were predictors of longer stay at ED in the

overall sample of patients. Therefore, development of delirium may reflect both an exposure to more serious environmental and biological stressors and/or an increased vulnerability of elderly patients.

Because incident delirium during hospital stay is associated with short- and long-term adverse outcomes (7, 9-11), there seems to be a rationale to evaluate whether interventions addressed to shorten the ED length of stay (or to make it more comfortable) may reduce the incidence of delirium in older vulnerable patients. Finally, present findings reinforce the clinical and educational potential for implementing geriatric evaluation, including the systematic use of tools such as the 4AT, the CAM and bCAM (29, 30) at ED admission to accurately address the complexity of older patients within this clinical setting. Furthermore, since the relevant proportion of patients developing incident delirium post-ED discharge, the study suggests that training and educational approaches are needed for healthcare workers to identify patients at risk and rapidly start initiatives for prevention (9, 16, 17).

A strength of the study is that, according to a previous experience (8), the diagnosis of delirium was performed by senior geriatricians who did not participate in the clinical care of enrolled patients, thus reducing the risk of influencing the outcomes of the study. Another strength is that delirium was diagnosed using both a validated tool (i.e., the 4-AT) and current gold standard (i.e., DSM-5) criteria which, however, are time consuming and require specific knowledge. We do believe that in such a way we have increased both our sensitivity in delirium detection and our accuracy in diagnosing this condition. Some limitations should also be addressed. Firstly, the sample studied was enrolled in two tertiary hospitals in Piemonte, northern Italy; therefore, these findings should be wisely generalized to different clinical settings. A second limitation is the relatively small sample size which, however, is not different from previous studies on delirium incidence in medical settings (25). Thirdly, we cannot exclude that, due to the fluctuating nature of this syndrome, we may have

misclassified some patients who were diagnosed as not having delirium at ED arrival; however, it is unlikely that a misclassification may have occurred only in patients without delirium at ED. Fourth, it could be argued that a period of observation longer than 72 hours after admission to geriatric/medical wards might have increased the number of cases of incident delirium, but would have also diluted the contributing role of ED length of stay to delirium occurrence.

In conclusion, in this observational cohort study we observed that ED length of stay greater than 10 hours is associated with increased risk of delirium onset in hospitalized older patients after adjusting for age and cognitive impairment. Although ED length of stay was mainly determined by greater comorbidity burden and severity of clinical conditions, these findings suggest that efforts should be made in order to reduce undue permanence of frail older patients in this unfriendly clinical setting.

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Conflict of Interest Disclosures:

Elements of Financial/Personal Conflicts	All authors		Author 2		Author 3		Author 4	
	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X						
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Stocks		X						
Royalties		X						
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Table 1. Main demographic and clinical variables in the overall sample of patients (330 patients). #: median (interquartile range); *: Number (%)

Age (years) #	82.8 (79.2 – 87.0)
Males*	171 (51.8%)
Home dwelling * nursing home residents *	290 (87.9%) 36 (10.9%)
Living * alone with relatives with carer	 95 (31.5%) 184 (60.9%) 23 (7.6%)
Hospital admissions during last year * 0 1-2 ≥ 3	 213 (64.9%) 102 (31.1%) 13 (4.0%)
Daily number of drugs * < 5 5-10 ≥ 11	 106 (32.2%) 190 (57.8%) 33 (10%)
ADL (score) #	2.0 (0.0 – 5.0)
Functional Dependence (ADL ≥ 3)*	158 (49.1%)
Bedridden *	17 (5.2%)
IADL (score) #	7.0 (4.0 – 10.0)
SPMSQ (score) #	4.0 (1.0 – 7.0)
Moderate-severe cognitive impairment (SPMSQ ≥ 6)*	110 (35.6%)
CIRS 2 (score) #	3.0 (2.0 – 5.0)
Severe comorbidity (CIRS ≥ 5)*	84 (26.0%)
APACHE (score) #	11.0 (5.2 – 15.4)
Severe APACHE score (APACHE>15)*	34 (10.5%)
Pain (score) #	0.0 (0.0 – 1.0)
Severe pain (NRS > 2)*	103 (33.3%)
Hematocrit < 30%*	42 (12.9%)
Blood Urea/Creatinine ratio > 18*	122 (39.9%)
Sodium (Na) serum levels< 133 mEq/l*	39 (11.8%)
Blood glucose (HGT) serum levels > 140 mg/dl*	144 (43.9%)
Albumin serum levels < 3.4 g/dl*	49 (44.5%)
Length of stay in ED (hours) #	5.0 (3.0 – 10.0)
Urinary catheter placement in ED *	40 (12.1%)
Length of stay in ward (days) #	10.0 (5.6 – 15.1)

