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## Complications in Post-Acute Care are Associated with Persistent Delirium

**Corrie P. Anderson, MA, Long H. Ngo, PhD, and Edward R. Marcantonio, MD, SM**

University of New England College of Osteopathic Medicine, Biddeford, ME (Anderson) and the Division of General Medicine and Primary Care (Marcantonio, Ngo) and Gerontology (Marcantonio), Department of Medicine, Beth Israel Deaconess Medical Center, and Harvard Medical School (Marcantonio, Ngo), Boston, MA

### Abstract

**Background**—Delirium is highly prevalent and persistent in post-acute care (PAC). However, few risk factors have been identified for delirium persistence.

**Objectives**—To investigate whether complications in PAC are associated with delirium persistence 30 days after PAC admission.

**Design**—Observational cohort study

**Setting**—8 Boston-area PAC facilities

**Participants**—350 patients with delirium at PAC admission

**Measurements**—We interviewed participants at PAC admission and 30 days later. Delirium presence was determined using the Confusion Assessment Method. We performed medical record reviews to ascertain new cardiac, non-cardiac, and geriatric syndrome complications in PAC. We also determined complication status 30 days after admission or at PAC discharge, whichever came first.

**Results**—The participants (mean age 83.6 years, 66% women) experienced the following incidence of PAC complications: cardiac complications 7%, non-cardiac complications 21%, geriatric syndrome complications 39%. Delirium persisted in 56% of participants one month after PAC admission. Neither cardiac nor non-cardiac complications were associated with delirium persistence. Delirium persistence at one month was significantly greater in patients with more geriatric syndrome complications (no complication 51%, one complication 61%, 2 complications 100%, adjusted  $p=0.048$ ). There was also a trend toward greater delirium persistence in patients with unresolved geriatric syndrome complications (no complication 51%, resolved complication 61%, unresolved complication 68%, adjusted  $p=0.1$ ).

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Corresponding author: Edward R. Marcantonio, Address: Beth Israel Deaconess Medical Center, 330 Brookline Ave, CO-218, Boston, MA. 02215. Phone: (617) 754-1405, Fax: (617) 754-1440, emarcant@bidmc.harvard.edu.

**Conflicts of Interest:** No authors report any conflicts of interest—see attached sheet for details.

**Data access and integrity:**

Dr. Marcantonio had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Author Contributions:**

Anderson: Conception and design, Analysis and interpretation of data, drafting the manuscript

Ngo: Statistical Analysis, Interpretation of the data, Critical revision of the manuscript

Marcantonio: Conception and design, acquisition of data, Analysis and interpretation of data, Critical revision of the manuscript, Obtained funding, Supervision

**Conclusion**—Geriatric syndrome complications are common in patients admitted to post-acute care with delirium, and are associated with the persistence of delirium one month later. Proactively addressing risk factors for geriatric syndromes may improve outcomes of vulnerable patients in post-acute care.

### Keywords

delirium; complications; geriatric syndromes; post-acute care

## INTRODUCTION

Delirium (acute confusional state) is characterized by an acute decline in attention and cognition (1, 2). More than one-third of hospitalized patients aged 70 and older are affected by delirium, resulting in longer, more costly hospital stays, increased nursing home placement, and poor functional recovery (3, 4). A previous study reported that hospital iatrogenic complications are precipitating factors associated with the development of delirium (5). This information is useful to identify patients at risk for delirium and for the design of interventions to reduce delirium.

Delirium can persist for weeks to months (6, 7), often beyond hospital discharge into the post-acute care (PAC) setting. An emerging literature demonstrates that persistent delirium confers an even worse prognosis than any delirium (8), including worse functional recovery (9) and a 2.9 times increased risk of death (10). Although much work has been performed to identify risk factors for the development of delirium (5, 11), fewer studies have examined risk factors for delirium persistence (12). The objectives of this study are: 1) to describe the spectrum of new onset complications in PAC experienced by patients admitted with delirium, and, 2) to examine the association between these complications with delirium persistence. We hypothesize that PAC complications would be common and independently associated with the persistence of delirium. We also hypothesized that successfully treated complications would be less likely to contribute to delirium persistence than complications that did not resolve by the time of PAC discharge or 30 days after PAC admission.

