Undiagnosed long-term cognitive impairment in acutely hospitalised older medical patients with delirium

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DOI:
10.1093/ageing/afw064

Document Version
Peer reviewed version

Citation for published version (Harvard):
Jackson, T, MacLullich, AMJ, Gladman, J, Lord, J & Sheehan, B 2016, 'Undiagnosed long-term cognitive impairment in acutely hospitalised older medical patients with delirium: a prospective cohort study', *Age and Ageing*, vol. 45, no. 4, pp. 493-499. https://doi.org/10.1093/ageing/afw064

Undiagnosed long-term cognitive impairment in acutely hospitalised older medical patients with delirium: a prospective cohort study

Abstract

Background

Delirium and dementia are common in the general hospital, being present in nearly 50% of older unselected admissions to hospital. Cognitive impairment is a risk factor for delirium, but the prevalence of previously undiagnosed cognitive impairment (dementia or mild cognitive impairment) in patients with delirium is unknown.

Methods

We performed a prospective cohort study of people over 70 years admitted to hospital with delirium to establish the prevalence of previously unrecognised prior cognitive impairment. Delirium was diagnosed at baseline using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). Mild cognitive impairment and dementia were diagnosed 3 months following recruitment in survivors using the International Working Group on Mild Cognitive Impairment criteria and DSM-IV criteria, respectively.

Results

Delirium was identified in 17.9% of older patients and 82 participants with delirium were assessed at 3 months: 5 (6%) had persistent delirium, 14 (17%) had mild cognitive impairment and 47 (57%) had dementia. In 17 participants with prior dementia and 14 with prior mild cognitive impairment the diagnosis had been unrecognised, amounting to 31/82 (38%) of all patients with delirium having some form of previously undiagnosed cognitive impairment.

Conclusion

Given that over 1/3 of older patients with delirium were found to have a previously undiagnosed cognitive impairment, the development and evaluation of services to follow-up and manage patients with delirium is warranted.

Key words: Delirium, dementia, mild cognitive impairment, MCI, general hospital, prevalence, aged

Key Phrases:

17% of patients with delirium had mild cognitive impairment

57% of patients with delirium had DSM-IV dementia

One third of patient with dementia had previously undiagnosed dementia

1/3 of older patients with delirium were found to have a previously undiagnosed cognitive impairment

Background

Delirium is a neuropsychiatric syndrome characterised by an acute change in cognition, attentional deficits and altered arousal [**1**]. It accounts for 20% of emergency hospital admissions in older people [**2**]. Delirium is associated with multiple adverse consequences including increased mortality and new institutionalisation [**3**].

Dementia is a chronic neurodegenerative syndrome with multiple causes, usually characterised by progressive cognitive change including amnesic and executive deficits and functional decline [**4**]. It is common in the general hospital setting, affecting up to 40% of acute hospital admissions [**5**]. The true contribution of dementia on the demand for unplanned hospital care of older people may be underestimated because up to half of all cases of dementia found in hospital in research had been previously undiagnosed [**5**]. Older people with dementia admitted to general hospitals also have increased adverse events [**6**] and higher mortality [**7**]. In fact delirium and/or dementia was present in 49% of older unselected admissions in a recent cohort study [**8**].

People with dementia are six times more likely to be admitted to hospital with delirium [**9**]. Given the high proportion of undiagnosed dementia in acutely hospitalised patients in general, we hypothesised that patients with delirium are likely to have an especially high prevalence of undiagnosed dementia.

Mild cognitive impairment (MCI) is a syndrome of reported memory loss and measurable cognitive deficit, but with the deficit not severe enough to affect activities of daily living. MCI affects approximately 5% of older people, and is associated with a 5-10% yearly risk of

development into dementia [**10**]. MCI is a risk factor for delirium [**11**]. Little is known about the prevalence of MCI in general hospital or in hospitalised people with delirium.

The prevalence of dementia in older hospital patients with delirium ranges from 51% to 68% from eight individual cohort studies [**8**, **12-20**]. Only two studies however used recognised reference criteria for the diagnosis of both delirium and dementia [**19, 20]**. Two studies reported the prevalence of unrecognised cognitive impairment. No studies reported the prevalence of mild cognitive impairment. These studies are summarised in supplemental table 1 in the supplementary data on the journal website http://www.ageing.oxfordjournals.org/. No previous studies to our knowledge report the true prevalence of undiagnosed dementia in hospital inpatients patients with delirium by reference criteria. The objective of this prospective study was to identify accurately the proportion of people admitted as unplanned admissions to hospital with delirium with both previously diagnosed and undiagnosed dementia and mild cognitive impairment. By determining these proportions, we aimed to determine the extent to which prevalent delirium is a marker of previously undiagnosed dementia and mild cognitive impairment.

