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Hospital use, institutionalisation and mortality associated with delirium

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Abstract

Background: delirium is a disorder affecting consciousness, which gives rise to core clinical features and associated symptoms. Older patients are particularly prone, owing to higher rates of pre-existing cognitive impairment, frailty, co-morbidity and polypharmacy.

Objectives: the aim of this study was to investigate the hypotheses that delirium affects the most vulnerable older adults and is associated with long-term adverse health outcome.

Methods: this prospective cohort study evaluated 278 medical patients aged ≥75 years admitted acutely to a district general hospital in South Wales. Patients were screened for delirium at presentation and on alternate days throughout their hospital stay. Assessments also included illness severity, preadmission cognition, co-morbidity and functional status. Patients were followed for 5 years to determine rates of institutionalisation and mortality. Number of days in hospital in the 4 years prior to and 5 years after index admission were recorded.
Results: delirium was detected in 103 patients and excluded in 175. Median time to death was 162 days (interquartile range 21–556) for those with delirium compared with 1,444 days (25% mortality 435 days, 75% mortality>5 years) for those without ($P < 0.001$). After adjusting for multiple confounders, delirium was associated with an increased risk of death (hazard ratio range 2.0–3.5; $P \leq 0.002$). Institutionalisation was higher in the first year following delirium ($P = 0.03$). While those with delirium tended to be older with more preadmission cognitive impairment, greater functional dependency and more co-morbidity, they did not spend more days in hospital in the 4 years prior to index admission.
Conclusions: delirium is associated with high rates of institutionalisation and an increased risk of death up to 5 years after index event. Prior to delirium, individuals seem to compensate for their vulnerability. The impact of delirium itself, directly or indirectly, may convert vulnerability into adverse outcome.

Keywords: *delirium, institutionalisation, mortality, frailty, elderly*

Introduction

Delirium is a disorder affecting consciousness, which gives rise to core clinical features (acute onset, inattention, fluctuation) and associated symptoms (psychiatric, sleep–wake and psychomotor disturbance) [1]. Commonly, delirium is triggered by acute illness: this accounts for its prevalence in the hospital setting, where up to 61% of patients are affected [2]. Older patients are particularly prone, owing to higher rates of pre-existing cognitive impairment, frailty, co-morbidity and polypharmacy [3, 4].

The diagnosis is often missed, allowing unrecognised precipitants to go untreated and potentially worsen outcome [4]. The spectrum of clinical presentation, delirium sub-types and fluctuation in symptoms are barriers to successful identification [5]. The diagnostic challenge may in part be overcome by recognition of high risk groups combined with targeted screening and prevention strategies [6].

If not prevented, delirium is associated with multiple short-term adverse outcomes, including greater risk of institutionalisation [7, 8], functional impairment [9, 10], dementia [10, 11] and death [7, 12–14]. Survivors often have impaired quality of life [9]. Cohort studies have provided valuable insights into clinical outcomes of delirium but have been limited by lack of prospective clinical evaluation [8], small numbers of patients [12, 13], infrequent serial assessment [14] and short follow-up periods (from 6 months [12–14] up to a maximum of 3 years) [10].

While the pathophysiology of delirium remains unclear [15], advanced age and pre-morbid dementia are the greatest risk factors [16]. Delirium may represent an interaction between vulnerability, or baseline predisposing factors, and triggers, such as acute illness [4, 9, 17]. Hence, high vulnerability states confer the highest risk of delirium. In such circumstances, a small insult, innocuous in a more robust individual, may precipitate delirium.

This study investigated two hypotheses: that delirium is associated with long-term adverse health outcome and that it affects the most vulnerable older adults. A cohort of patients with and without delirium was followed for 5 years to determine rates of institutionalisation and mortality. Demographics at baseline and pattern of acute hospital admission 4 years prior to and 5 years after index admission were calculated as markers of vulnerability.

Methods

Participants were men and women aged ≥75 years admitted acutely to a general medical service at a district general hospital in South Wales [18]. Patients were screened for inclusion on alternate days over a 6-month period. Of 393 eligible patients, 278 were recruited. Readmissions during the recruitment period ($n=5$) were not included in the study population. Reasons for non-participation were refusal of consent ($n=98$) or assent (10) and the unavailability of proxy consent (7). Patients were screened for delirium at presentation using DSM-IV criteria [1]. Illness severity was stratified using the Greenfield Index, a subjective assessment based on clinical judgement and physiological variables, with scores ranging from 1 point (not ill) to 9 points (moribund) [19]. This scale has been validated in inpatients, including older persons, and shown to be predictive of in-hospital death and 1-year mortality [20]. Assessment also included place of residence, preadmission cognition (IQCODE-10) [21], baseline cognition (Mini-Mental State Examination) [22] and co-morbidity (Charlson morbidity score) [23]. Barthel Index score [24] was used to measure baseline activities of daily living, with scores of 0–8 out of 20 reflecting medium to high functional dependency [25].

