Important factors in predicting mortality outcome from stroke: findings from the Anglia Stroke Clinical Network Evaluation Study

Phyo Kyaw Myint1,2,3, Max O. Bachmann3, Yoon Kong Loke3,4, Stanley D. Musgrave3, Gill M. Price3, Rachel Hale4, Anthony Kneale Metcalfe3,4, David A. Turner3, Diana J. Day5, Elizabeth A. Warburton5,6, John F. Potter3,4

1Epidemiology Group, Institute of Applied Health Sciences, School of Medicine, Medical Sciences & Nutrition, University of Aberdeen, Scotland, UK
2Clinical Gerontology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK
3Norwich Medical School, University of East Anglia, Norwich, UK
4Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK
5Addenbrooke’s Hospital, Cambridge, UK
6Department of Clinical Neuroscience, University of Cambridge, Cambridge, UK

Address correspondence to: P. K. Myint. Tel: (+44) (0) 1224 437841; Fax: (+44) (0) 1224 437911. Email: phyo.myint@abdn.ac.uk

Abstract

Background: although variation in stroke service provision and outcomes have been previously investigated, it is less well known what service characteristics are associated with reduced short- and medium-term mortality.
Method: data from a prospective multicentre study (2009–12) in eight acute regional NHS trusts with a catchment population of about 2.6 million were used to examine the prognostic value of patient-related factors and service characteristics on stroke mortality outcome at 7, 30 and 365 days post stroke, and time to death within 1 year.

Results: a total of 2,388 acute stroke patients (mean (standard deviation) 76.9 (12.7) years; 47.3% men, 87% ischaemic stroke) were included in the study. Among patients characteristics examined increasing age, haemorrhagic stroke, total anterior circulation stroke type, higher prestroke frailty, history of hypertension and ischaemic heart disease and admission hyperglycaemia predicted 1-year mortality. Additional inclusion of stroke service characteristics controlling for patient and service level characteristics showed varying prognostic impact of service characteristics on stroke mortality over the disease course during first year after stroke at different time points. The most consistent finding was the benefit of higher nursing levels; an increase in one trained nurse per 10 beds was associated with reductions in 30-day mortality of 11–28% (P < 0.0001) and in 1-year mortality of 8–12% (P < 0.001).

Conclusions: there appears to be consistent and robust evidence of direct clinical benefit on mortality up to 1 year after acute stroke of higher numbers of trained nursing staff over and above that of other recognised mortality risk factors.

Keywords: older people, stroke, services, staffing, outcome, mortality

Introduction

Stroke is one of the leading causes of death and the leading cause of long-term disability worldwide [1]. Langhorne et al. [2] demonstrated the clear clinical benefits of organised stroke unit care in their landmark systematic review, although the exact mechanisms for this effect were unclear. It appears that clinical benefits associated with stroke units are being observed up to 10 years post discharge [3]. Further work identified processes of care (e.g. therapy assessments) and management strategies (e.g. early mobilisation), and having access to facility (e.g. MRI) as characteristics of a stroke unit associated with a good outcome [4, 5].

Stroke care in United Kingdom is still far from ideal, patients having a worse outcome in terms of death and dependency than many other European countries [6–8], at least in part probably due to differences in care provided [9]. There is also variation in outcomes between different localities within the United Kingdom; results from a series of national stroke audits in the United Kingdom have repeatedly highlighted the differences in stroke services and care between hospitals and mortality outcome [10–12]. Examples of such differences include staffing levels, presence of early supported discharge, stroke specialist on call rota for thrombolysis and access to neurovascular/neurosurgical service [13].

Examination of the variation in stroke services and outcome in the UK setting could provide a valuable insight into which stroke service characteristics are associated with the best outcomes. This can only be achieved by assessment of the relationship between robustly collected detailed service level characteristics and relevant outcomes using representative observational sample taken into account of case-mix and access to care (e.g. urban vs rural setting). The study aimed to describe the regional variation in stroke mortality and to identify the characteristics of the services that were associated with better outcomes after accounting for case-mix differences and individual prognostic factors in a mostly rural population in East of England.