Method

A prospective cohort study was carried out. Unselected patients aged 70 years and over with an unplanned medical admission to a UK teaching hospital between March 2013 and November 2014 were screened by a single trained assessor (a specialist in geriatric medicine) for delirium. The screening used the Confusion Assessment Method (CAM) [21], Abbreviated Mental Test Score (AMTS) [22], the Digit Span test, and a detailed review of the medical notes. Participants were eligible for the study if they met the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV-TR) criteria for delirium [23]. The screening took place on 143 days evenly spread over the period. Potential

participants who were unable to communicate because of severe sensory impairment or inability to communicate in English were excluded, as were those deemed to be at risk of imminent death.

Patients with delirium were then invited to participate. Informed consent was sought from the potential participant if they had the mental capacity to give it. For those who lacked the mental capacity to give informed consent, the next of kin was consulted in accordance with the provisions of the Mental Capacity Act with respect to participation in research, and they were asked also to agree to act as informants.

Baseline data were collected including demographic data, the Charlson Co-morbidity Index and the Clinical Frailty Index [24, 25]. Review of the medical record accompanied an informant interview that enquired about a previous diagnosis of dementia or MCI, and a history of prior cognitive function, but no new diagnoses of dementia were made at baseline due to the difficulties of distinguishing dementia from delirium in the presence of the latter.

At 3 months, a follow-up assessment was undertaken in survivors, at the patient's own home or hospital if they were still an in-patient, by the same assessor who had seen them at baseline. The presence of persistent delirium was first established using DSM-IV-TR criteria for delirium. If no delirium was present a standardised history and examination, including the Addenbrooke's Cognitive Examination III (ACEIII) [26], was performed to establish the presence or absence of dementia or mild cognitive impairment before the onset of the delirium. Dementia and subtype was diagnosed using the DSM-IV-TR criteria [27]: (1) the development of multiple cognitive deficits, including memory impairment, and (2) the impairment is sufficiently severe to cause impairment in occupational or social function. MCI was diagnosed using the current consensus definition [28]: (1) the person is neither normal

nor demented, (2) there is evidence of cognitive decline, and (3) that activities of daily living are preserved and complex instrumental functions are either intact or minimally impaired.

The final diagnosis was made synthesising all available information in relation to the 6 month period before delirium hospitalisation, to make the diagnosis of either dementia or MCI at the index admission. The symptoms of cognitive and functional decline had to have been present for at least 6 months prior to the admission with delirium, as indicated by DSM-IV. It is not possible to diagnose DSM-IV dementia in the presence of delirium so follow-up at three months was chosen as the best balance to allow recovery from delirium and ensuring an accurate and near-contemporaneous diagnosis of dementia at the index admission.

Data were analysed using IBM SPSS version 20 for Windows. Descriptive statistics were used to describe the proportions of cognitive diagnoses given to the cohort with 95% confidence interval calculated. Differences between common clinical variables were analysed, using the independent t-test, Kruskall-Wallis test or chi-squared test depending on the normality of the variables and whether the variables were continuous or categorical. Odds ratios to predict the risk of having previously undiagnosed dementia were calculated using univariate binary logistic regression.

The study was reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [29].

Ethics, consent and permissions

Ethical and regulatory approvals were obtained (Bradford Ethics Committee, part of the Yorkshire and Humber National research and Ethics Service, ref: 12/YH/0534). The consent process is described in the methods.

Results

Of 1668 available older people admitted to hospital, 1327 were screened for delirium between March 2013 and November 2014. Of these, 228/1327 (17·2%) were diagnosed with DSM-IV-TR delirium. 125 of 228 (54·8%) were recruited. The main reason for non-recruitment was lack of an available next of kin to act as consultee (57/103).

Of the 125 recruited, 45 (36%) had a previously recognised diagnosis of dementia. The diagnosis had been made by a GP in 4/45 (9%) cases, a geriatrician in 7/45 (16%) cases and an old age psychiatrist in 34/45 (76%) cases. 32/45 (71%) had been assessed in a memory clinic and 17/45 (38%) were on cognitive enhancing drugs.

