Admitting Acute Ischemic Stroke Patients to a Stroke Care Monitoring Unit Versus a Conventional Stroke Unit

A Randomized Pilot Study

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Background and Purpose—Pathophysiological considerations and observational studies indicate that elevated body temperature, hypoxia, hypotension, and cardiac arrhythmias in the acute phase of ischemic stroke may aggravate brain damage and worsen outcome.

Methods—Both units were organized with the same standard care and multidisciplinary approach to nursing and rehabilitation. A blinded observer assessed functional outcome at 3 months with the modified Rankin scale (mRS) and Barthel Index (BI). End points were (1) poor outcome, defined as either mRS $\geq$4 or BI $<$60 or the need for institutional care and (2) mortality.

Results—Fifty-four patients meeting the inclusion criteria were randomized. The groups were well matched for baseline characteristics, stroke subtype, stroke severity, vascular risk factors, and prognostic factors. Poor outcome was seen in 7 (25.9%) patients in the SCMU group and in 13 (48.1%) in the SU group (P=0.16). Mortality was lower in the SCMU group than in the SU group (1 [3.7%] vs 7 [25.9%]; odds ratio, 0.11 [95% CI, 0.02 to 0.96], P=0.05).

Conclusions—This pilot study suggests that admission of acute stroke patients to an SCMU may reduce mortality and poor outcome. A larger trial is required to confirm these findings. **(*Stroke*. 2003;34:101-104.)**

Key Words: ischemia ■ stroke assessment ■ stroke management ■ treatment outcome

Several studies have shown that organized stroke-unit care after stroke reduces death, dependency, and the need for institutional care. Key features of stroke-unit care are a dedicated multidisciplinary team, early rehabilitation, prevention and adequate treatment of complications, and involvement of both patient and relatives in the rehabilitation process.[1–6] From animal experiments and human observational studies, a number of factors have been identified that appear to aggravate initial brain damage and worsen outcome after ischemic stroke. Besides hyperglycemia, these include elevated body temperature, hypoxia, hypotension, and cardiac arrhythmias.[7–13] Despite a lack of randomized trials, strategies to correct elevated body temperature, hypoxia, and hypotension have become standard practice in some acute stroke units.[13] However, based on pathophysiological considerations, these variables should be corrected as soon as they develop during the acute phase of stroke. This can be achieved by intensive monitoring of body temperature, oxygen saturation, blood pressure, and ECG. We performed a randomized study to compare survival and functional outcome between patients admitted to a stroke-care monitoring unit (SCMU) and those admitted to a conventional stroke unit (SU).

Subjects and Methods

Subjects

During a 1-year period, patients with acute ischemic hemiparetic stroke were randomly allocated to an SCMU or a conventional SU within the Academic Hospital Groningen. Patients with a clinical diagnosis of acute ischemic stroke in the carotid artery territory were eligible for inclusion in the study if (1) they were between the age of 18 and 80 years, (2) there was a hemiparesis, with the affected outstretched arm unable to hold a 90° position for 10 seconds, (3) they were conscious, (4) symptoms had started within 24 hours before admission, and (5) they were ineligible for intravenous thrombolysis according to the NINDS (National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group) criteria.[14] Patients treated with intravenous tissue-type plasminogen activator (tPA) were not included in the study to avoid interference from a second intervention. Patients who had had a previous stroke with residual neurological impairment, who had suffered from any other disorder interfering with neurological or functional assessments, or who had a life-threatening concurrent illness were excluded. Ethics Committee approval was obtained, and the patients or their legal representatives gave written, informed consent to participate in the trial.

