Randomized Controlled Study of Stroke Unit Care Versus Stroke Team Care in Different Stroke Subtypes

Andrew Evans, MRCP; Farzaneh Harraf, MBBS; Nora Donaldson, PhD; Lalit Kalra, PhD

Background and Purpose—The benefits of stroke unit management may vary according to stroke subtype. A post hoc analysis of the influence of stroke subtype on stroke unit effectiveness was undertaken by using prospective data collected in a randomized controlled trial.

Methods—Two hundred sixty-seven patients with moderately severe ischemic stroke (164 with large-vessel infarcts and 103 with lacunar infarcts) were randomly allocated to treatment in stroke units or in general medical wards with specialist stroke team support. Mortality, institutionalization, neurological, functional, and quality-of-life scores and resource use were assessed at 3 and again at 12 months after stroke onset. An intention-to-treat analysis was undertaken, and logistic regression was used to evaluate the independent effect of stroke unit intervention.

Results—Stroke team–supported management was associated with higher mortality (odds ratio [OR] 4.9, 95% CI 1.3 to 18.6) and higher mortality or institutionalization (OR 2.9, 95% CI 1.1 to 7.4) at 3 months (OR 3.6, 95% CI 1.5 to 8.7) and at 1 year (OR 2.8, 95% CI 1.3 to 6.2) in patients with large-vessel infarcts. In contrast, there were no significant differences in outcome in patients with lacunar strokes managed in the stroke unit or by the stroke team. In patients with lacunar strokes, stroke unit care was associated with a longer length of hospital stay (18 versus 13.5 days for stroke unit care versus stroke team care, respectively; P<0.01) and significantly greater use of therapy.

Conclusions—Stroke units improve the outcome in patients with large-vessel infarcts but not in those with lacunar syndromes. For lacunar strokes, stroke unit management may be associated with higher initial health costs for equivalent benefit. (Stroke. 2002;33:449-455.)

Key Words: lacunar infarction ■ large-vessel infarct ■ outcome ■ rehabilitation ■ stroke units

The effectiveness of organized stroke care in reducing mortality, institutionalization, and dependence has been established,1 but there is great variability in outcome between individual studies, with some studies showing no effect2-3 and others showing an extreme positive effect.4,5 Although this variability has been attributed to differences in patient selection, definitions of organized care, or experimental design between trials, the meta-analysis had strict criteria for experimental design and stroke care that were uniform across studies.6 Patient selection criteria were less well-defined in most studies, leaving the possibility that differences in the types of patients or their stroke characteristics may have contributed significantly to the variability in outcome between studies.

The influence of age and stroke severity on the effectiveness of stroke unit care has been demonstrated previously.1,2,7,8 The benefits of stroke unit care may also vary by stroke subtype. Dedicated stroke unit care may be particularly advantageous in patients with large-vessel infarcts (whether atherosclerotic or cardioembolic) because of the relatively higher risk of mortality, early recurrence, and multiple deficits compared with patients with lacunar stroke, who have less severe deficits, low mortality or recurrence, and few specialist needs (beyond diagnosis and acute investigations).9 Support for this hypothesis is provided by the observation that there is little difference in outcome between specialist and nonspecialist care for patients with milder stroke and in elderly patients, groups in which lacunar infarcts are likely to be more prevalent.1,2,8

There have been no direct comparisons of the effectiveness of stroke unit care in patients stratified by type of stroke. Information on stroke subtypes is either incomplete or superficial in most studies included in the meta-analysis, and it will not be possible to use existing data to answer this question. A prospective randomized controlled trial is not justified because it is unethical to assign any stroke patient (regardless of subtype) to a potentially less effective treatment based on existing evidence.10 However, this information is important because acute stroke units remain a limited resource,11 and their effectiveness can be improved by targeting toward appropriate patients.
We have previously reported a randomized controlled trial in 457 patients with acute stroke showing that stroke units were more effective than a specialist stroke team or specialist domiciliary care in reducing mortality and dependence. These patients were investigated comprehensively for stroke etiology and subtype as a part of stroke assessment. In addition, outcome was assessed by using a range of functional and quality-of-life measures at fixed time points up to 1 year after stroke. It was possible to categorize patients by stroke subtype and use prospective data to compare stroke unit care with that provided by a specialist stroke team on general wards for different stroke subtypes.

The objective of the present study was to compare mortality, institutionalization, disability, handicap, quality of life, and resource use in patients categorized as having large-vessel or small-vessel (lacunar) infarcts and managed either on a dedicated stroke unit or by a stroke team on general medical wards.

