Delirium in an acute stroke setting,occurrence and risk factors

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Table 1. Associations with delirium.

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Background and Purpose:Delirium is a common and serious complication of acute illness. We describe delirium occurrence in an unselected, acute stroke population.

Methods: We collected data from consecutive stroke admissions. We performed comprehensive cognitive assessment within first week including Diagnostic Statistical Manual-5 based delirium diagnosis. We reported proportion with delirium and the clinical and demographic associations with delirium using multiple logistic regression.

Results: Of 708 patients, median age:71 years (inter-quartile range:59-80), we recorded delirium in 187/708 (26.4%;95% Confidence Interval:23.0-30.0). Across 395 patients with complete risk factor data (105 delirium), factors independently associated with delirium were:age (Odds Ratio:1.05; 95%CI:1.03-1.08), drug/alcohol misuse (OR:2.64; 95%CI=1.10-6.26) and stroke severity (OR:1.22; 95%CI:1.14-1.31).

Discussion: Delirium is common in acute stroke, affecting one in four. It may be possible to predict those at risk using pre-stroke and stroke specific factors.

Protocol:1147 (researchregistry.com).

INTRODUCTION

Delirium is a syndrome of cerebral decompensation in response to pathophysiological stressors and is a common complication of acute illness.[1] Delirium complicating stroke carries a particularly poor prognosis, being associated with increased length of stay, disability and mortality.[2]

Reported rates of delirium in stroke range from 2-66% depending on study design, population, and diagnostic approach.[3] Some published studies may have underestimated delirium in stroke by excluding high risk groups such as those with pre-stroke dementia, severe stroke and aphasia.[3] General risk factors for delirium have been described, but post stroke delirium could be driven by other, stroke-specific, factors.

An estimate of delirium occurrence and its associations, based on an unselected acute stroke group, could inform clinical practice, research and policy. We assessed occurrence of delirium (incident and prevalent cases) in a consecutive, unselected, stroke population, and described the factors associated with delirium.

METHOD

The data that support the findings are available from corresponding author upon reasonable request.

We conducted an observational, cross-sectional study. The project was approved by West of Scotland Research Ethics Committee (16/WS/0001), and allowed for inclusion of routine clinical data from patients unable to consent.

Setting and population: Data were collected from admissions to the Acute Stroke Unit (ASU) of a University teaching hospital. The unit admits all strokes (including TIA but not aneurysmal subarachnoid haemorrhage) from a geographical catchment, except those requiring multi-organ support. Recruitment occurred in waves:Feb 2016-Feb 2017; April-June 2017; October-December 2017; July-August 2018. Sampling was consecutive and did not exclude patients with dementia, severe stroke or aphasia.

Study assessments occurred in first week (5 days) after admission, with direct assessments ideally within first 48 hours. Assessments were performed by trained researchers, in liaison with clinical team. We performed a single, structured assessment, but testing could be performed over more than one session if needed, for example if patient become too tired. The assessments were integrated into routine care and made use of clinical notes, and reports from clinical staff, family and other informants.

Delirium assessment: We used an operationalised[4] system that allowed categorisation of all patients, based on DSM-5 criteria.(Figure 1) Patients too drowsy to be assessed were automatically assigned the delirium label. Final diagnostic formulation was agreed with the treating team. Problematic assessments were discussed with a delirium specialist (TQ).

Delirium assessment used clinical observations and screening battery of:4A's test (4AT, multi-domain delirium assessment validated in stroke[5]) and Hodkinson's Abbreviated Mental Test[6] (AMT10, general cognitive screen, cut- off<8/10) to assess undifferentiated

cognitive impairment. Pre-stroke cognitive impairment was assessed using a combination of medical records (prior history of cognitive syndrome) and GP-Cog[7] informant questionnaire (cut off≥3/6).

Clinical and demographic assessment: We collected data on:age (years), previous stroke(s), previous depression, pre-stroke cognitive impairment (defined previously), illicit drug and/or alcohol misuse (use of illegal non prescribed medication/greater than five units alcohol daily), pre-stroke function (modified Rankin Scale [mRS]), stroke severity (NIHSS) and presence of sensory (visual or hearing) impairment (patient self-report or recorded in case-notes), prescribed medications and any medications known to precipitate delirium (using a list of 'culprit' medications[8]). Patient and/or informant interview was supplemented by case-notes review and discussion with the treating clinical team. Routine inclusion of NIHSS was introduced after the first assessment wave and so these data were missing for some.

Analyses: Primary analysis was occurrence of delirium, described as proportion with corresponding 95% confidence interval (95%CI). Minimum sample size to allow this estimate, assuming, 25%[3] prevalence and 0.05 error, was 288 participants.

We conducted sensitivity analysis, excluding those patients where delirium assessment was based on partial data due to inability to complete the full cognitive assessment.

We assessed univariable then multivariable associations with delirium using logistic regression. Variables included in the full model (Table 1) were chosen based on previous

literature.[9] Our primary analysis was a complete data approach including NIHSS, and so used data from waves 2-4 only. With expected delirium prevalence of 25-30%, we required 350-400 patients (10 outcomes per included variable). Results were described as odds-ratio (OR, +/-95%CI). We described missing data, comparing groups (included vs excluded in full model), and ran a partially adjusted (age,sex) model that allowed greater use of data. All analyses were completed using SPSS version:22 (IBM,USA).