Methods

We conducted a cohort study in the East of England through the Anglia Stroke & Heart Clinical Network (ASHCN), with 1 year of follow-up after admission for stroke, or stroke while in hospital. The detailed description of the study has been previously reported [13]. Ethical approval was obtained from the NRES Committee East of England—Norfolk (REC Reference number 10/H0310/44). A consecutive sample of these patients was systematically selected in all eight acute NHS trusts in Norfolk, Suffolk and Cambridgeshire, with total catchment population of 2.6 million, between October 2009 and September 2011 [14].

Anonymised individual patient data on patients’ prognostic factors on admission, health care received and mortality outcomes, as well as relevant characteristics of each provider organisation were collected prospectively. Baseline data on patients’ prognostic characteristics on admission were prospectively recorded as a part of routine clinical data collection by ASHCN. Dates of death from any cause until 13 March 2013 were obtained by linkage with the NHS Central Register.

Data on the service capabilities and population and patient load of the eight units were also collected by research staff at each site. Information on the population served, staffing numbers and training at all levels and availability of essential clinical services was recorded at each site for each of four 6-month blocks spanning the 2 years in which stroke patient admissions were included in the study. For each field analysed, if a service characteristic at a site varied over the 2 years, then the mean of the values was used in the analysis.
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Statistical analysis

Mortality outcome was examined at four time points: death within 7 (acute), 30 (sub-acute) or 365 days after admission (binary variables) (longer term) and time to death (with follow-up censored 365 days after admission). Analysis was conducted at individual patient level, with each patient also ascribed the characteristics of the stroke unit and hospital to which they were admitted. Intra-unit correlation of outcomes was accounted for using Huber-White robust adjustment [15].

First, we identified patient characteristics independently associated with above mortality outcome, using logistic regression or Cox-proportional hazards models as appropriate. The variables were selected based on well validated off the shelf stroke mortality predictors [16]. For Cox models, the proportionality of hazards during follow-up was assessed for each prognostic variable using complementary log–log plots. Second, we examined each characteristic of the stroke units separately, estimating its association with each outcome after adjustment for all of the prognostic variables selected in the first step. Staff to bed ratios were used in these analyses, because they are better indicators of the adequacy of staffing in each unit than are crude staff numbers. These ratios were expressed as whole time equivalent staff per 10 beds, which is a more realistic reflection of staffing levels in NHS stroke units than staff per single bed. Third, we modelled combinations of stroke unit characteristics, together with the same prognostic characteristics used in steps one and two. Stroke unit characteristics that were independently associated with each outcome were selected in the same way as prognostic characteristics selected in step one.

We excluded 4.3% of patients who were transferred between the sites because transferred patients tend to have more severe disease, so bias would be introduced depending on whether they were assigned to initial site or recipient site. We imputed missing prognostic data using multiple imputation with chained equations [17]. Ten data sets were created for each outcome, and regression results from each were combined using Rubin’s rules [18]. Complete case sensitivity analyses were done, repeating all analyses but excluding anyone with any missing prognostic data. We estimated the proportion of outcome variance explained by each model, using pseudo $R^2$ for logistic regression models and Royston’s $R^2$ for Cox models [19]. Analyses were performed using Stata SE 12.0 statistical software [20].

Table 1 shows the distribution of the sample characteristics with regard to demographics, stroke-related factors (subtype, severity taken as reflected by Oxfordshire Community Stroke Project (OCSP) type), prestroke disability as modified Rankin score (mRS) and major cardiovascular co-morbidities. The total sample characteristics and the sample characteristics of those who died within 1 year or not (primary outcome) are presented separately. Table 1 also shows the multiple logistic regression model results adjusted for all patient-related characteristics shown in the table and for intra-hospital correlation of outcome, after multiple imputation of missing covariate data. Increasing age, haemorrhagic stroke type, total anterior circulation stroke, increasing prestroke frailty depicted by mRS, higher glucose level on admission, history of ischaemic heart disease and hypertension were identified as patient level prognostic factors that were independently associated with significant effect on mortality at 1 year. These prognostic variables explained 29% of the variance in 1 year mortality (pseudo $R^2 = 0.29$). For the equivalent logistic regression models with 7-day and 30-day mortality as outcomes, the pseudo $R^2$ values were 0.31 and 0.32, respectively. For the equivalent Cox model, the $R^2$ value was 0.62 (data not shown).