All screening tests were performed by a single geriatrician (SVW) with training in the diagnosis of delirium and the assessment of vulnerable older people. Subsequent assess-

Table 1. Baseline characteristics of participants aged ≥75 years admitted acutely to a general medical service by delirium status (expressed as means or proportions)

Baseline	Delirium $n=103$	No delirium $n=175$	Significance
Age in years (SD)	83.7 (5.8)	81.8 (5.3)	$P=0.005$
Male	41%	42%	NS
Pre-existing dementia (IQCODE-10)	57%	20%	$P<0.0001$
Barthel Index score (SD)	13.7 (5.3)	17.4 (3.8)	$P<0.001$
Charlson co-morbidity score	2.0 (1.4)	1.7 (1.4)	$P=0.03$
Greenfield illness severity index	3.9 (1.4)	3.3 (1.3)	$P=0.001$

ments were carried out every 48 h for the first 2 weeks of admission. Assessments were done daily if the patient was delirious or thought to be developing delirium. Medical notes were reviewed every 48 h and ward staff interviewed about possible symptoms of delirium in those with a length of stay >2 weeks. Patients were clinically assessed if there was any suggestion of delirium symptoms. Otherwise, the patient had a full assessment at weekly intervals until discharge or death. Baseline assessment was taken to be the first day of evaluation.

Local hospital electronic records were used to determine length of stay for each acute hospital admission in the 4 years prior to and 5 years after discharge from index event. Length of index admission was excluded from the calculation of number of days in hospital before and after index event. Time to death and institutionalisation from the point of index admission were established from hospital records, supplemented by the local register of births and deaths. Risk of death was adjusted for potential confounders such as age, gender, illness severity and co-morbidity.

We analysed data using the Statistical Package for Social Sciences version 15.0 and Stata version 10.0. Non-parametric tests were used to compare differences in hospitalisation between those with and without delirium. We constructed Kaplan–Meier curves to compare time to death and calculated median survival. The significance of differences in survival was calculated using the log-rank test. Cox proportional modelling with backwards selection was used to adjust for the effects of delirium and potential confounders on the risk of death. Risk of death was adjusted for potential confounders. A single patient had suspected persistent delirium [26] and this was not included as a confounder in the analysis. The effect of delirium on survival was estimated as a time-varying covariate to account for the change in delirium status in those whose delirium was acquired in hospital. Preliminary tests of proportional hazards using Schoenfeld residuals showed that the effect of delirium varied with time ($P=0.026$). The effect of delirium was consequently estimated within three time periods: during the index admission, in the first year after the index admission and in the remaining 4 years of follow-up. No further deviation from the proportional hazards assumption was detected within these time periods.

The study was approved by the South East Wales Research Ethics Committee. Informed consent for inclusion into the study was sought for each patient. In cases where individual capacity to undertake healthcare decision was impaired, relative assent was obtained.

Results

Mean age of participants was 82.5 years (SD 5.6 years); 117 were men. Delirium was detected in 103 patients and excluded in 175. For 80 patients, delirium was present on admission and 23 patients developed delirium during their inpatient stay. Seventy-two patients with delirium (70%) were living in their own home prior to admission compared with 158 patients without delirium (90.3%) ($P<0.001$). Those with delirium tended to be older, with more preadmission cognitive impairment, greater functional dependency and more co-morbidity (Table 1).

Thirty-seven patients with delirium (35.9%) and 12 patients without delirium (6.9%) died during the index admission. A minority of patients in whom delirium was detected were discharged to their own home (37: 35.9%) compared with 141 (80.6%) of those without delirium ($P<0.001$).

Mortality or institutionalisation data were captured in 278 patients (100%) and 9-year hospitalisation data in 277 (99.6%). Figure 1 shows a Kaplan–Meier plot of survival in those with delirium and those without. Median time to death was 162 days [interquartile range (IQR) 21–556] for those with delirium compared with 1,444 days (25% mortality 435 days, 75% mortality >5 years) for those without ($P<0.001$).

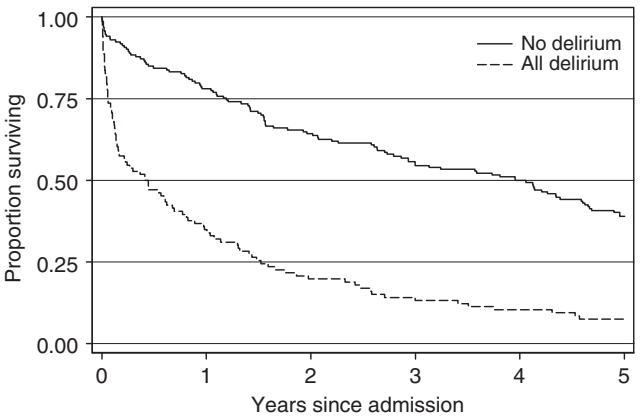

Figure 1. Five-year survival in patients aged ≥75 years admitted to a general medical service.