## METHODS

### Study Sample

Participants were enrolled in a previously described randomized trial of a Delirium Abatement Program (DAP) involving eight greater-Boston skilled nursing facilities specializing in post-acute care between October 1, 2000 and December 31, 2003 (13). Eligible patients were aged 65 and older, admitted directly from an acute medical or surgical hospitalization, English speaking, communicative prior to acute illness, not admitted for terminal care (life expectancy > 6 months), did not have end stage dementia, were not completely dependent in activities of daily living prior to hospitalization, and lived within 25 miles of the research site. In addition, all participants had CAM-defined delirium based on a screening assessment performed by research personnel within 5 days of PAC admission (average time to interview 2.5 days). Due to the compromised cognitive status of the patients, family caregivers, acting as proxies, provided informed consent by a protocol approved by the Institutional Review Board.

### Delirium Assessment and Outcomes

At PAC admission and one-month later, all participants underwent a structured delirium assessment (14) by trained interviewers consisting of the Mini-Mental State Examination (MMSE) (15), Digit Span (16), and the Delirium Symptom Interview (DSI) (17). Using these data, the interviewer completed the Memorial Delirium Assessment Scale (MDAS)

(18) to determine delirium severity and the Confusion Assessment Method (CAM) (19) diagnostic algorithm to determine the presence or absence of delirium. The combination of these assessments resulted in a highly reliable (inter-rater kappa = 0.95) procedure for determining the presence or absence of delirium (14). In general, the same assessor performed the PAC admission and one-month follow up interview for a given patient. Notably, we attempted to complete the one-month follow-up assessment regardless of the location of the participant, whether still in the PAC, discharged to the community, or readmitted to the hospital. Our primary study outcome was the presence of CAM-defined delirium at the one-month follow-up.

### **Complications in the Postacute Setting**

A single, experienced research nurse performed a structured PAC facility medical record review for all participants masked to the delirium status of the patient. The reviews focused on the development of new medical complications in the PAC setting. Based on our previous work (4, 11), we ascertained the presence of 28 complications, including 6 cardiac complications, 14 non-cardiac complications, and 8 geriatric syndrome complications (other than delirium). Each complication met a standardized definition with documentation in one or more progress notes in the PAC medical record. For each complication, the nurse recorded the status of the complication (resolved or not resolved) at either the time of PAC discharge or 30 days after admission, whichever came first. The medical record abstractor underwent extensive training prior to study initiation and continual quality monitoring to ensure accuracy of data collection.

### **Potential Confounders**

We examined several potential confounders of the association between PAC complications and delirium persistence. This included PAC admission factors we previously identified as significantly associated with delirium persistence one month later: age dichotomized at 85, preexisting dementia (yes/no), PAC admission Memorial Delirium Assessment Scale (MDAS) score (dichotomized at 15), and PAC admission Delirium Symptom Interview (DSI) (yes: presence of all 8 items) (12). We considered the following additional variables as potential confounders: gender, race (white vs. non-white), and DAP trial intervention status (yes/no). Pre-existing dementia was determined from two sources: 1) the International Classification of Diseases, Ninth Revision, Clinical Modification (20) diagnosis codes documented in the discharge summaries for the hospitalization immediately preceding the PAC admission (21); 2) a standardized interview from the patient's proxy to ascertain the presence or absence of diagnoses in the Charlson comorbidity index, including dementia. (22, 23).

