Role of Monitoring in Management of Acute Ischemic Stroke Patients

Anna Cavallini, MD; Giuseppe Micieli, MD; Simona Marcheselli, MD; Silvana Quaglini, PhD

Background and Purpose—Although several studies have demonstrated the effectiveness of specialist Stroke Unit (SU) care of stroke patients, there is still disagreement over how these units are best organized. We sought to clarify the role of continuous monitoring of physiological parameters in acute ischemic stroke.

Methods—We conducted a prospective study of 268 first-ever ischemic stroke patients admitted to our Cerebrovascular Department and allocated, according to the availability of beds, to the SU or Cerebrovascular Unit (CU). Statistical analysis compared mortality and outcome at discharge, medical and neurological complications, and length of hospitalization in the 2 care settings.

Results—Two hundred sixty-eight patients were enrolled. A good outcome at discharge, observed in 114 SU patients (85%) and 78 CU patients (58%) (odds ratio, 2.63; 95% CI, 1.4 to 4.8; \(P<0.02\)), was found, on multivariate analysis, to be significantly related to type of care (SU versus CU). A significantly greater proportion of SU patients showed adverse changes in monitored parameters, which required acute medical treatment (SU: 64%; CU: 19%; \(P<0.0001\)). The mean duration of these complications was significantly shorter in the SU patients (SU: 1.0 day; CU: 2.4 days; \(P<0.02\)), and the outcome in patients experiencing complications covered by the monitoring protocol was significantly better in the SU (66%) than in the CU (35%) group (\(P<0.0001\)).

Conclusions—Admission of acute stroke patients to a monitoring SU may positively influence their outcome at discharge. Confirmation of our findings in larger trials will indicate the need for a revision of the minimum requirements of SUs, with the addition of monitoring as a new requirement. (Stroke. 2003;34:2599-2603.)

Key Words: monitoring ■ stroke, ischemic ■ stroke management ■ stroke units

Meta-analysis of randomized controlled studies has demonstrated that the care of stroke patients in specialist Stroke Units (SUs) can significantly reduce mortality, institutionalization, and dependence. Accordingly, admission to a SU that offers well-organized multidisciplinary care is currently considered to be the most effective course of action in acute stroke.\(^1\) Factors that appear to significantly distinguish SU from conventional stroke management include thrombolysis in selected patients,\(^2\) physiological homoeostasis,\(^3\) early prescription of aspirin,\(^4\) anticoagulation in patients with atrial fibrillation,\(^5\) and early mobilization.\(^6\) Additionally, the implementation of evidence-based guidelines\(^7\) can significantly reduce mortality and dependence after stroke. Evans et al\(^8\) recently reported the superiority of specialist SU care over care in a general ward with specialist stroke team support and concluded that all patients with acute stroke should be managed in SUs according to standardized stroke care protocols.

Despite this evidence, organized SU care is not widely available, and there are still significant variations between different countries’ definitions of SU. Indeed, different types of SU have been proposed, characterized by different levels of intensity of care (ranging from acute intensive SUs to rehabilitation SUs). As minimum requirements, a SU must guarantee 24-hour availability of CT scanning facilities and neurologists or other stroke-oriented physicians, the presence of nursing staff specializing in stroke care, and adherence to recognized treatment and management guidelines.\(^1\) Moreover, it has been established that neurological status and vital functions (blood pressure, pulse rate, temperature) should be continuously or discontinuously monitored in all stroke patients.\(^9\)

The past few years have seen the development of acute SUs in which heart rate, blood pressure, body temperature, and oxygen saturation are monitored continuously. The importance of monitoring stroke patients is supported indirectly by the evidence that fever,\(^10,11\) hypertension/hypotension,\(^12\) cardiac arrhythmias, and hypoxia play an important role in determining a poor or good outcome.\(^13\) However, despite this evidence and despite the suggestion in a very recently published pilot study\(^14\) that admitting acute stroke patients to a Stroke Care Monitoring Unit can reduce mortality and poor
outcome, the effective role of monitoring is still debated. We sought to analyze the importance, in terms of both outcome and length of stay (LOS), of continuous physiological monitoring in the stroke care process.

Subjects and Methods

We conducted a prospective study of 268 first-ever ischemic stroke patients admitted to our Cerebrovascular Department (within 36 hours of stroke onset) between January 1999 and April 2001. These patients represent approximately 32% of all the patients admitted during that period (total = 831). The Cerebrovascular Department comprises 2 sections: a SU and a Cerebrovascular Unit (CU).