Table 2. Hazard ratio for death within 5 years for patients aged ≥75 years admitted acutely to a general medical service

	Hazard ratio (95% confidence interval)		
	Unadjusted	Adjusted[a]	*P*-value
Effect of delirium on mortality during index admission	4.5 (3.0–6.8)	3.5 (2.3–5.6)	<0.0001
Effect of delirium on mortality during first year after admission	4.0 (2.8–5.9)	3.2 (2.1–4.8)	<0.0001
Effect of delirium on mortality from second to fifth year after admission	2.4 (1.6–3.6)	2.0 (1.3–3.2)	0.002
Dementia	2.1 (1.6–2.8)	1.3 (0.9–1.8)	0.14
>85 years	1.8 (1.3–2.4)	1.5 (1.1–2.0)	0.01
Male gender	1.1 (0.8–1.5)	1.2 (0.9–1.6)	0.31
Institutionalised	2.8 (2.0–3.9)	1.4 (0.9–2.1)	0.17
Greenfield illness severity[b]	1.9 (1.4–2.6)	1.8 (1.3–2.6)	<0.0001
Charlson co-morbidity[c]	1.6 (1.2–2.2)	1.4 (1.1–2.0)	0.02
Dependency on admission[d]	2.5 (1.5–4)	1.6 (0.9–2.9)	0.14

[a]Adjustment made for multiple confounders age, dementia, placement, illness severity, co-morbidity and dependency.
[b]Greenfield severity score >4.
[c]Charlson co-morbidity score >2.
[d]Barthel Index score <8.

Hospital-acquired delirium had the worst survival of 88 days (IQR 31–607) versus community-acquired 199 days (IQR 21–524) although this difference was not statistically significant (log-rank test $P=0.43$).

The effect of delirium during admission varies with time since admission. The effect on mortality in hospital during the index admission [hazard ratio (HR) = 4.5, 95% confidence interval (CI) = 3.0–6.8] is greater than the effect during the first year after the index admission (HR = 4.0, 95% CI = 2.8–5.9) and during the subsequent years of follow-up (HR = 2.4, 95% CI = 1.6–3.6). After adjustment for multiple confounders (placement, age, gender, illness severity and co-morbidity), delirium remained significantly associated with a higher risk of death in all time periods (Table 2).

In the 5 years following index admission, residential or nursing home placement was higher for patients post-delirium. This was statistically significant for the first 2 years (Year 1: 40.5 versus 17.6%, $P=0.03$; Year 2: 33 versus 15.1%, $P=0.05$) (Table 3).

Five-year survivors of delirium ($n=8$) were less dependent at baseline (median Barthel Index scores 19.5; IQR 3) than those with delirium who died (median Barthel Index scores 14; IQR 8) ($P=0.05$). These 'delirium survivors' had the same functional status as patients without delirium who survived for ≥5 years (whose median Barthel Index score was 20: IQR 3) ($P=1.00$). Furthermore, the effect of functional status on survival in those without delirium (HR = 1.5, 95% CI = 0.6–4.1) was less than in those with delirium (HR = 2.7, 95% CI = 1.3–5.4) although this interaction effect was not statistically significant ($P=0.29$). No difference in other measures were found in comparing survivors with non-survivors of delirium (age, $P=0.16$; illness severity, $P=0.24$; co-morbidity, $P=0.13$; dementia, $P=0.18$; admitted from their own home versus institution, $P=0.26$).

Length of index admission was significantly higher for those with delirium; mean 13.1 days absent delirium and 26.1 days with delirium ($P<0.001$). Preadmission hospitalisation tended to increase in each year leading up to admission with no significant differences between those with and without delirium. For example, in the 1 year preceding admission, those with delirium spent a mean of 13.5 ± 24.5 days compared with 10 ± 36.1 (SD) days absent delirium in hospital ($P=0.61$). Delirium was associated with greater time spent in acute hospital care in the first year following index admission: mean 30.3 days (SD 54.3) versus 17.0 days (SD 36.1) ($P=0.01$). Hospitalisation rates subsequently stabilised in both groups with a trend towards reduced hospitalisation after 2 years. For example, in Year 4 following admission, 14 delirium survivors spent 10.1 days in hospital (SD = 19.5) compared with 13.4 days (SD 23.8) for the 94 survivors who had no delirium ($P=0.44$). There was no significant difference in the frequency of hospitalisation between the two groups in any year prior to or following index admission. Adjusting for illness severity did not alter the significance of these relationships.