**Subjects and Methods**

**Patients**

Four hundred fifty-seven acute-stroke patients with moderately severe stroke were randomly allocated to treatment on a stroke unit (n=152), to general medical wards with specialist stroke team support (n=152), or to specialist domiciliary stroke care (n=153) at the time of presentation. The study setting and population, recruitment procedures, inclusion and exclusion criteria, and random allocation methods have been described in detail in our previous study. Moderately severe stroke was defined as persistent neurological deficit affecting continence, mobility, or self-care abilities and requiring multidisciplinary treatment. Although the Barthel score was not a criterion for inclusion, Barthel scores at the time of inclusion (within 72 hours of stroke onset) ranged between 2 and 15. Patients with mild stroke, patients with severe stroke (unconsciousness, swallowing problems not amenable to dietary modification, and/or heavy nursing needs), patients admitted to other hospitals, and patients with unusual or atypical neurological features were excluded. Patients allocated to the domiciliary limb of the original randomized trial were also excluded from the present study because a third (n=51) of patients were admitted to the stroke unit, and it would not be possible to exclude significant bias regarding this group.

**Assignment of Stroke Subtype**

Baseline assessments for patients included the following: demography; comorbidity; premorbid function; Orgogozo score for neurological deficits; Orpington Prognostic Scale for the level of motor, proprioceptive, and cognitive impairments; and Barthel Index for basic activities of daily living. The diagnosis and pathology of stroke was confirmed by CT scanning undertaken within 48 hours of admission (median duration 42 hours after stroke onset). Further CT (n=69) or MRI (n=18) scans were undertaken in patients in whom initial scan findings were unhelpful (eg, normal CT scan, scan undertaken in <24 hours, atypical features, lack of correlation with clinical findings, or unexplained clinical worsening). Duplex ultrasound of the carotid and vertebral arteries was undertaken in 114 (88%) of 129 patients on the stroke unit and 111 (80%) of 138 patients in general wards. Echocardiography was undertaken in patients with atrial fibrillation or in those suspected to have had a large-vessel or small-vessel (lacunar) infarcts and managed either on a dedicated stroke unit or by a stroke team on general medical wards.

All ischemic strokes were assigned to 1 of the 2 major categories: (1) those due to large-vessel disease and (2) those due to small-vessel occlusion. Large-vessel strokes were defined as cortical or subcortical syndromes with infarcts >1.5 cm in diameter on CT scans in the presence of (1) vascular risk factors (hypertension, diabetes, hyperlipidemia, or smoking) and carotid/vertebral artery disease (>70% stenosis or heterogeneous plaques) or (2) atrial fibrillation and/or history of cardiac disease with an abnormal echocardiogram. Strokes due to small-vessel occlusion were defined as clinical lacunar syndromes with either small, deep, oval, white matter or basal ganglia infarcts <1.5 cm in diameter, periventricular hypodensity, or no lesions on CT scan. Cortical/subcortical syndromes with infarcts >1.5 cm in diameter for which an etiology could not be found, lacunar syndromes with CT scan lesions >1.5 cm in diameter, and strokes in which >1 etiology was equally likely were categorized as being due to large-vessel disease. Because it is difficult to assign an accurate subtype to stroke patients without completing all investigations, the majority of subtypes were assigned after randomization. There were no significant differences in the frequency and type of investigations between the 2 settings. The accuracy of categorization was verified by an independent review of masked clinical details and investigations by another specialist who was not involved in patient care and unaware of the stroke subtype allocated to the patient. A joint review was undertaken for patients in whom the 2 assessors disagreed on stroke subtype.

**Interventions**

**Stroke Unit**

Care on the stroke unit (acute care and rehabilitation) was provided by a stroke physician supported by a multidisciplinary team with specialist experience in stroke management. The acute medical treatment was standardized for diagnostic evaluation, monitoring, and prevention of complications. The role of thrombolyis in acute stroke had not been established at the time of the present study and was not used in any patient. Antiedema agents were used selectively and were limited to patients with rapidly deteriorating consciousness levels and midline shift on CT scan. A coordinated multidisciplinary approach was adopted toward rehabilitation, with emphasis on early mobilization. All patients had an individualized rehabilitation plan with clearly defined goals based on joint assessments. Patient participation was encouraged, with focus on motivation and the providing of an enriched environment.