### **Data Analysis**

We report the mean and standard deviation of continuous variables, and the sample proportion of categorical variables. Descriptive statistics are reported for both the 350-patient sample with a delirium assessment at one-month, and the original DAP trial 455-patient sample. We compare the incidence of 28 individual PAC complications and total cardiac, non-cardiac, and geriatric syndrome complications among patients with and without persistent delirium at one month. Because we found different relationships between the three classes of complications and persistent delirium, all subsequent analyses were performed by class, rather than total complications. We used the Mantel-Haenszel chi-square trend test to examine univariate associations between the number of cardiac, non-cardiac, and geriatric syndrome complications (none, one, 2 or more) with delirium presence at one month. Subsequently, we used multivariable logistic regression to obtain the adjusted effect of the number of each class of complications on delirium persistence, controlling for the potential confounders described above. To improve statistical power, only those potential

confounders associated with delirium persistence were retained in the model. Similar analyses were used to evaluate the association between complication resolution status (no complications, all complications resolved, at least 1 unresolved complication) and delirium persistence at 1 month. A type-I error of 0.05 was used to define statistical significance. All analyses were performed using SAS software, Version 9.2 (SAS Institute, Inc., Cary, NC).

## RESULTS

### Study population characteristics, complications, delirium persistence

The screening and enrollment process of the DAP trial are well described previously (13). Briefly, during the enrollment period at our 8 participating facilities, there were 6352 eligible admissions, of whom 4744 underwent screening, and 667 were diagnosed with delirium. Table 1 displays the baseline characteristics and complication rates of the analytic sample (N=350) compared to the overall trial sample (N=455), which were very similar to each other. Typical of PAC patients, this was a very elderly study population with mean age nearly 84 years old, modest pre-hospital dependency in basic activities of daily living functional status (mean score 13.3 out of a total of 16, with 16 representing total independence), and a high prevalence of medical comorbidities, including a 37% rate of dementia. Table 1 also shows that most study patients had mild delirium at PAC admission (only 19% with an MDAS score of over 15), with over 75% having normal or hypoactive psychomotor features. During the PAC stay, cardiac complications occurred least frequently in the study cohort, with a 7% incidence, compared to a 21% incidence of non-cardiac complications and a 39% incidence of geriatric syndrome complications. The majority of cardiac and non-cardiac complications resolved by PAC discharge or 30 days after admission; in comparison, over half of geriatric syndrome complications remained unresolved. Delirium persisted 30 days after PAC admission in 197 (56%) of the participants.

### Incidence of PAC complications and associations with delirium persistence

Table 2 reports the definitions of the 28 PAC complications examined, grouped into cardiac, non-cardiac, and geriatric syndromes, along with the incidence of these complications in the group with persistent delirium at one month vs. the group with resolved delirium. Cardiac complications did not show an association with delirium persistence status at one month. Non-cardiac complications had a slightly higher incidence in patients with persistent delirium vs. those with resolved delirium (22.8% vs. 19%). Geriatric syndrome complications as a whole had a substantially higher incidence in the persistent vs. resolved delirium group (45% vs. 31%), with each of the individual geriatrics syndromes showing a similar pattern, with the exception of poorly controlled pain and fecal impaction.

### Association of number of PAC complications with delirium persistence

Table 3 shows the associations between number of the three classes of PAC complications and delirium persistence one-month after PAC admission. There was no association between the number of cardiac or non-cardiac complications and delirium persistence status. In contrast, for geriatric syndrome complications, delirium persisted in 51% of those with no such complications, 61% of those with 1 complication, and 100% of those with 2 or more complications. These differences were statistically significant in univariate analyses and after multivariable adjustment ( $p=0.0004$ ,  $p=0.048$ , respectively).

### Association of PAC complication resolution status with delirium persistence

Table 3 also displays the association of complication resolution status with delirium persistence one-month after PAC admission. There was a non-significant trend toward

greater delirium persistence in patients with unresolved cardiac and non-cardiac complications. For geriatric syndrome complications, delirium persisted in 51% of those with no such complications, 61% of those with resolved complications, and 68% of those with unresolved complications. These differences were statistically significant in univariate analyses, but became only borderline significant after multivariable adjustment ( $p=0.016$ ,  $p=0.1$ , respectively).