Supplementary Table 1, available at *Age and Ageing* online shows the characteristics of each stroke unit and their mortality rates at 7 and 30 days and 1 year after admission stroke event. There was wide variation in characteristics of services but there were no obvious outliers.

Table 2 shows the associations between the selected stroke unit characteristics and odds of mortality for the three time points, as well as hazards of death during 1 year of follow-up, adjusted for patient's prognostic factors. Overall all service characteristics indicative of a better resourced unit, that is, with higher staffing levels, were associated with better outcomes across these time points. Type of hospital (district general or university) and ratio of stroke admissions per bed per month were less consistently associated with lower mortality. Having an early supported discharge service was not associated with a reduction in mortality but higher trained nursing staff levels were consistently associated with decreased death rates.

Table 3 shows the stroke unit characteristics independently associated with each outcome after mutual adjustment for other influential hospital characteristics. A consistent finding was that higher trained nurse (NHS staff grade 5 and above, i.e. staff nurse or senior staff nurse) to bed ratios were associated with lower all-cause mortality. In addition, more beds per stroke unit and fewer admissions per bed per month were independently associated with higher mortality within a year and not having an early discharge policy were also associated with greater odds of death within 7 days. Fewer beds per stroke unit, more rehabilitation beds, not having an early discharge policy and being in a university hospital were associated with higher odds of death within 30 days. Complete case analyses without imputed data produced similar results.

Results

Of 2,656 consecutive admissions during the study periods, after exclusion of 157 admissions with other diagnoses (see Supplementary data, available at *Age and Ageing* online), transfers ($n = 108, 4.3\%$) and those with missing data for admission dates ($n = 3, 0.1\%$), 2,388 patients (mean age (SD) 76.9 (12.7) years; 47.3% men, 87% ischaemic stroke) were included in the study.
In this study, we found that whilst there was considerable variations in stroke service provision amongst the stroke units even within a relatively small geographical region, variation in mortality outcomes following acute stroke was not significantly different, if unadjusted data were used. Stroke mortality, however, appeared to be strongly influenced by certain known patient level characteristics and certain service characteristics. Higher nursing:beds ratio was strongly and consistently associated with a better mortality outcome even after controlling for patient level prognostic factors. These results suggest that increasing stroke unit staff by one whole time equivalent trained nurse for every 10 beds could reduce 1 year mortality significantly by 8–12% (Table 3).

Some of these findings, however, require cautious interpretation as they may be partly explained by confounding factors that are not adequately adjusted for e.g. more severe cases being admitted to larger units with neurosurgical facility. Larger units are not necessarily equipped with better resources; indeed as evident in our study many indicators of better resources are associated with a lower mortality (see Table 2). This study has focused on type of services/staffing and outcome relationship rather than process measures and outcome. Care processes after admission are not confounders but intermediate variables that lie on casual pathways between prognostic characteristics and outcomes.