Patients were stratified for stroke subtype (total anterior circulation syndrome, partial anterior circulation syndrome, or lacunar anterior syndrome), according to the criteria described by Bamford et al,[15] and were randomly assigned to the SCMU or SU by an envelope system in a 1-to-1 manner. All patients received a CT scan of the

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TABLE 1. Acute Stroke Unit Protocol*

Parameter	Values	Interventions
Blood pressure (BP)	Systolic BP≤220 and mean BP≤130 mm Hg	No intervention, except in conditions when lowering of BP is warranted (eg, acute myocardial infarction or aortic dissection).
	Systolic BP>220 or mean BP>130 mm Hg	10% reduction in BP Labetalol 100–200 mg orally or 1 mg/min, (maximum 200 mg) IV Enalapril 2.5–5 mg orally or 0.5–1 mg IV
	Mean BP≤80 mm Hg	Volume expander (Gelofusine)
Oxygen saturation	<95%	Oxygen via nasal prong or mask; start with 2–5 L/min
Body temperature	>37.5°C	Acetylsalicicylic acid (500 mg) or paracetamol suppository (1000 mg)
Blood glucose	>10 mmol/L	Actrapid insulin via infusion pump
Arrhythmias		Cardiologist

Mean BP=[Systolic BP+2 Diastolic BP]: 3
*Adapted from Reference 13.

head before randomization. ECG and routine blood tests were performed on admission, and other diagnostic procedures were performed when indicated. Neurological examination and the National Institute of Health stroke scale (NIHSS, a 46-point scale that assesses neurological deficit) scoring were performed by NIHSS-trained neurologists before randomization.

For ethical reasons, we decided to treat all patients in a similar way according to a standardized protocol. Thus, strategies to correct hypotension or excessive hypertension, hypoxia, elevated body temperature, and hyperglycemia, once detected, were identical for both groups (Table 1). Glucose concentrations were determined every 6 hours. Patients in the SCMU were continuously monitored with Marquette Eagle 4000 monitors for at least 48-hours (and longer if required) for cardiac rhythm (5-lead ECG), body temperature (rectal thermometer), oxygen saturation (pulse oximeter), and blood pressure (noninvasive automatic measurement every 15 minutes), thereby allowing immediate interventions. After the first 48 hours, monitoring was stopped when the condition of patient was stable and the physiological variables showed no abnormality over the last 24 hours. After the monitoring period, patients were further treated in the conventional SU. In the conventional SU, observations consisted of manual measurement of body temperature, blood pressure, and heart rate 4 times a day. Oxygen saturation levels were determined when deemed necessary by the attending physician.

The protocol for both units also included a swallowing test for the detection of dysphagia.[16] A positive test led to immediate precautions to prevent aspiration (nil per os and nasogastric tube feeding). A bladder scan was used to assess urine retention. Saline solutions were administered intravenously 24 hours after admission to avoid or treat dehydration. Aspirin 100 mg was routinely given in the first 12 hours after admission. A low dose of nadroparin (2850 IU subcutaneously once a day) was used for deep venous thrombosis prophylaxis. In patients with suspected cardioembolic stroke or stroke progression, nadroparin 5700 IU subcutaneously was administered twice a day. Both units were organized with a team approach to nursing and rehabilitation. Key members of the team were trained stroke nurses and physiotherapists who developed a specific mobilization program, consisting of functional training and a modified motor relearning program. In the first 2 days after admission, patients were trained in bed; after 48 hours, patients were mobilized. Further plans were developed during weekly multidisciplinary stroke team meetings. An important goal was early discharge (within 14 days after admission) to a specialized stroke rehabilitation unit in either an affiliated nursing home or a rehabilitation clinic.

End Points

End points were assessed at 3 months and included (1) poor outcome, defined as either a modified Rankin scale (mRS) score ≥4 or a Barthel Index (BI) <60 or the need for institutional care due to the stroke[17] and (2) mortality. The mRS is a 7-point scale that assesses overall function; death is rated as 6. The BI is a 100-point scale that assesses activities of daily living. A trained stroke nurse who was unaware of which treatment unit each patient had been allocate to determined both scales. Further end points were the number of abnormalities in physiological parameters that were detected during the acute phase of stroke and the number of interventions.

Statistical Analysis

Means, SD, and statistical tests for significance were calculated and performed using the statistical program SPSS for Windows. A *t* test was used to compare group means for continuous variables (eg, age, NIHSS). Fisher's exact test and odd ratios (95% CIs) were used to test group differences for nominal variables (eg, stroke subtype, mortality, poor outcome). No corrections were made for multiple testing.