Table 3. Rate of institutionalisation (residential or nursing home) over the 5-year post-index admission

	Institutionalisation % (n = number of survivors)		
	Delirium	No delirium	*P*-value
Year 1	40.5%, 37	17.6%, 136	0.03*
Year 2	33%, 21	15.1%, 112	0.05
Year 3	28.5%, 14	13.7%, 95	0.15
Year 4	18%, 11	12.6%, 87	0.61
Year 5	13%, 8	11.5%, 61	0.85

Discussion

Delirium was associated with an increased risk of death and institutionalisation up to 5 years after index event. The risk of death following delirium remained after adjustment for multiple potential confounders. At baseline, compared with those without delirium, those with delirium were older and more cognitively impaired, had higher co-morbidity and greater illness severity, and were more functionally dependent. Delirium was associated with significantly more

days in hospital in the first year following index admission but not with increased hospital use in the four preceding years.

Delirium was detected in 37.1% of our cohort, which is comparable to previous studies of older inpatients reporting delirium rates of 25 [13] to 51.5% [27]. Our results confirm an association between delirium and death [7, 11, 27] but with a somewhat higher adjusted hazard ratio for mortality (2.7).

Our study has certain strengths. Investigations of delirium are challenged by its sporadic and unpredictable occurrence, fluctuating course and diverse clinical presentation. In our study, patients were well characterised at baseline with comprehensive serial clinical evaluation. This optimised the detection of delirium at presentation and tracked its evolution through the course of admission. Screening all older patients admitted to hospital increased the generalisability of results. The number of patients recruited is relatively large and the 5-year follow-up is, to our knowledge, the longest period reported in relation to mortality and institutionalisation. Minimal loss of data assists with reliability of observed relationships, and this is the first study to evaluate specifically the pattern of hospital admission as a marker of health need in relation to an episode of delirium.

We also acknowledge methodological weaknesses. The absence of clinical follow-up data denies the opportunity to explore the causation of subsequent hospital admissions. Admission to hospital outside the trust was a potential confounder not captured in this data. As only a single patient moved out of area in the 5-year follow-up period, this was unlikely to have influenced our findings. The use of Cox proportional hazards models assumes the effect of covariates is constant during follow-up. We were able to show that the effect of delirium during hospital admission decreases with time since admission ($P=0.026$) and consequently reported the effect in three time periods. No further time-dependent effects within these groups were detected but the power to detect these differences was limited. The effects of all other covariates were assumed constant with time. Including interactions between age and time since follow-up did not affect our estimates of the effect of delirium, and so this was not included in the final model.

Here, we have used hospitalisation as a marker of decompensation and functional dependency, cognitive status and co-morbidity to estimate vulnerability. The use of acute hospitalisation as a marker of health need is a dichotomous and imprecise tool. Nevertheless, geriatricians well recognise that a change in physiological or social well-being that can no longer be tolerated results in acute and ongoing hospital management [28]. Hospitalisation as a marker of decompensation in older people is therefore a justifiable place to start. Our vulnerability measures are indicators, but not a direct quantification, of frailty status [29].

Previous cohort studies have reported the association of delirium with adverse outcomes in the short term, and we have confirmed these associations up to 5 years after index admission. Yet, it remains unclear how delirium imposes such a heavy toll. Relating poor outcomes to antecedent events may help refine the conceptualisation of delirium. Delirium is perceived as an interaction of precipitants and acute illness upon vulnerability. Hitherto, the lack of comprehensive patient description prior to delirium onset hindered the interrogation of this model. We hypothesised that patients with delirium had a lower threshold, and greater vulnerability, for delirium. Certainly considering baseline factors (greater age, dependency and co-morbidity), the patients with delirium can be considered more vulnerable to adverse events. However, this did not translate into differing rates of hospitalisation prior to index admission. These individuals appear able to compensate for their vulnerability. We propose that the impact of delirium itself, directly or indirectly, converts vulnerability into adverse outcome. Furthermore, vulnerability seems to modulate the outcome of delirium: those with worse functional status who had delirium were more likely to die. Better functional status may be a marker of low vulnerability or high resilience, making delirium less likely and conferring some protection in terms of health outcome after the event.

Amongst older inpatients, delirium was associated with an increased risk of death and institutionalisation up to 5 years after index event. Understanding individual vulnerability may yield important insights into the causation and outcomes of delirium and provide a model for delirium causation in frail older patients. The measurement of individual vulnerability, particularly in relation to frailty status, is a focus of further studies by our group.

Key points

- Delirium is associated with an increased risk of death and institutionalisation up to 5 years after index event.
- Prior to delirium, individuals seem to compensate for their vulnerability.
- The impact of delirium itself, directly or indirectly, may convert vulnerability into adverse outcome.

Conflicts of interest

All authors declare no conflict of interest.

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