**Stroke Team**

Patients allocated to specialist stroke team care were managed on general wards and remained under the care of admitting physicians. Patients were assessed at the time of admission by the specialist team, who undertook a comprehensive diagnostic evaluation and assessment for medical, nursing, and therapy needs. A plan for management based on standardized guidelines as used on the stroke unit was recommended for implementation by the ward team. Patients were reviewed regularly by the specialist team, who continued to advise on treatment. Rehabilitation was provided by the generic nursing and therapy staff on the ward, but the specialist team provided input for assessments, goal setting, planning of treatment, discharge arrangement, and liaison with patients and relatives.

Stroke unit and stroke team care were based within the same hospital but provided by different teams. Both teams were comparable in seniority and specialist experience and had access to similar resources in the hospital and community. Treatment after discharge from the stroke unit and general medical wards with specialist team support was provided by community services.

**Assessments of Outcome and Resource Use**

Outcome was assessed at 3 and 12 months after stroke onset to represent early and long-term recovery from stroke. An independent observer who was unaware of treatment allocation or stroke subtype and who was not involved with patient care assessed the patients in their own environment. Validated measures within a hierarchy of domains were used for a comprehensive assessment of recovery from stroke. These included mortality, mortality or institutionalization, Orgogozo score for neurological recovery (impairment), Barthel activities of daily living score and Frenchay Activities Index for personal and extended activities of daily living, modified Rankin score (mRS) for handicap, and Euroqol for quality of life.
amount of therapy received by patients in the first 3 months after stroke (whether it be in the hospital or in the community) and duration of hospital stay (acute care and rehabilitation) were recorded in “real time” by the therapists providing the treatment.

Although the researcher undertook neurological assessments, the patients themselves were encouraged to complete the questionnaires on activities of daily living and quality of life to reduce observer bias. If patients were unable to comply because of dysphasia or other impairments, caregivers were allowed to assist with the responses.

Statistical Analysis
Sample size calculation for the present study has been described in detail in our previous study.12 This was based on mortality and institutionalization as the primary outcome measure,12 but the study also had 80% power to detect a 2-point difference in Barthel Index, a 5-point difference in the Frenchay Activities Index, a 7-point difference in Euroqol scores, and 20% difference at the 5% level in the proportion of patients with a good outcome on dichotomized Rankin score.

Intention-to-treat analysis was used to compare baseline and outcome data between the 2 settings in patients divided according to type of stroke. The mRS at 1 year was dichotomized for patients who were independent and those who required minor or severe assistance for activities of daily living (mRS 0, 1, 2, or 3) as having a good outcome.12 The Barthel Index was similarly dichotomized for dependence, and Barthel scores of 15 to 20 were classified as having a good outcome.12 Means, standard deviations, medians, and interquartile ranges were used, as appropriate for data. The Mann-Whitney test was used to compare medians for continuous variables (eg, Frenchay Activities Index and Euroqol scores). The Fisher exact test was used for mortality. The χ² test was used for comparing proportions (institutionalization, dichotomized mRS, and Barthel Index), and the Student t test was used to compare continuous parametric data (age, length of stay, and Orgogozo score).

In addition to univariate analyses, logistic regression models were fitted to the whole data set at 3 and 12 months to adjust for the effects of prognostic variables and differences in resource use when assessing for the independent effect of stroke unit intervention. Models were constructed for each of the outcome variables of mortality, mortality or institutionalization, and dichotomized Rankin, Barthel, and Orgogozo scores. In addition to strategy of care, prognostic variables known to affect outcome (age, sex, premorbid function, living alone, comorbidity, and measures of stroke severity) and resource use (length of hospital stay and duration of therapy input) were included in these analyses.

Results
Patient Characteristics
Of the 304 patients randomized, 33 were excluded because of hemorrhagic stroke, and 4 were excluded because of a nonstroke diagnosis. The remaining 267 patients with ischemic stroke were included in the present study, 164 (61%) of whom had large-vessel infarcts and 103 (39%) of whom had infarcts due to small-vessel occlusion. The reviewers agreed on the subtype of stroke (atherosclerotic, cardioembolic, lacunar, or indeterminate) in 209 (78%) of the patients. Consensus on subtype was arrived at in a further 54 patients on joint review. The 4 patients for whom consensus could not be reached were assigned to the indeterminate group.

There were no significant differences in age, sex, neurological deficits, level of impairment, and initial disability between patients with large-vessel infarcts allocated to the stroke unit or to general medical wards with support of the specialist stroke team (Table 1). The baseline characteristics of patients with small-vessel occlusion were also comparable.