The SU is a 6-bed, semi-intensive care unit in which bedside monitors continuously record vital functions (blood pressure, ECG, oxygen saturation, respiratory frequency, body temperature, electroencephalography). All subjects undergo, on admission, at least 72 hours of continuous monitoring. This level of instrumental control is not available in the CU, where blood pressure and heart rate are recorded automatically every 4 hours during the first 3 days of hospitalization and 4 times a day thereafter, while body temperature is measured 3 times daily. Oxygen saturation, respiratory frequency, and ECG are performed on admission to the CU. These parameters are measured again in the event of an adverse change in clinical conditions.

Both care units follow the same acute management and early rehabilitation guidelines. Thus, diagnostic assessment procedures, medical treatments for acute stroke and adverse events, nursing protocols, rehabilitation treatments, and prevention of complications are standardized. The same multidisciplinary stroke team works in both the SU and the CU. Moreover, both units employ the same kind of electronic patient record chart, which is completed daily by all those involved in the management of the stroke patient. In the SU, the monitoring instruments enter parameter values directly into the relevant sections of the patient’s chart. All the data collected can be automatically exported into a format suitable for further statistical analysis. This software was introduced in 1997, and all the stroke team personnel have been specifically trained in its use.

At the time of this study, patients consecutively admitted to the Cerebrovascular Department were allocated to the SU or the CU purely on the basis of availability of beds, with the SU beds always filled first. This allocation of patients was the responsibility of the ward administrator, who was blind to the aims of the study.

To determine the number of patients to enroll in the study, we considered that, in conventional units, approximately 70% of ischemic stroke patients have a good outcome. We decided to collect enough patients to allow detection of a clinically relevant difference of 15% in the SU, with a type I error α = 0.05 and a type II error β = 0.2 (the power of the study was 80%). The number of patients computed was 268. Similarly, we calculated the number of patients needed to show a 2-day difference in LOS (considering the LOS in a CU to be approximately 15 days) and a complication ratio difference of ≥ 15% (on the basis of a CU complication ratio of 50%), and neither exceeded 268 (160 and 226, respectively). Thus, patient enrollment was continued until 134 patients were available in each unit.

All the patients underwent the standardized initial assessment, as follows: (1) demographic data, comorbidity, premorbid function (modified Rankin Scale), stroke subtype, neurological deficit (National Institutes of Health Stroke Scale [NIHSS]), functional disability (Barthel Index [BI]), (2) physiological measurements: blood pressure, heart rate, body temperature, oxygen saturation, respiratory frequency; (3) laboratory tests: complete blood cell count, blood glucose level, chemical analysis of kidney and liver function, serum electrolytes, prothrombin time, partial thromboplastin time; (4) 12-lead ECG; (5) imaging: chest x-ray, brain CT scan without contrast, extracranial carotid and vertebral duplex ultrasonography, transcranial Doppler ultrasonography; and (6) physical evaluation.

If the baseline CT scan failed to reveal the ischemic lesion, a repeated CT scan, to confirm the diagnosis, was performed within 7 days of symptom onset or at discharge if earlier.

The initial assessment was performed within 90 minutes of hospital admission to either the SU or the CU. In accordance with our standardized care plan, neurological status was assessed every 6 hours for the first 24 hours and once a day thereafter, and functional disability was assessed after 24 hours, after 3 days, and at discharge. The modified Rankin Scale was also applied at discharge. All the subjects had started their personalized rehabilitation programs within 24 hours.

Any medical and/or neurological complication occurring during hospitalization in any patient was recorded. In particular, we considered the following adverse events, related to the monitored parameters: cardiac complications (new onset/worsening of arrhythmias, worsening of preexisting cardiac disease, new changes on ECG, heart failure); arterial hypertension (systolic blood pressure > 200 mm Hg, diastolic blood pressure > 105 mm Hg) or hypotension (systolic blood pressure < 80 mm Hg); fever (body temperature > 37.8°C); and hypoxia (SpO2 < 91%). The other complications recorded, defined according to Davenport et al., are reported in Table 4.

The LOS, date and cause of death or type of discharge, and modified Rankin Scale score at discharge were also evaluated.

Data were extracted and analyzed by an operator (S.Q.) blind to the aims of the study. For each patient, we evaluated clinical data; type, number, and duration of any medical/neurological complication; LOS; and date and cause of death or type of discharge.

A good outcome was recorded if the patient was able to live at home (even with intermittent support) or was considered suitable for an intensive rehabilitation program. In our series a good outcome corresponds to a Rankin Scale score of 0 to 3. In contrast, a poor outcome was recorded if the patient died or was recommended for admission to a long-term care department (Rankin Scale score 4 to 6). Outcome at discharge was the primary end point of the study.