RESULTS

We completed delirium assessment in all 708 stroke patients admitted. Median age:71 years (IQR:59-80), 372/695 (53.5%) male.(Supplementary Materials) Occurrence of delirium was 26.4% (95%CI:23.0-30.0) (187/708 patients). Sensitivity analysis removing forty-six patients with partially complete cognitive assessment (labelled delirium as default) gave delirium occurrence of 22.9% (95%CI:20-26%).

In an illustrative analysis of 552 patients with complete cognitive test data, 229 (41.5%) had cognitive impairment, comprising a mix of cognitive syndromes.(Figure 2)

Variables associated with delirium in unadjusted analyses (restricted to those with complete data, 395 patients [105 with delirium]):age, sex, pre-stroke function, NIHSS, pre-stroke cognitive impairment, previous depression, and medications.(Table 1)

Semi-adjusted models, controlling for age and sex only, suggested association with pre-stroke function, pre-stroke cognitive impairment, NIHSS, and drug/alcohol misuse.(Supplementary Materials)

For the fully adjusted model, independent associations were observed for:age (OR:1.05; 95%CI:1.03-1.08 per year), NIHSS (OR:1.22; 95% CI:1.14-1.31 per point increase) and drug/alcohol misuse (OR:2.64; 95%CI=1.10-6.26).(Table 1). Comparing those included/not included due to missing data, the only significant difference was less aphasia in those included.(Supplementary Materials)

DISCUSSION

In this unselected, acute stroke population, rates of delirium were one in four. This delirium may be partly predictable based on stroke severity as well as more established delirium risk factors. Our delirium occurrence is broadly similar to estimates from our systematic review.3 However, our data may be more representative of acute stroke, since pre-stroke dementia, severe stroke, and aphasia were not excluded.

These findings add further support to the evidence that delirium is a common complication of stroke. There is increasing interest in the concept of post-stroke transient cognitive impairment, a syndrome related to, but not synonymous with, delirium.[10] Our data suggest that a proportion of patients with acute stroke have cognitive impairments that are not delirium or dementia.

Factors predictive of delirium were a combination of premorbid and stroke-specific variables. These risk factors are non-modifiable but could potentially be used to identify patients at risk of delirium where preventative measures could be employed.[11]

Delirium assessment is not straightforward. We used a multimodal approach, combining clinical assessment with structured tools. Assessing for delirium in those with the greatest

impairments is reliant on potentially subjective observations. Severe stroke can be associated with altered arousal and a delirium label was frequently applied to those with reduced consciousness. There is debate around whether this presentation should be labelled delirium[12], but the poor cognitive and functional outcomes seen in such patients suggests they are a group that require special attention.

We have conducted a large, highly inclusive study that is less biased by exclusions that may have limited previous research. Our assessment of delirium was robust, including a clinical synthesis of information from validated assessment tools, informants and ward staff.

We recognise that the single centre nature of our study may limit external validity, although the evidence based acute stroke care we offer is similar to most centres. Missing data is the reality of a system embedded in clinical care. Data were not missing at random and while sensitivity and subgroup analyses attempted to mitigate the effects of missing data, multivariable models still need to be interpreted with caution. Resulting reduced sample size may explain why some factors traditionally associated with delirium were not positive in our work.

We have shown the feasibility of inclusive recruitment for stroke studies concerned with cognitive disorders. Research concerned with neuropsychological sequela of stroke must make active efforts to include those most at risk.[13] Post-stroke cognitive assessment is mandated in guidelines.[14] Our data would suggest that assessment is possible in routine practice and that any screening battery should include a measure of delirium.

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Conflicts of interest: None.

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Figure 1: Delirium assessment protocol.

Figure 2: Cognitive syndromes in acute stroke.

Table 1. Associations with delirium

	Delirium N=105	**No delirium** N=290	**Univariable** OR (95% CI)	**Multivariable** OR (95%CI)
Age (years) (Median IQR)	79 (70-87)	65 (55-76)	1.07 (1.05-1.09)	1.05** (1.03-1.08)
Sex (Male)	173	48	0.71 (0.51-0.99)	0.61 (0.34-1.08)
Pre-stroke disability (mRS 2-5)	62	91	2.86 (2.01-4.08)	1.54 (0.84-2.81)
Pre-stroke cognitive impairment	31	28	3.51 (2.27-5.43)	1.99 (0.98-4.08)
NIHSS (Median, IQR)	5 (2-11)	2 (1-4)	1.28 (1.20-1.36)	1.23** (1.15-1.32)
Previous depression	9	59	0.51 (0.31-0.85)	0.52 (0.22-1.22)
Previous stroke	34	83	1.17 (0.81-1.71)	0.96 (0.52-1.77)
Drug or alcohol misuse	15	29	1.41 (0.82-2.42)	2.64* (1.10-6.26)
Deliriogenic drugs	32	82	1.10 (0.75-1.62)	0.92 (0.50-1.71)
Medication count (Median, IQR)	8 (6-11)	6 (3-10)	1.07 (1.03-1.12)	1.02 (0.95-1.10)
Sensory impairment	14	20	1.70 (0.97-2.99)	1.16 (0.47-2.84)

Analysis limited to those with full data

OR:Odds Ratio, IQR:inter-quartile range, mRS:modified Rankin Scale

All data are n (%) unless otherwise specified

**=p<0.05; **=p<0.001 (multivariable model)*

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Illustrative classification of all patients who completed the cognitive screening battery. Post-stroke cognitive impairment was defined by cognitive test score (AMT-10). A proportion with delirium were unable to complete assessment.