The median Barthel Index placed all groups at the moderately severe level.21 Although there was a trend toward patients with large-vessel disease having lower neurological scores and greater impairment and disability on initial assessment, these differences did not achieve statistical significance. Three patients in the stroke team group were lost to follow-up at 12 months. All completed assessments in these patients were included in the analysis.

Outcome
Large-Vessel Disease
Mortality was significantly higher in patients with large-vessel infarcts managed on general medical wards with stroke team support compared with those managed on the stroke unit at 3 months (15% versus 4%, respectively) and at 1 year (26% versus 10%, respectively) (Table 2). The combined endpoint of mortality or institutionalization was also significantly higher in patients managed by the stroke team on general medical wards. Stroke unit care was associated with a favorable effect on dependence both at 3 months and at 1 year, with a higher proportion of patients achieving good outcome on the dichotomized Barthel and Rankin scores. The median Frenchay Activities Index score, a measure of extended activities of daily living,18 was significantly higher at 1 year in patients treated on the stroke unit. There were no significant differences in neurological scores or quality-of-life measurements between the 2 settings at 3 months and 1 year.

The multiple regression analyses assessed the independent effect of stroke unit care on mortality, institutionalization, and functional recovery after adjusting for other prognostic variables in patients with large-vessel infarcts (Table 3). These analyses showed that the odds of dying were nearly 5 times greater within 3 months and nearly 4 times greater within 1 year for patients on general wards with stroke team care.
care compared with the stroke unit. The odds for dying or being institutionalized were also increased nearly 3-fold in stroke team patients. Stroke unit care in patients with large-vessel infarcts was associated with a trend toward lesser dependence at 3 and 6 months, but this just failed to achieve statistical significance.

**Small-Vessel Occlusion**

There were no significant differences in mortality, mortality or institutionalization, level of neurological recovery, or dependence in patients with small-vessel (lacunar) strokes managed on the stroke unit or by the stroke team on general medical wards at 3 months or at 12 months (Table 2). Patients in both settings showed good recovery with low mortality and low institutionalization rates. Logistical regression modeling showed that mortality, institutionalization, and dependence at 3 months and 1 year were influenced by age and stroke severity but not by management strategy (Table 3).

**Resource Use**

The total duration of the hospital stay was comparable between patients with large-vessel infarcts managed on the stroke unit and patients managed on general wards with support from the stroke team (Table 4). In contrast, patients with lacunar syndromes managed by the stroke unit had a significantly longer length of stay compared with patients managed by the stroke team. Nearly all stroke patients received physiotherapy input regardless of strategy of care.

However, stroke unit care was associated with a significantly longer duration of physical treatment, both for patients with large-vessel infarcts (24.2 hours [stroke unit] versus 12.7 hours [stroke team], P<0.001) and with small-vessel occlusion (18.5 hours [stroke unit] versus 3.7 hours [stroke team], P<0.0001). Although the proportions of patients with large-vessel infarcts receiving occupational therapy and speech and language therapy were comparable between the stroke unit and the stroke team, there were significant differences in the duration of therapy received by patients. Significantly fewer patients with lacunar strokes managed by the stroke team, compared with those in the stroke unit, received occupational or speech therapy input (Table 4). The duration of treatment received by these patients was also less than the duration of treatment for patients in stroke unit.

**Discussion**

The present study suggests that although the outcome in stroke patients is improved by organized management and rehabilitation, not all types of stroke patients benefit to the same extent by dedicated stroke unit care. The benefits of a dedicated stroke unit care appear to be considerable in patients with large-vessel stroke, in whom mortality, institutionalization, and dependence are reduced both at 3 months and at 1 year. More important, this benefit of stroke unit care is independent of age or initial severity of stroke. In contrast, mortality, institutionalization, and dependence in patients...
TABLE 3. Adjusted Regression Analysis of Factors Influencing Outcome at 3 and 12 mo