## DISCUSSION

In our large prospective cohort of patients admitted to PAC facilities with delirium, we found a high incidence of new complications, with geriatric syndromes being the most common and the most likely to remain unresolved by PAC discharge or 30 days after admission. Geriatric syndrome complications were also the most strongly associated with delirium persistence one month after PAC admission. Our findings support previous studies that have shown common risk factors for geriatrics syndromes (24), and further suggest that these complications may be risk factors for both incidence and persistence of each other. Proactively addressing risk factors for geriatric syndrome complications may improve outcomes of vulnerable patients in PAC.

Investigators have examined the relationship between acute hospital complications and the incidence of delirium (5), but we are not aware of previous studies that have examined the relationship between complications and the persistence of delirium. Our finding that PAC complications are associated persistent delirium is consistent with the “vicious spiral to bad outcomes” previously described in the literature (25). Delirium, initiated in the hospital and still present on PAC admission, may predispose to other complications in the PAC such as falls, dehydration, pressure ulcers, and urinary retention. These complications, or their treatment, subsequently predispose to persistence of delirium. This vicious spiral is associated with worse functional recovery (4, 9), long-term nursing home placement, and increased healthcare costs (26). Ultimately, persistent delirium is associated with high one-year mortality, with patients whose delirium persists nearly three times as likely to die as patients whose delirium resolves (10).

There are a number of notable strengths in this study. Our sample represents the largest cohort of patients with delirium ever enrolled in a research study (13). Additionally, the delirium assessments utilized for the initial screening and outcome measurements are valid and highly reliable (14). We used standard definitions of complications, and our single experienced medical records abstractor underwent extensive training and continual quality review. Furthermore, assessment of complications was performed masked to delirium status at one-month. Finally, one-month follow-up interviews were completed whether the participant was still in the PAC, discharged home or another community setting, or readmitted to the hospital

There are several limitations to our study. Despite our attempt to follow up all DAP trial participants regardless of location, only a subset of 350 had delirium follow-up interviews at one month due to death, withdrawal, and other losses to follow-up. However, the 350 participants with one month delirium status available have very similar baseline characteristics and complication data as the full cohort (Table 1), suggesting our results are generalizable. Ascertainment of PAC medical complications was dependent on documentation in the PAC medical record, but this is the standard approach for ascertainment of complications. While our medical record review captured 28 PAC complications, there are other common complications that can be harder to identify, such as constipation and urinary incontinence, which we did not include in our study. The data for this study was collected from eight Boston-area PAC facilities and may not generalize to

other locations. Lastly, since we conducted an observational study, the statistical associations we identified do not necessarily imply causality.

In conclusion, geriatric syndrome complications are common in patients admitted to post-acute care with delirium, and are associated with the persistence of delirium. Our findings may begin to elucidate how delirium instigates a vicious spiral leading to new complications, persistent delirium, and eventually, long term decline and death. Moreover, these findings reinforce the need to implement programs to prevent and/or to promptly detect and treat geriatric syndrome complications in post-acute patients, especially those admitted with delirium.

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**Table 1**  
Study Population Characteristics, PAC Complications, Comparison to Overall DAP Trial Enrollees

CHARACTERISTICS	Analytic Cohort for this Study* (N=350)	DAP Trial Enrollees Full Cohort (N=455)
<b>Demographics</b>		
Age in years, mean ± sd	83.6 ± 6.9	83.8 ± 6.9
Female, % (n)	66 % (230)	65% (294)
White, not Hispanic, % (n)	90% (316)	92% (417)
Education > high school, % (n/N)	21% (68/324)	23% (95/409)
<b>Pre-hospital functional status, comorbidities</b>		
Baseline ADL total score (0 worst, 16 best)	13.3 ± 3.2	13.3 ± 3.3
Dementia*, % (n)	38% (133)	37% (170)
Myocardial Infarction	22% (75/337)	22% (93/423)
Congestive Heart Failure	22% (76/342)	23% (98/428)
Peripheral Vascular Disease	10% (33/339)	10% (41/426)
Stroke or Transient Ischemic Attack	33% (109/329)	33% (136/412)
Asthma	6% (20/346)	5% (23/434)
COPD, Emphysema, bronchitis	8% (26/344)	9% (37/430)
Peptic ulcer disease	7% (24/340)	7% (29/428)
Diabetes	22% (76/346)	21% (92/434)
Renal disease	9% (32/345)	9% (39/433)
Connective tissue disease	10% (33/331)	9% (38/417)
Liver disease	2% (7/344)	2% (8/430)
Leukemia or polycythemia	0.3% (1/348)	0.2% (1/436)
Lymphoma	2% (6/348)	2% (8/436)
Cancer, not skin	8% (29/346)	10% (45/432)
<b>PAC admission cognitive function, delirium characteristics</b>		
Baseline Mini-Mental State Examination total score	12.3 ± 6.8	12.1 ± 6.7
Presence of all 8 Delirium Symptom Interview Items, % (n)	9% (33)	10% (45)
Memorial Delirium Assessment Scale score > 15	19% (67)	21% (97)