### Table 1. Sample characteristics on admission, and their independent association with 1-year mortality in Anglia Stroke Clinical Network Evaluation Study (2009–12)

| Patients’ characteristic | Total (N = 238,888) | % | Death (N = 759) | % Who died | OR \(^a\) | 95% CI \(^a\) | \(P^b\) |
|-------------------------|---------------------|---|----------------|------------|---------|-----------|------|
| Age quintiles (years)   |                     |   |                |            |         |           |      |
| 18–64                   | 463                 | 19.4 | 54             | 11.7       | 1.0     | –         | <0.001\(^b\) |
| 65–75                   | 434                 | 18.2 | 85             | 20.0       | 1.5     | 1.0–2.2   | 0.028 |
| 76–81                   | 491                 | 20.6 | 133            | 27.1       | 2.3     | 1.7–3.1   | <0.001 |
| 82–86                   | 452                 | 19.0 | 187            | 41.4       | 3.8     | 2.5–5.6   | <0.001 |
| 87–101                  | 544                 | 22.8 | 298            | 54.8       | 6.1     | 3.5–10.4  | <0.001 |
| Sex                     |                     |   |                |            |         |           |      |
| Female                  | 1,256               | 52.6 | 454            | 36.2       | 1.0     | –         |       |
| Male                    | 1,130               | 47.4 | 305            | 27.0       | 1.2     | 0.8–1.6   | 0.36  |
| Type of stroke          |                     |   |                |            |         |           |      |
| Infarct                 | 1,990               | 86.8 | 569            | 29.6       | 1.0     | –         | <0.001\(^b\) |
| Haemorrhage             | 288                 | 12.6 | 147            | 51.0       | 2.3     | 1.5–3.6   | <0.001 |
| Haemorrhagic infarct    | 16                  | 0.70 | 5              | 31.3       | 0.7     | 0.2–2.8   | 0.65  |
| OCSP classification     |                     |   |                |            |         |           |      |
| PACS                    | 825                 | 39.6 | 184            | 22.3       | 1.0     | –         |       |
| LACS                    | 517                 | 24.8 | 78             | 15.1       | 0.8     | 0.5–1.1   | 0.20  |
| POCS                    | 295                 | 14.1 | 68             | 23.1       | 1.4     | 1.0–2.1   | 0.06  |
| TACS                    | 449                 | 21.5 | 315            | 70.2       | 7.4     | 5.9–9.3   | <0.001 |
| Prestroke mRS           |                     |   |                |            |         |           |      |
| 0                       | 959                 | 50.0 | 163            | 17.0       | 1.0     | –         | <0.001\(^b\) |
| 1                       | 360                 | 18.8 | 110            | 30.6       | 1.8     | 1.3–2.4   | <0.001 |
| 2                       | 206                 | 10.7 | 74             | 36.0       | 2.4     | 1.6–3.6   | <0.001 |
| 3                       | 208                 | 10.8 | 109            | 52.4       | 4.3     | 2.9–6.4   | <0.001 |
| 4                       | 131                 | 6.8  | 88             | 67.2       | 6.5     | 4.3–10.0  | <0.001 |
| 5                       | 55                  | 2.9  | 43             | 78.2       | 8.9     | 3.8–21.2  | <0.001 |
| Glucose quintile (mmol/L)|                     |   |                |            |         |           |      |
| <5.6                    | 386                 | 18.7 | 97             | 25.1       | 1.0     | –         |       |
| 5.7–6.4                 | 428                 | 20.7 | 107            | 25.0       | 0.9     | 0.6–1.3   | 0.47  |
| 6.5–7.3                 | 418                 | 20.3 | 106            | 25.4       | 1.0     | 0.7–1.3   | 0.86  |
| 7.4–8.9                 | 409                 | 19.8 | 151            | 36.9       | 1.5     | 1.1–2.0   | 0.02  |
| >8.9                    | 423                 | 20.5 | 199            | 47.0       | 1.9     | 1.4–2.5   | <0.001 |
| Ischaemic heart disease |                     |   |                |            |         |           |      |
| No                      | 1,700               | 75.1 | 517            | 30.4       | 1.0     | –         | <0.001 |
| Yes                     | 565                 | 24.9 | 220            | 38.9       | 1.3     | 1.1–1.6   | 0.01  |
| Diabetes                |                     |   |                |            |         |           |      |
| No                      | 1,889               | 83.0 | 607            | 32.1       | 1.0     | –         |       |
| Yes                     | 388                 | 17.0 | 135            | 34.8       | 0.9     | 0.6–1.3   | 0.52  |
| Hypertension            |                     |   |                |            |         |           |      |
| No                      | 949                 | 41.7 | 316            | 33.3       | 1.0     | –         |       |
| Yes                     | 1,329               | 58.3 | 426            | 32.1       | 0.8     | 0.7–1.0   | 0.02  |

\(^a\)Multiple logistic regression model, adjusted for all other variables in the table and for intra-hospital correlation of outcome, after multiple imputation of missing covariate data. Pseudo R2 for complete case analysis = 0.29.

