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

This is the author's manuscript

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1592790> since 2018-10-16T09:23:03Z

Published version:

DOI:10.1111/jgs.14103

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(Article begins on next page)

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

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32 **ABSTRACT**

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

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

38 **DESIGN:** Prospective cohort study

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

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

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

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

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

57

58 INTRODUCTION

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

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

81

82 **METHODS**

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

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

93 *Delirium assessment*

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

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

113 In this study the 4AT was carried out as soon as possible in all patients after their ED arrival
114 (3.3±1.1 hours since ED entry) by four geriatric postgraduate students, two for each hospital,
115 trained over a 1-month period in using the 4AT scale to detect delirium within an acute
116 geriatric ward. At the same time, two senior geriatricians, one at each hospital, supervised
117 the administration of 4AT at ED arrival and diagnosed delirium, according to DSM-5 (4).
118 This approach was undertaken because DSM-5 criteria represent the gold standard method
119 for the diagnosis of delirium. The post-graduate students were not allowed to know the
120 diagnosis made by the senior geriatricians and the senior geriatricians were not involved in
121 the care of patients during their stay in ED. For those patients who were critically ill, proxy
122 respondents were used as the primary source of information, using a hierarchy of proxies (8).
123 Each proxy was specifically asked whether he or she could report on the patient's functional
124 and mental abilities as evident before the patient's hospital admission. Patients who had not
125 exclusion criteria, provided informed consent and were admitted to an acute medical or
126 geriatric ward of the two hospitals, constituted the study sample.

127 Multidimensional geriatric assessment

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

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

138 Outcome measures

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

143 Data analysis

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

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

151 Covariates were selected as categorical variables according to a recent review by Ahmed et al
152 (25) on delirium among older hospitalized patients, and included severe cognitive
153 impairment (SPMSQ ≥ 6), severe comorbidity (CIRS ≥ 5), severe acute clinical conditions
154 (APACHE > 15), functional dependence (ADL ≥ 3), polypharmacy (daily drugs taken ≥ 11),
155 one or more hospital admissions during last year, presence of urinary catheter, low albumin
156 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 \geq 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^o percentile identified those who
165 had a ED length of stay greater than 10 hours.

166

167 **RESULTS**

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

180 During the first three days from ward admission, delirium was diagnosed in 52 patients
181 (15.8%): 16 (4.8%) cases occurred in the first day, 20 (6.2%) during the second day and 16
182 (4.8%) during the third day. Increasing age, moderate-severe cognitive impairment, urinary
183 catheter placement and ED length of stay longer than 10 hours were associated with delirium
184 occurrence at univariate analysis (Table 2). All of these variables, with the exception of
185 urinary catheter placement in ED, were found to be independently associated with delirium
186 occurrence (Table 3).

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

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

196 **DISCUSSION**

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

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

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

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

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

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

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

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

254 **ACKNOWLEDGMENTS**

255

256 **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						
Grants/Funds		X						
Honoraria		X						
Speaker Forum		X						
Consultant		X						
Stocks		X						
Royalties		X						
Expert Testimony		X						
Board Member		X						
Patents		X						
Personal Relationship		X						

257

258

259 **Author Contributions:** All authors contributed to this paper.

260

261 **Sponsor's Role:** None.

262

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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