CHARACTERISTICS	Analytic Cohort for this Study* (N=350)	DAP Trial Enrollees Full Cohort (N=455)
Psychomotor Features of Delirium on Admission		
Normal	31% (142)	30% (106)
Hypoactive	46% (211)	47% (164)
Hyperactive	10% (47)	11% (38)
Mixed	12% (55)	12% (42)
<b>Incidence of New PAC Complications</b>		
At least 1 cardiac complication, % (n)	7% (25)	6% (26)
At least 1 non-cardiac complication, % (n)	21% (74)	19% (86)
At least 1 geriatric syndrome complication, % (n)	39% (136)	36% (168)
<b>Resolution status of Complications at PAC Discharge or One-Month after PAC Admission</b>		
At least 1 unresolved cardiac complication, % (n)	1% (5)	4% (20)
At least 1 unresolved non-cardiac complication, % (n)	5% (19)	6% (29)
At least 1 unresolved geriatric syndrome complication, % (n)	24% (85)	24% (108)

Table Abbreviations: PAC—post-acute care, ADL—Activities of Daily Living, DAP—Delirium Abatement Program COPD-Chronic Obstructive Pulmonary Disease

Footnotes:

\* Dementia status based on proxy interview and ICD-9 from hospital discharge summary

**Table 2**  
Association of Individual Complications and Complication Groups with Delirium Status One Month after Post-acute care Admission

Complications	Definition used in Medical Record Review	Incidence in patients with delirium at 1 month (N=197)	Incidence in patients without delirium at 1 month (N=153)
<b>Cardiac Complications</b>			
Severe Hypertension	BP>200 systolic, 110 diastolic, requiring treatment	1.0% (2)	0.7% (1)
Hypotension	Systolic BP<90, or greater than 1/3 drop from admission, requiring immediate treatment	1.5% (3)	2.6% (4)
Unstable Angina	Cardiac chest pain at rest or with minimal exertion	0.5% (1)	1.3% (2)
New Arrhythmia	New sustained arrhythmia requiring treatment	0% (0)	0.7% (1)
Congestive Heart Failure	Symptomatic left or right sided heart failure requiring treatment	2.0% (4)	5.9% (9)
Myocardial infarction	New clinical myocardial infarction based on symptoms, electrocardiogram, and/or cardiac enzymes	0% (0)	0% (0)
Any Cardiac Complication		5% (10)	10% (15)
<b>Non-cardiac complications</b>			
Deep Vein Thrombosis	Confirmed proximal lower extremity venous thrombosis	1.0% (2)	0% (0)
Pulmonary Embolism	Clinical pulmonary embolism confirmed by appropriate radiographic testing	0% (0)	0% (0)
Pneumonia	Clinical pneumonia confirmed by radiographic testing	6.1% (12)	4.6% (9)
Respiratory Failure	Respiratory failure requiring intubation or other ventilatory support	0.5% (1)	0% (0)
COPD Exacerbation	Respiratory exacerbation in patient with known COPD	0% (0)	0% (0)
Renal Failure	Worsening renal function requiring treatment	1.0% (2)	0% (0)
Stroke	New clinical stroke with appropriate confirmatory testing—consultation or radiographic	0% (0)	0% (0)
Gastrointestinal Bleed	Clinical gastrointestinal bleeding with accompanying drop in blood count—upper or lower source	1.0% (2)	0% (0)
Skin/Soft Tissue Infection	New clinical skin or soft tissue infection requiring antibiotics and/or local treatment	5.1% (10)	5.9% (9)
Bacteremia	Clinical sepsis confirmed with positive blood cultures	0% (0)	0% (0)
Urinary Tract Infection	New clinical urinary tract infection, usually confirmed by urine culture, requiring treatment	9.6% (19)	9.2% (14)
Fever	New fever to 101°F, not otherwise explained	1.0% (2)	0.7% (1)
Clostridium Difficile Colitis	Diarrheal illness with positive Clostridium difficile toxin assay requiring treatment	1.5% (3)	2.6% (4)
Hypoxia	Oxygen saturation <90%, requiring treatment	2.0% (4)	1.3% (2)
Any Non-Cardiac Complication		22.8% (45)	19% (29)
<b>Geriatric Syndrome Complications</b>			
Dehydration	Clinically evident dehydration, supported by exam and laboratory data, requiring treatment	7.6% (15)	2.0% (3)