\(^b\)Wald test for all categories of variable. PACS, partial anterior circulation stroke; LACS, lacunar stroke; OCSP, Oxfordshire Community Stroke Project; POCS, posterior circulation stroke; TACS, total anterior circulation stroke.
Table 2. Associations between mortality at various time points and single stroke unit characteristics, adjusted for patients’ prognostic characteristics on admission

| Outcome | Time to deatha | Died within 7 daysb | Died within 30 daysb | Died within 365 daysb |
|---------|----------------|--------------------|---------------------|----------------------|
|         | Hazard ratio   | 95% CI             | Odds ratio          | 95% CI               | Odds ratio          | 95% CI | P   |
|         | P              |                    | Odds ratio          | 95% CI               | Odds ratio          | 95% CI | P   |
|         |                |                    |                     |                      |                     |        |     |
| Stroke unit characteristic |                |                    |                     |                      |                     |        |     |
| District general vs university hospital | 0.91 | 0.70–1.18 | 0.474 | 0.80 | 0.98–1.11 | 0.018 | 0.69 | 0.52–0.93 | 0.013 | 0.59 | 0.61–1.31 | 0.568 |
| Early supported discharge service | 1.27 | 1.08–1.49 | 0.003 | 1.28 | 0.95–1.71 | 0.099 | 1.41 | 1.04–1.91 | 0.029 | 1.40 | 1.04–1.88 | 0.028 |
| No. of stroke admissions per month (per 10 beds) | 1.04 | 1.00–1.07 | 0.037 | 1.07 | 1.01–1.12 | 0.017 | 1.07 | 1.03–1.13 | 0.001 | 1.07 | 1.02–1.11 | 0.003 |
| No. of stroke admissions per month (per 10 admissions) | 1.09 | 1.05–1.13 | <0.001 | 1.14 | 1.05–1.12 | 0.001 | 1.21 | 1.12–1.29 | <0.001 | 1.13 | 1.07–1.21 | <0.001 |
| Ratio stroke admissions per month: stroke unit beds | 0.92 | 0.64–1.31 | 0.166 | 1.07 | 0.62–1.86 | 0.089 | 0.89 | 0.47–1.66 | 0.094 | 1.09 | 0.65–1.83 | 0.747 |
| No. of rehabilitation beds in unit (per 10 beds) | 1.09 | 0.96–1.23 | <0.001 | 1.17 | 1.01–1.36 | 0.036 | 1.23 | 1.05–1.44 | 0.010 | 1.08 | 0.90–1.28 | 0.418 |
| Staff: bed ratios (No. of staff per 10 stroke unit beds) Trained nurses | 0.94 | 0.91–0.96 | <0.001 | 0.94 | 0.89–0.99 | 0.018 | 0.93 | 0.86–0.99 | 0.032 | 0.90 | 0.88–0.92 | <0.001 |
| Stroke consultants | 0.65 | 0.47–0.89 | 0.007 | 0.93 | 0.51–1.71 | 0.826 | 0.54 | 0.29–1.02 | 0.058 | 0.56 | 0.38–0.82 | 0.003 |

* Each hazard ratio is from a separate regression model. All regression models adjusted for age, type of stroke, OCSP classification, modified Rankin score, ischaemic heart disease, hypertension, blood glucose level on admission; not mutually adjusted for the other stroke unit characteristics.

aCox regression models, censored at 365 days.
bLogistic regression models.
cNHS Band 5 and above (bands 5, 6 and 7).
that even in rural areas if stroke units were equipped with optimal staffing mortality outcome can be improved. Indeed, Fulop et al. [26] recently highlighted challenges in evaluation of health system changes due to the different timings of the reconfigurations; the retrospective nature of the evaluations; and the current organisational turbulence in the English NHS.