Univariate and multivariate logistic analyses were performed to investigate relationships between outcome and risk factors. All dichotomous variables were codified as 1 = absent and 2 = present, in such a way that a negative coefficient indicates an inverse correlation of the risk factor with the good outcome.

As a complementary statistical tool, a classification tree was used. Tree-based modeling is an exploratory technique for uncovering structure in data. The result is a collection of rules displayed in the form of a binary tree. The importance of the splitting variables decreases from the root to the leaves of the tree. The leaves show the probability of the outcome for the various paths, in terms of outcome occurrence frequency. Compared with classic regression or classification models, the tree allows more general interaction between predictors, and the results are easier to interpret, particularly when independent variables are a mixture of continuous and categorical variables, as in this study.

In addition, we compared the 2 care settings (SU versus CU) by analyzing the proportion of patients showing specific complications in each of the 2 groups. The differences are presented as odds ratios (ORs) to provide an estimate of the association between effect and type of care.

**Table 1. Population Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>SU Patients</th>
<th>CU Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y (range)</td>
<td>73 (41–88)</td>
<td>72 (40–92)</td>
</tr>
<tr>
<td>Male sex, % (n)</td>
<td>59 (79)</td>
<td>57 (77)</td>
</tr>
<tr>
<td>Median NIHSS on admission (range)</td>
<td>8 (5–20)</td>
<td>7 (3–21)</td>
</tr>
<tr>
<td>Median BIS on admission (range)</td>
<td>9 (0–19)</td>
<td>9 (0–19)</td>
</tr>
<tr>
<td>Mortality at discharge, % (n)</td>
<td>4 (6)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Good outcome,* % (n)</td>
<td>85 (114)</td>
<td>58 (78)</td>
</tr>
</tbody>
</table>

*Modified Rankin Scale score at discharge 0–3.
The local ethics committee decided that this study, which was not of a predominantly biomedical nature, did not fall within its sphere of competence. The committee nevertheless had no objections to the study proceeding in the proposed form.

Results

Of the 268 stroke patients, 134 (median age, 73 years) were allocated to SU and 134 (median age, 72 years) to CU care. Sex distribution, NIHSS score, and BI score on admission were similar in the 2 groups (Table 1). Fifty-six of the 268 patients, partial anterior circulation infarct (PACI) in 104 (39%), lacunar infarct (LACI) in 121 (45%), and posterior circulation infarct (POCI) in 27 (10%). Additionally, the distribution of the patients across these 3 time intervals was similar in the 2 groups (SU: 22%, 42%, and 36%; CU: 20%, 40%, 40%).

The clinical diagnosis of stroke was total anterior circulation infarct (TACI) in 16 (6%) of the 268 patients, partial anterior circulation infarct (PACI) in 104 (39%), lacunar infarct (LACI) in 121 (45%), and posterior circulation infarct (POCI) in 27 (10%). Additionally, the distribution of stroke diagnoses was similar in both groups (SU: TACI, 7%; PACI, 39%; LACI, 45%; POCI, 10%; CU: TACI, 5%; PACI, 39%; LACI, 45%; POCI, 11%). The mean time taken to complete baseline assessment was 76±12 minutes in the SU and 79±6 minutes in the CU. A positive history of coronary heart disease was detectable in 28 SU patients (21%) and in 28 CU subjects (21%), of atrial fibrillation in 22 (16%) and 18 (13%), of hypertension in 86 (64%) and 80 (60%), of diabetes in 18 (13%) and 24 (18%), of hypercholesterolemia in 6 (4%) and 16 (15%), of transient ischemic attacks in 20 (15%) and 12 (9%), of intermittent claudication in 4 (3%) and 10 (7%), and of smoking in 18 (13%) and 40 (30%). No significant differences were detectable between the distribution of the risk factors in the SU and CU subjects.

The mean LOS was 9.2 days in the SU patients and 17.1 days in the CU patients (P<0.0001).

Fourteen patients (5%) died during hospitalization, 6 (4%) in the SU and 8 (6%) in the CU group. The cause of death was intracranial hypertension in 5 patients (SU: 3; CU: 2), cardiac disorders in 4 patients (SU: 1; CU: 3), sepsis in 1 patient (SU: 0; CU: 1), acute renal insufficiency in 3 patients (SU: 1; CU: 2), and pneumonia in 1 patient (SU: 1; CU: 0).

A good outcome at discharge was found in 114 SU patients (85%) and in 78 CU patients (58%) (OR, 2.63; 95% CI, 1.4 to 4.8; P<0.02).

Univariate logistic analysis revealed a highly significant relationship between outcome and coronary heart disease, NIHSS and BI score on admission, type of care, and age (Table 2).