Of the 125 recruited, 82 (66%) were followed up at 3 months: 25 (20%) had died, 10 (8%) declined the follow-up visit and 8 (6%) were not contactable. There was no difference in age, gender or admission dementia status between those followed up and those not. The mean age of the followed up sample was 84.4 years and 65.9% were female. 21/82 (24%) were from a care home. Figure 1 shows participant flow.

At 3 months 5/82 (6%) had persistent delirium, 14/82 (17%) were diagnosed with prior MCI, 47/82 (57%) were diagnosed with dementia and 16/82 (20%) had no evidence of prior cognitive impairment. Of the 47 with dementia, 31/47 (66%) had Alzheimer's disease, 12/47 (26%) had vascular dementia, 3/47 (6%) had mixed dementia and 1/47 (2%) had dementia with Lewy bodies: 17 (21%) had probable dementia that was present at index admission but

not diagnosed. MCI had not been previously diagnosed in any of those in whom it was diagnosed at the 3-month follow up. Of these newly diagnosed cases, 12 were diagnosed with Alzheimer's disease and 5 with vascular dementia. In total, 31/82 patients who had been admitted to hospital with delirium had previously undiagnosed cognitive impairment, that is either dementia or MCI. Figure 2 illustrates these proportions with 95% confidence intervals.

The group with prior cognitive impairment had a higher burden of co-morbidity (median co-morbidity index 2·0 vs 0·0, p=0.002) and frailty (median clinical frailty scale 5·5 vs 4·0, p<0·0005) than the group with no prior cognitive impairment. See table 1.

Fifty of the 82 had no recognised diagnosis of dementia when admitted to hospital with 17/50 (34%) of those diagnosed with dementia at follow-up. When trying to predict unrecognised dementia at admission from the group admitted with no recognised diagnosis of dementia, age and frailty were significantly associated with having unrecognised dementia. Univariate logistic regression demonstrates every increased year of age was associated with a 12% increased risk of having unrecognised dementia (OR 1.12, 95% CI 1.01-1.25) and every increased point in the Rockwood clinical frailty scale was associated with a two and a half fold increased risk of having unrecognised dementia (OR 2.58, 95% CI 1.34-4.97). Please see supplementary table 2 in the supplementary data on the journal website http://www.ageing.oxfordjournals.org/ .

Discussion

The main findings in this study are that nearly 4 in 5 older emergency medical patients with delirium also have dementia or MCI, and that half of those with dementia or MCI did not

have a prior diagnosis. Our findings are consistent with previous studies of dementia prevalence in older patients with delirium, which report a range of 51-68% **[8, 17]**. Delirium was diagnosed on admission in 17% of older people in our cohort, which also is in keeping with previously reported prevalence rates (15-25%) **[2, 30]**.

This study adds to prior reports finding that unrecognised cognitive impairment is common among patients with delirium. However, no previous studies have reported the proportion of cases of delirium who had undiagnosed dementia at presentation diagnosed according to the reference standard, and none have previously reported the prevalence of prior mild cognitive impairment patients presenting with delirium. Two studies report the prevalence of unrecognised cognitive impairment. In a study measuring drug metabolism in older patients with delirium, 'probable dementia' was recorded using a validated informant questionnaire (Informant Questionnaire of Cognitive Decline in the Elderly, IQCODE) and informant interview **[15]**. The assessment was carried out at the time of admission and 63/105 patients with delirium had probable dementia. Of those 37/105 (35%) had no prior diagnosis. A further study reported the proportion of undiagnosed cognitive impairment in delirium, reporting that in only 5 of 28 participants with delirium and cognitive impairment, a diagnosis of dementia was recorded in medical notes **[18]**. Here the IQCODE administered over the telephone was used to classify previous cognitive impairment.

The ascertainment at three months of pre-delirium dementia and MCI used standardised diagnostic processes which included the assessment of cognition at that point, and hence post-delirium cognitive impairment could potentially have led to an over-estimation of the number of cases of prior dementia or prior MCI in borderline cases. We judge this risk to be small, as the amount of post delirium cognitive impairment is small, and the diagnoses of prior MCI and prior dementia rarely relied solely upon the cognitive assessment made at three months.

Although the study did not recruit all patients admitted to hospital with delirium, the main reason for non-recruitment was a lack of a consultee. There was no difference between the age or sex of those who were and were not recruited, so this is unlikely to have caused a significant bias in our results. Recognising the difficulty of separating delirium from dementia, we applied formal reference standard criteria for the diagnosis of delirium and dementia, using a trained assessor and using assessment at three months rather than solely on admission: for these reasons we believe these findings to be robust. Persistent symptoms of delirium were present at three months in 5 (6%) participants, though this may have represented a new episode at assessment.