Complications	Definition used in Medical Record Review	Incidence in patients with delirium at 1 month (N=197)	Incidence in patients without delirium at 1 month (N=153)
Pressure Ulcers	New Stage II or greater pressure ulcers noted in the medical record requiring treatment/management plan	7.6% (15)	4.6% (7)
Poorly Controlled Pain	Pain that is poorly controlled, requiring specialized management	2.5% (5)	2.6% (4)
Urinary Retention	Clinically recognized urinary retention requiring treatment with medication or catheterization	2.5% (5)	0% (0)
Fecal Impaction	Clinically recognized fecal impaction requiring treatment with enemas, suppositories, or laxatives	2.0% (4)	3.3% (5)
Malnutrition	Clinically recognized poor nutritional status requiring a specialized management plan	0.5% (1)	0% (0)
Aspiration	Clinically recognized aspiration, with supportive studies as indicated, and management	2.0% (4)	0% (0)
Falls	Clinically recognized falls, requiring evaluation and management plan	32% (63)	21% (32)
Any Geriatric Syndrome Complication		45% (89)	31% (47)

Table Abbreviations: BP—blood pressure; COPD—chronic obstructive pulmonary disease

**Table 3**

Association between Complications and Delirium Persistence at 1-Month

	No Complications	1 Complication	2 Complications	Univariate Analysis P-value*	Multivariable Analysis P-value <sup>†</sup>
<b>Delirium Persistence among those with Cardiac Complications</b>	58% (188/325)	33% (7/21)	50% (2/4)	0.069	0.118
<b>Delirium Persistence among those with Non-Cardiac Complications</b>	55% (152/276)	59% (34/58)	69% (11/16)	0.279	0.580
<b>Delirium Persistence among those with Geriatric Syndrome Complications</b>	51% (108/214)	61% (74/121)	100% (15/15)	0.0004	0.048
	<b>No Complication</b>	<b>All Complications Resolved</b>	<b>At least 1 Unresolved Complication</b>	<b>Univariate Analysis P-value*</b>	<b>Multivariable Analysis P-value<sup>†</sup></b>
<b>Delirium Persistence among those with Cardiac Complications</b>	58% (188/325)	30% (6/20)	60% (3/5)	0.108	0.117
<b>Delirium Persistence among those with Non-Cardiac Complications</b>	55% (152/276)	55% (30/55)	79% (15/19)	0.135	0.165
<b>Delirium Persistence among those with Geriatric Syndrome Complications</b>	51% (108/214)	61% (31/51)	68% (58/85)	0.016	0.100

\* Mantel-Haenszel  $\chi^2$  trend test;

<sup>†</sup> Multivariable logistic regression adjusted for age (dichotomized at 85), MDAS (dichotomized at 15), baseline DSI