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<th>Large-Vessel Disease</th>
<th>Small-Vessel Disease</th>
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<td>3 mo</td>
<td>12 mo</td>
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<td>Mortality</td>
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<tr>
<td>Age</td>
<td></td>
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<tr>
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<td>Orgogozo score on admission</td>
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<td>OR (95% CI)</td>
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<td>Barthel score on admission</td>
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<td>Stroke team:stroke unit care</td>
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<tr>
<td>OR (95% CI)</td>
<td>4.9</td>
<td>(1.3–18.6)</td>
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<tr>
<td>P</td>
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<tr>
<td>MRS (0–3)</td>
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<td>OR (95% CI)</td>
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<td>Barthel score on admission</td>
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<td>Stroke team:stroke unit care</td>
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<tr>
<td>OR (95% CI)</td>
<td>2.9</td>
<td>(1.1–7.4)</td>
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<td>P</td>
<td>0.03</td>
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<td>Mortality and institutionalization</td>
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<td>Stroke team:stroke unit care</td>
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<tr>
<td>OR (95% CI)</td>
<td>0.44</td>
<td>(0.18–1.1)</td>
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<td>P</td>
<td>0.07</td>
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with lacunar strokes managed on general wards with specialist stroke team support were no different from those values seen in the dedicated stroke unit. Most patients had good outcome, which was influenced by age and initial stroke severity rather than strategy of care. Paradoxically, stroke unit care was associated with longer hospital length of stay and increased therapy use in the first 3 months (whether this be in the hospital or in the community) in this group of patients, suggesting increased initial health costs for equivalent benefit.

These findings need to be interpreted with caution because of the limitations imposed by study design. The study was a
The validity of the findings of the present study is also dependent on the accuracy of subtyping of stroke and lack of bias in assessment procedures. All patients were comprehensively investigated for stroke subtype, and the criteria for the different subtypes were specified in advance. Subtyping was undertaken at 2 different levels: (1) an initial clinical assessment of patients and (2) later verification by an independent observer using masked clinical findings and investigations. There was a high level of agreement between the 2 assignments, and the exclusion of patients for whom there was disagreement from the initial analysis did not affect the results.

Observer bias was kept to a minimum by using end points not subject to bias (mortality and institutionalization) and by simple objective measures (Rankin score, Barthel Index, Frenchay Activities Index, and Euroqol) that are known to have high reliability and validity in stroke patients and that were reported by the patients themselves as far as possible. It is accepted that bias may have been introduced in some patients with communication or cognitive problems in whom caregivers helped to complete questionnaires, but this was unavoidable. Although the observer was unaware of allocation and although all assessments were conducted in the patients’ home or nursing home to avoid inadvertent unmasking of allocation, observer bias may not have been eliminated completely because some patients may have inadvertently divulged the location of acute care during the interview. The effect of any such disclosure is likely to be minimal because the observer could correctly identify the location in just over half the patients, which is no greater than can be expected by chance alone.

In the present study, the proportion of patients with lacunar stroke was higher than can be expected because all patients with severe strokes (more likely to have large-vessel infarcts) were managed on the stroke unit and excluded from the study. The possibility of selection or statistical bias was reduced by undertaking regression and sensitivity analyses, in addition to direct comparisons of data, to account for the effect of other confounding variables, such as age or stroke severity and patients lost to follow-up. These analyses continued to support the findings and showed that stroke unit management had an independent favorable effect on outcome in large-vessel infarcts but not in lacunar stroke.

The findings of the present study do not disagree with existing evidence on the effectiveness of organized specialist care in improving stroke outcome because both groups received coordinated stroke management that was organized in different ways. The study provides further insight into stroke unit care by showing that the higher level of monitoring, interventions, and therapy input are particularly advantageous for patients with higher risks of mortality and recurrence or greater rehabilitation needs. The study further suggests that stroke units may have limited effectiveness in patients with lacunar stroke and that the culture on stroke units may result in these patients staying in the hospital longer and receiving more therapy input than can be justified by the outcome. A similar observation was made in a recent study, which showed an early beneficial effect of stroke units on mortality but not on any other measure of outcome in elderly patients with mild stroke.

Differences in the benefits of stroke unit care according to stroke subtype have important implications. Although there can be no doubt that all stroke patients need access to specialist care for monitoring, for investigations to establish severity, etiology, and subtype of stroke, and for possible thrombolysis in the acute phase, patients with lacunar syndromes in the postacute phase may be equally well managed in generic settings as long as arrangements are made to provide ongoing specialist support. The present study also highlights the need for an education program to change “culture effects” that are not evidence-based on stroke units. There is a possibility that the effects of stroke unit management may be more subtle (eg, reduced need for community resources and diminished burden on caregivers); this topic has not been described in the present study. The cost-effectiveness of alternate approaches to managing lacunar stroke, the feasibility of early subtyping, and the accuracy of such subtyping in clinical practice are also not known. The present study provides evidence to support an adequately powered prospective, randomized, controlled trial in patients with lacunar syndromes to compare the benefits and cost-effectiveness of stroke unit care with organized care in other settings in the postacute phase.

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References


15. Evans et al Stroke Units Aid Outcome in Large-Vessel Infarcts 455


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