### Table 2: Univariate Logistic Regression Analysis on the Outcome at Discharge

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Standard Error</th>
<th>t Value</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>0.6099</td>
<td>0.1653</td>
<td>-3.6899</td>
<td>0.0003</td>
<td>0.54 (0.39–0.75)</td>
</tr>
<tr>
<td>Initial NIHSS score</td>
<td>-0.2692</td>
<td>0.0359</td>
<td>-7.4927</td>
<td>&lt;0.00001</td>
<td>0.76 (0.71–0.82)</td>
</tr>
<tr>
<td>Initial Barthel Index score</td>
<td>0.2809</td>
<td>0.0461</td>
<td>6.0879</td>
<td>&lt;0.00001</td>
<td>1.32 (1.21–1.45)</td>
</tr>
<tr>
<td>Care setting (1=SU, 2=CU)</td>
<td>-0.3693</td>
<td>0.1544</td>
<td>-2.3919</td>
<td>0.0175</td>
<td>0.69 (0.51–0.93)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.1013</td>
<td>0.0203</td>
<td>-4.9768</td>
<td>&lt;0.00001</td>
<td>0.90 (0.87–0.94)</td>
</tr>
<tr>
<td>Sex (1= M, 2= F)</td>
<td>-0.2624</td>
<td>0.1506</td>
<td>-1.7427</td>
<td>0.08</td>
<td>0.77 (0.57–1.03)</td>
</tr>
<tr>
<td>Time to admission, h</td>
<td>0.0193</td>
<td>0.0116</td>
<td>1.6611</td>
<td>0.09</td>
<td>1.02 (0.98–1.04)</td>
</tr>
<tr>
<td>Atrial fibrillation*</td>
<td>-0.2862</td>
<td>0.1917</td>
<td>-1.4928</td>
<td>&gt;0.1</td>
<td></td>
</tr>
<tr>
<td>Hypertension*</td>
<td>0.0327</td>
<td>0.1537</td>
<td>0.2128</td>
<td>&gt;0.1</td>
<td></td>
</tr>
<tr>
<td>Diabetes*</td>
<td>-0.1228</td>
<td>0.1994</td>
<td>-0.6156</td>
<td>&gt;0.1</td>
<td></td>
</tr>
<tr>
<td>Hypcholesterolemia*</td>
<td>0.4406</td>
<td>0.3795</td>
<td>1.1608</td>
<td>&gt;0.1</td>
<td></td>
</tr>
<tr>
<td>Previous TIA*</td>
<td>0.3208</td>
<td>0.2731</td>
<td>1.1746</td>
<td>&gt;0.1</td>
<td></td>
</tr>
<tr>
<td>Claudicatio intermittens*</td>
<td>3.4618</td>
<td>4.8991</td>
<td>0.7066</td>
<td>&gt;0.1</td>
<td></td>
</tr>
<tr>
<td>Smoking*</td>
<td>-0.1646</td>
<td>0.1775</td>
<td>-0.9271</td>
<td>&gt;0.1</td>
<td></td>
</tr>
</tbody>
</table>

*1= absent, 2= present.

### Table 3: Multivariate Logistic Regression Analysis on the Outcome at Discharge

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Standard Error</th>
<th>t Value</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>9.1884</td>
<td>2.7227</td>
<td>3.3747</td>
<td>0.0008</td>
<td></td>
</tr>
<tr>
<td>Care setting</td>
<td>-0.8607</td>
<td>0.2458</td>
<td>-3.5022</td>
<td>0.0005</td>
<td>0.42 (0.26–0.68)</td>
</tr>
<tr>
<td>Time to admission</td>
<td>-0.0367</td>
<td>0.0184</td>
<td>-1.9945</td>
<td>0.0472</td>
<td>0.96 (0.93–0.99)</td>
</tr>
<tr>
<td>Initial Barthel Index score</td>
<td>0.1858</td>
<td>0.0726</td>
<td>-2.5597</td>
<td>0.011</td>
<td>1.20 (1.04–1.39)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.0927</td>
<td>0.0314</td>
<td>-2.9487</td>
<td>0.0036</td>
<td>0.91 (0.86–0.97)</td>
</tr>
<tr>
<td>CHD</td>
<td>-0.4641</td>
<td>0.2352</td>
<td>-1.9728</td>
<td>0.049</td>
<td>0.63 (0.39–0.99)</td>
</tr>
<tr>
<td>Initial NIHSS score</td>
<td>-0.1299</td>
<td>0.0562</td>
<td>-2.3114</td>
<td>0.0216</td>
<td>0.88 (0.79–0.98)</td>
</tr>
</tbody>
</table>
To be conservative, multivariate analysis was performed with $P<0.1$ as the cutoff level. Table 3 shows the variables that emerge as significant independent predictors of outcome. While care setting is still highly significant, sex, no longer an important factor, is omitted.