Results

A total of 162 patients were assessed for eligibility. Of these, 6 patients received intravenous thrombolysis, 23 patients had a primary intracerebral hemorrhage, 23 no longer had a hemiparesis at time of recruitment, 15 had recovered completely, 12 refused participation, 11 were admitted later than 24 hours after stroke onset, 11 had posterior circulation stroke, and 7 had severe comorbidity or were dependent in daily life before their stroke (mRS>2). The remaining 54 patients meeting the inclusion criteria were randomized: 27 were assigned to the SCMU and 27 to the conventional SU.

The groups were well matched for baseline characteristics, stroke subtype, stroke severity, vascular risk factors, and prognostic factors (Table 2). One patient in the SCMU group was admitted to the Intensive Care Unit within 48 hours after admission owing to ventricular fibrillation. Mean±SD time to discharge from the hospital was less in the SCMU group than in the conventional SU group (16±5 vs 25±7 days). None of the patients were lost to follow-up. The number of patients with poor outcome, defined as either mRS≥4 or BI<60, or institutionalization due to stroke was less in the SCMU group than in the SU group (7 [25.9%] vs 13 [48.1%]; odds ratio, 0.37 [95% CI, 0.12 to 1.18], $P=0.15$). Mortality was lower in the SCMU group than in the SU group (1 [3.7%] vs 7 [25.9%]; odds ratio, 0.11 [95% CI, 0.02 to 0.96], $P=0.05$). Causes and time of death are listed in Table 3.

The number of complications and interventions during the first 48 hours after admission are shown in Table 4. Hypoxia was detected in a higher proportion of patients in the SCMU. Accordingly, in the SCMU more patients promptly received

TABLE 2. Demography and Baseline Characteristics

	Stroke Care Unit (n=27)	Conventional Stroke Unit (n=27)	*P*
Mean age (SD), y	68.0 (14.7)	67.6 (16.0)	0.92
Male gender (%)	15 (56)	10 (37)	0.28
Stroke type			
TACS, PACS, LACS	9, 7, 11	9, 7, 11	
Baseline stroke severity (NIHSS)			
Mean (SD)	11. (7.4)	11.2 (7.5)	0.94
≤5, 6–13, ≥14, n	8, 9, 10	8, 9, 10	
Mean (SD) time to admission	7 h 12 min	7 h 50 min	0.74
Risk factors			
Hypertension, n	11	10	1.00
Diabetes Mellitus, n	3	7	0.29
Previous stroke or transient ischemic attack, n	5	4	1.00
Cardiac disease, n	8	10	0.77
Peripheral vascular disease, n	3	2	1.00
Current smoker, n	11	8	0.68
Prognostic factors			
Glucose concentration on admission, mmol/L (SD)	7.1 (4.0)	7.5 (4.3)	0.62
Diastolic blood pressure on admission, mm Hg (SD)	90.5 (16.2)	88.7 (15.3)	0.70
Body temperature on admission, °C (SD)	36.7 (0.6)	37.0 (0.5)	0.06

oxygen therapy because of drops in oxygen saturation. Hypotension was observed more often in the SCMU, and plasma expanders were administered more frequently. The proportion of patients in whom elevated body temperature (>37.5°C) was identified was similar between the SCMU and conventional SU. In the conventional SU, antipyretics were given on the basis of 6-hourly temperature recordings, whereas in the SCMU antipyretics were given immediately after continuous rectal temperature monitoring detected a rise above 37.5°C. Continuous monitoring detected more patients with prior unknown (paroxysmal) cardiac arrhythmias, and 1 patient who developed ventricular fibrillation was successfully resuscitated.