The UK NHS system is health care model as a universal free at the point of care health care system, which has been shown to be very cost efficient [27]. Our results highlight the importance of staffing levels and having a reasonable catchment population/stroke service as key factors associated with a better mortality outcome in stroke, which is one of the biggest killers globally. Our study thus provides useful information to local populations, clinicians and service providers across the world to design stroke services that would address these key determinants of stroke mortality outcome.

**Key points**

- Variation in stroke services explained very little of the variation in mortality in stroke.
- Patient level prognostic variables explained 29% of the variance in 1-year mortality in stroke.
- Every 1 point increase in trained nurses per 10 beds was associated with significant reduction in stroke mortality.

**Supplementary data**

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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ASCNES Group (alphabetical order)

- Max O Bachmann (UEA)
- Garry R Barton (UEA)
- Fiona Cummings (ASHCN)
- Genevieve Dalton (ASHCN)
- Diana J Day (ASHCN/AH)
- Abraham George (JPUH)
- Rachel Hale (UEA)
- Anthony Kneale Metcalf (NNUH/UEA)
- Stanley D Musgrave (UEA)
- Phyo Kyaw Myint (UoA/UEA)
- Joseph Ngeh (IPH)
- Anne Nicholson (WSH)
- Peter Owusu-Agyei (PH)
- John F Potter (UEA/NNUH)
- Gill M Price (UEA)

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**Table 3.** Associations between mortality outcomes and mutually adjusted stroke unit characteristics, also adjusted for prognostic characteristics on admission

| Outcome | Hazard Ratio | 95% CI | P | Odds ratio | 95% CI | P | Odds ratio | 95% CI | P | Odds ratio | 95% CI | P |
|---------|--------------|--------|---|------------|--------|---|------------|--------|---|------------|--------|---|------------|--------|---|
|         |              |        |   |            |        |   |            |        |   |            |        |   |            |        |   |
| Time to deatha |        |        |   |            |        |   |            |        |   |            |        |   |            |        |   |
| Died within 7 daysb |        |        |   |            |        |   |            |        |   |            |        |   |            |        |   |
| Died within 30 daysb |        |        |   |            |        |   |            |        |   |            |        |   |            |        |   |
| Died within 365 daysb |        |        |   |            |        |   |            |        |   |            |        |   |            |        |   |
| District general vs university hospital | 0.62 | 0.49–0.79 | <0.001 | 0.79 | 0.62–1.00 | 0.007 | 0.79 | 0.62–1.00 | 0.007 | 0.79 | 0.62–1.00 | 0.007 |
| Early stage discharge policy during study | 0.48 | 0.29–0.82 | 0.007 | 0.50 | 0.28–0.89 | 0.018 | 0.50 | 0.28–0.89 | 0.018 | 0.50 | 0.28–0.89 | 0.018 |
| No. of stroke unit beds (per 10 beds) | 1.07 | 1.03–1.12 | 0.0003 | 1.41 | 1.17–1.71 | <0.001 | 0.86 | 0.74–0.99 | 0.042 | 0.86 | 0.74–0.99 | 0.042 |
| No. of rehabilitation beds in unit (per 10 beds) | 1.24 | 1.02–1.50 | 0.028 | 1.24 | 1.02–1.50 | 0.028 | 1.24 | 1.02–1.50 | 0.028 | 1.24 | 1.02–1.50 | 0.028 |
| Ratio stroke admissions per month: stroke unit beds | 0.84 | 0.74–0.96 | 0.010 | 0.84 | 0.74–0.96 | 0.010 | 0.84 | 0.74–0.96 | 0.010 | 0.84 | 0.74–0.96 | 0.010 |
| No. of nurses per 10 stroke unit beds | 0.94 | 0.92–0.95 | <0.001 | 0.74 | 0.75–0.94 | 0.002 | 0.80 | 0.72–0.89 | <0.001 | 0.90 | 0.88–0.92 | <0.001 |
| R² for modelc | 0.62 | 0.31 | 0.33 | 0.30 |