Table 2. Main demographic and clinical variables according to incidence of delirium within 72 hours since ward admission: univariate analysis. #: median (interquartile range); *: Number (%)

	Overall sample (330 patients)	WITH Delirium 52 patients (15.8%)	WITHOUT Delirium 278 patients (84.2%)	p value
Age (years) #	82.5 (79.2 – 87.0)	85.3 (80.3 – 90.0)	82,3 (78,8 – 86.4)	**0.009**
Men* Women *	171 (51.8%) 159 (48.2%)	31 (18.1%) 21 (13.2%)	140 (81.9%) 138 (86.8%)	0.282
Functional dependence ADL ≥ 3 * ADL <3 *	158 (49.1%) 164 (50.9%)	24 (15.2%) 26 (15.9%)	134 (84.8%) 138 (84.1%)	0.992
Moderate-severe cognitive impairment SPMSQ ≥ 6 * SPMSQ < 6 *	119 (36.3%) 209 (63.7%)	37 (31.1%) 14 (6.7%)	82 (68.9%) 195 (93.3%)	**0.000**
Severe Comorbidity CIRS ≥ 5 * CIRS < 5 *	91 (27.6%) 239 (72.4%)	21 (23.1%) 31 (13%)	70 (76.9%) 208 (87%)	0.667
Severe APACHE score APACHE >15 * APACHE <=15 *	34 (10.5%) 291 (89.5%)	5 (14.7%) 47 (16.2%)	29 (85.3%) 244 (83.8%)	1.000
Severe Pain* NRS > 2 * NRS <=2 *	103 (33.3%) 206 (66.7%)	21 (20.4%) 27 (13.1%)	82 (79.6%) 179 (86.9%)	0.134
Bedridden Yes * Not *	17 (5.2%) 312 (94.8%)	4 (23.5%) 48 (15.4%)	13 (76.5%) 264 (84.6%)	0.579
Urinary catheter in ED Yes * Not *	40 (12.1%) 290 (87.9%)	12 (30%) 40 (13.8%)	28 (70%) 250 (86.2%)	**0.016**
Anemia Htc < 30% * Htc ≥ 30% *	42 (12.9%) 283 (87.1%)	8 (19%) 44 (15.5%)	34 (81%) 239 (84.5%)	0.725
Dehydration/Renal failure Blood Urea/Creatinine ratio > 18 * Blood Urea/Creatinine ratio <=18 *	122 (39.9%) 184 (60.1%)	21 (17.2%) 28 (15.2%)	101 (82.8%) 156 (84.8%)	0.759
Low sodium levels Na < 133 * Na ≥ 133 *	39 (11.8%) 291 (88.2%)	4 (10.3%) 48 (16.5%)	35 (89.7%) 243 (83.5%)	0.441
High glucose levels HGT > 140 * HGT <=140 *	144 (43.9%) 184 (56.1%)	23 (16%) 29 (15.8%)	121 (84%) 155 (84.2%)	1.000
Low albumin levels Albumin < 3.4 * Albumin ≥ 3.4 *	49 (44.5%) 61 (55.5%)	7 (14.3%) 9 (14.8%)	42 (85.7%) 52 (85.2%)	1.000
Length of stay in ED (hours) 50° > 5 * <= 5 *	188 (57%) 142 (43%)	29 (15.4%) 23 (16.2%)	159 (84.6%) 119 (83.8%)	0.970
Length of stay in ED (hours) 75° > 10 * <= 10 *	91 (27.6%) 239 (72.4%)	21 (23.1%) 31 (13%)	70 (76.9%) 208 (87%)	**0.037**

Table 3. Variables independently associated with incident delirium in the overall sample of patients

	B	Standard error	Exp (B)	95% C.I.
Length of stay in ED > 10 hours 75°	0.80	0.35	2.23	1.13 – 4.41
Moderate-severe cognitive impairment	1.70	0.35	5.47	2.76 – 10.85
Age (years)	0.65	0.03	1.07	1.01 – 1.13