The significance of the finding of a high proportion of people with delirium having prior undiagnosed cognitive impairment is that, not only is delirium an important diagnosis to make in older patients admitted to hospital **[31]**, it also presents a strong opportunity to identify dementia and MCI **[32]**. A timely diagnosis of dementia during hospital admission may ameliorate adverse events associated with a hospital stay [**6**], allow suitable resource allocation, such as signposting to a cohort ward **[33]** or a trigger for comprehensive geriatric assessment **[34]**. In the longer term, diagnosing patients with dementia allows identification of those who would benefit from pharmacological therapy **[35]**. Patients could then be counselled, advised and offered post diagnostic support, or offered the opportunity to participate in research. This would not be possible without these diagnoses being recognised. In the UK there is a government drive to improve dementia diagnosis rates through the National Dementia Strategy**[36]** and the Prime Minister's dementia challenge[37], and similar activities are also occurring worldwide. Routine follow up of patients who have presented with delirium could therefore be of value - to identify those with persisting delirium as well as to identify previously unrecognised dementia and mild cognitive impairment.

A frailty measure, the Clinical Frailty Scale, would appear to have discriminating ability in identifying those with delirium who also have dementia (Tables 1 and supplementary table 2). This suggests that there is also value in the assessment of frailty in this cohort.

Further work is now required to develop follow-up procedures to identify unrecognised dementia, and to evaluate their cost effectiveness. Although screening tools for dementia in the acute hospital setting exist **[38]** future work should concentrate on developing optimised tools to identify dementia and MCI accurately in people with delirium, as well as evaluating the potential benefits timely diagnosis in hospital offers.

Conclusions

Dementia in acutely hospitalised older patients is common and is associated with poor acute and long-term health outcomes, yet it is currently under diagnosed. Our findings confirm that older people in hospital with delirium are a high-risk group for undiagnosed cognitive impairment (dementia and MCI). Delirium is therefore a target condition to screen or case-find for dementia in general hospitals. However, improved identification in hospitals and validated methods of evaluation and follow-up of older people with delirium in hospitals are needed. Practitioners should consider adopting informant interviews and other methods in detecting possible dementia in older acute hospital patients with delirium.

Acknowledgements

TAJ is supported jointly by the Research into Ageing Fund; a fund set up and managed by Age UK and the British Geriatrics Society (#367)

We gratefully acknowledge all participants, consultees and informants for their participation in the study

Declaration of interests

The authors have no declaration of interests to declare

Author contributions

TAJ conceived and designed the study with significant contributions from AMJM, JRG, JML and BS. TAJ carried out all assessments, data analysis and wrote the first manuscript draft. All authors contributed to data interpretation and further revisions of the manuscript. The final paper has been approved by all authors.

Table 1: Demographic and illness data of patients organised by diagnosis at 3 month follow up. MCI=mild cognitive impairment, ACEIII = Addenbrooke's Cognitive Assessment III, carried out at 3 month follow-up, Difference = Difference between cognitive impairment and no cognitive impairment, using independent samples Kruskall-Wallis test as data not normally distributed, NS=not significant, *=statistically significant.

	Cognitive impairment at 3 months						
	Persistent delirium N=5	MCI N=14	Dementia – previously recognised N=30	Dementia – not previously recognised N=17	Combined cognitive impairment N=66	No cognitive impairment N=16	Difference
Age Years, mean, SD	84.4±3.7	82.7±5.0	84.6±6.5	87.2±7.0	84.4±6.5	82.3±7.6	NS
Gender % female	20.0	64.3	76.0	64.7	66.7%	62.5	NS
Co-morbidity (Charlson co-morbidity index) Median, IQR	3(3)	1.5(3)	2(2)	2(2)	2(2)	0.0 (2)	.002 *
Frailty (Rockwood clinical frailty scale) Median (IQR)	6(4)	5(1)	6(1)	6(2)	5.5(1)	4(2)	<0.0005*
Cognitive assessment (ACEIII) Mean, SD	NA	66.4 (8.7)	20.1(23.7)	29.4(26.5)	33.2(28.7)	86.8(7.2)	<0.0005*

Figure 1: Flowchart of participant flow through the study. ♀=female.

Figure 2: Flow chart of diagnosis of prior cognitive impairment made at 3-month follow-up. 95% confidence intervals for all proportions shown in brackets.

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PLEASE NOTE: The very long list of references supporting this report has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available on the journal website http://www.ageing.oxfordjournals.org/ as appendix 1

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