Each column of hazard ratios is from the same multiple regression model. All regression models adjusted for age, type of stroke, OCSP classification, modified Rankin score, ischaemic heart disease, hypertension, blood glucose level on admission; not mutually adjusted for the other stroke unit characteristics not listed in the table.

aCox regression model, censored at 365 days.
bLogistic regression models.
cRoyston R² for Cox model, pseudo R² for logistic regression models. Only nurses:bed as the service characteristic in ‘Died within 365 days’ model.
Committee East of England

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Authors’ contributions

P.K.M., D.J.D. and M.O.B. conceived the idea. P.K.M. is the PI of the ASCNES study. J.E.P., M.O.B., A.K.M., G.M.P. and E.A.W. are co-applicants of the grant and co-investigators of the ASCNES. D.J.D. is study steering committee member. R.H. developed electronic data collection forms with PKM and collected data at one site and provided secretarial support. S.D.M. coordinated the study and managed and cleaned the data with G.M.P. M.O.B. and G.M.P. performed the statistical analyses. P.K.M., M.O.B. and Y.K.L. drafted the manuscript and all co-authors contributed in the writing of the paper.

Conflicts of interest

None declared.

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Partial and no recovery from delirium after hospital discharge predict increased adverse events

MARTIN G. COLE¹,², JANÉ MCCUSKER²,³, ROBERT BAILEY⁴, MICHAEL BONNYCASTLE⁴,⁵, SHEK FUNG⁴, ANTONIO CIAMPI²,³, ERIC BELZILE²

¹Department of Psychiatry, St. Mary’s Hospital Center, McGill University, Montreal, Quebec, Canada
²St. Mary’s Research Centre, St. Mary’s Hospital Center, Montreal, Quebec, Canada
³Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada
⁴Division of Geriatric Medicine, St. Mary’s Hospital Center, McGill University, Montreal, Quebec, Canada
⁵Department of Medicine, St. Mary’s Hospital Center, McGill University, Montreal, Quebec, Canada

Address correspondence to: Martin G. Cole. Tel: (+3839) 514-345-3511; Fax: 514-734-2652. Email: martin.cole@ssss.gouv.qc.ca

Abstract

Background: the implications of partial and no recovery from delirium after hospital discharge are not clear. We sought to explore whether partial and no recovery from delirium among recently discharged patients predicted increased adverse events (emergency room visits, hospitalisations, death) during the subsequent 3 months.

Method: prospective study of recovery from delirium in older hospital inpatients. The Confusion Assessment Method was used to diagnose delirium in hospital and determine recovery status after discharge (T0). Adverse events were determined during the 3 months T0. Survival analysis to the first adverse event and counting process modelling for one or more adverse events were used to examine associations between recovery status (ordinal variable, 0, 1 or 2 for full, partial or no recovery, respectively) and adverse events.

Results: of 278 hospital inpatients with delirium, 172 were discharged before the assessment of recovery status (T0). Delirium recovery status at T0 was determined for 152: 25 had full recovery, 32 had partial recovery and 95 had no recovery. Forty-four patients had at least one adverse event during the subsequent 3 months. In multivariable analysis of one or more adverse events, poorer recovery status predicted increased adverse events; the hazard ratio (HR) (95% confidence interval, CI) was 1.72 (1.09, 2.71). The association of recovery status with adverse events was stronger among patients without dementia.

Conclusion: partial and no recovery from delirium after hospital discharge appear to predict increased adverse events during the subsequent 3 months. These findings have potentially important implications for in-hospital and post-discharge management and policy.

Keywords: older people, delirium, partial and no recovery, adverse events, aged