The results of the classification tree analysis are reported in the Figure. As shown, the most important predictor of a good outcome is NIHSS score on admission. Indeed, in patients with NIHSS score $<14$ and BI $\geq 13$, the outcome was good in 100% of our cases. When BI was $<13$ but $\geq 3$ and age was $<76$ years, the outcome was still good. However, if BI is $<3$, admission to a SU can help determine a good outcome, with a proportion of 87% versus 50% in CU. This is also true when NIHSS score is $<13$ but age was $<76$ years, and the time to admission is $<30$ hours. Returning to the root, when NIHSS score is $\geq 14$, only age $<72$ years and absence of coronary heart disease are predictive of a good outcome, regardless of SU or CU admission.

To investigate the role of monitoring in improving outcome, we also analyzed complications. One hundred sixty-five patients showed at least 1 complication during hospitalization. In detail, we observed a single complication in 26 SU patients and 51 CU subjects, 2 to 4 complications in 32 SU patients and 28 CU patients, 5 to 8 complications in 18 SU patients and 2 CU patients, and $>8$ complications in 8 SU patients and 0 CU patients. The total number of adverse events recorded in the SU and CU groups was 304 and 148, respectively, with a mean number of events per patient of 2.3±2.9 in the SU and 1.1±1.4 in the CU group ($P<0.0001$).

Medical/neurological complications were recorded in 73 SU patients (54%) and in 64 CU subjects (48%). The frequency of complications not covered by the monitoring procedures was similar in the SU and CU cases (Table 4). The mean duration of these unmonitored complications was also similar in the 2 groups (SU: 4.1±4.3 days; CU: 3.9±4.7 days).

On the other hand, a significantly greater proportion of SU patients showed adverse changes in the monitored parameters, which required acute medical treatment (SU: n=86, 64%; CU: n=26, 19%; $P<0.0001$). Cardiac complications as well as fever and hypertensive or hypotensive crises were significantly more frequently detected in SU patients (Table 5). The mean duration of the adverse events related to the monitored parameters was significantly shorter in the SU than in the CU patients (SU: 1.0 day; CU: 2.4 days; $P<0.02$).

The outcome in patients who experienced complications related to the monitored parameters was found to be good in 57 (66%) of the SU subjects compared with only 9 (35%) of the CU patients ($P<0.0001$).

**Discussion**

This study demonstrates that allocation to care in a monitoring SU (rather than a CU) increases 2.5-fold the probability of a good outcome at discharge in first-ever ischemic stroke patients. This is probably due to prompt therapeutic intervention after an earlier detection of complications, ie, before they become symptomatic. Indeed, in the SU patients we detected a significantly higher number of complications related to the monitored parameters, but the duration of these complications was shorter, which in turn resulted in a significantly shorter LOS in SU versus CU patients. These findings confirm that intensive, noninvasive physiological monitoring is feasible in
acute stroke patients and capable of improving the rate of detection of, and subsequent intervention for, adverse changes in physiological variables. It is probable that this optimized management of adverse events positively influences the outcome at 3 months. In our study, in which we evaluated only outcome at discharge, our 2 care settings were similar to those evaluated by Sulter et al. Indeed, the only difference between our 2 units was the presence or absence of monitoring, and thus our SU and CU can be considered the equivalents of their Stroke Care Monitoring Unit and Conventional Stroke Unit, respectively.

Previous studies have suggested that SU care can reduce the frequency of complications associated with stroke and that it is associated with better outcome. Moreover, mortality in the postacute phase has been associated with complications arising during the first week of management and related to the quality of care provided during this period. The monitoring of physiological parameters in the acute phase of ischemic stroke can be considered an important management tool that can improve significantly the quality of care provided, allowing easier detection and correction of complications and consequently having a favorable effect on outcome. Indeed, it is well known that elevated body temperature, hypoxia, excessive increases or decreases in blood pressure, and cardiac arrhythmias in the acute phase of ischemic stroke negatively affect stroke evolution and/or survival.

With only a few pilot studies available, evidence on this topic is currently scarce. Should larger trials confirm our findings, the minimum requirements of SUs will have to be revised, with monitoring added as a new requirement.

References

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Stroke. 2003;34:2599-2603; originally published online October 16, 2003; doi: 10.1161/01.STR.000094423.34841.BB
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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