TABLE 4. Detected Complications and Interventions During Monitoring Phase

	Stroke Care Unit (n=27)	Conventional Stroke Unit (n=27)	*P* Value
Complication			
Hypoxia	16	6	0.01
Cardiac failure	2	2	1.00
Atrial fibrillation	5	1	0.19
Ventricular arrhythmia	1	0	1.00
Aspiration pneumonia	2	2	1.00
Seizures	0	1	1.00
Hypotension (mean BP≤80 mm Hg)	12	7	0.25
Excessive hypertension (systolic BP>220 or mean BP>130 mm Hg)	1	3	0.61
Transtentorial herniation (edema)	1	0	1.00
Elevated body temperature (>37.5°C)	9	11	0.78
Urinary infection	0	1	1.00
Dehydration	0	1	1.00
Intervention			
Oxygen therapy	16	6	0.01
Antipyretics	9	11	0.78
Plasma expander	13	7	0.16
Antihypertensive medication	1	3	0.61
Insulin	3	3	1.00
Antibiotics	5	4	1.00
Antiarrhythmics	6	2	0.25

Discussion

Brain injury secondary to occlusion of a cerebral artery is a dynamic process. The penumbra or peri-infarct area, between the densely ischemic core and normally perfused brain, contains compromised but salvageable tissue in a zone of reduced blood flow.[18–21] The enlargement of the infarcted tissue with time is caused by unstable electrophysiological activity and associated neurotoxic changes involving energy metabolism and ion homeostasis. Depletion of the energy stores, whether persistent, as in the ischemic core, or transient/intermittent, as in the penumbra, is the essential trigger for all subsequent cytotoxic events that occur in focal cerebral ische-

TABLE 3. Time and Causes of Death

	Initial Stroke Severity NIHSS	mRS at Discharge	Cause of Death	Time After Admission, d
SCMU				
Patient 1	24	6	Cerebral edema and herniation	3
Conventional SU				
Patient 1	26	6	Respiratory insufficiency and aspiration pneumonia	4
Patient 2	16	6	Acute cardiac failure	4
Patient 3	10	6	Sudden death—cause unknown	8
Patient 4	17	5	Sudden death—cause unknown	28
Patient 5	5	4	Sudden death—cardiac lethal arrhythmia suspected	41
Patient 6	21	5	Respiratory insufficiency and aspiration pneumonia	45
Patient 7	26	5	Sepsis	64

mia.[19,22,23] Hypoxia further depletes the energy stores and can influence ischemic progression. Many patients with acute stroke develop abnormal respiratory function and drops in oxygen saturation levels.[12] An elevated body temperature (>37.5°C) aggravates ischemic brain damage because it increases metabolic demand in the penumbra and enhances the release of cytotoxic excitatory amino acids and the formation of free radicals.[7,25–29] Approximately 40% of the patients with acute ischemic stroke develop elevated body temperature within the first 48 hours.[30] In the ischemic brain area, arteries dilate in response to acidosis, resulting in a loss of autoregulation of the cerebral vessel.[23,31,32] Mild to modest reductions in blood pressure may therefore result in a critical fall in cerebral blood flow, worsening the degree of ischemia in the penumbra, and transform areas of reversible injury into infarction.[32]

The results of a case-control study conducted by the group of Langhorne et al[8] lend support to this concept that neurological impairment may be exacerbated by disturbances in these physiological variables. Patients who maintained physiological homeostasis showed improved outcomes. Acute medical interventions, targeted at maintaining these essential physiological variables (body temperature, oxygen saturation, and blood pressure) within a narrow physiological range, can be performed without delay when patients are intensively monitored.

To our knowledge, this is the first prospective, randomized study that examined whether intensive monitoring of acute stroke patients for body temperature, oxygen saturation, blood pressure, and cardiac rhythm further reduces poor outcome and mortality in addition to organized stroke-unit care. We found that admission to an SCMU was associated with a lower proportion of patients who died or had a poor outcome at 3 months. The latter was not significant, which is not unexpected in view of the relatively low number of patients that were included in the study. However, compared with other interventions in acute ischemic stroke, the effect of monitoring and normalization of physiological parameters on outcome was quite impressive. The beneficial effect can be attributed to the intensive physiological monitoring protocol because this was a single-center study wherein patients in both arms were very well matched and received the same standard care.

Patients with acute stroke are at risk of developing (ventricular) arrhythmias.[10] In our study, 1 patient in the SCMU could be successfully resuscitated because ventricular fibrillation was promptly identified. Cardiac rhythm monitoring also identified newly diagnosed atrial fibrillation in 5 stroke-care unit patients versus 1 patient in the traditional stroke unit. These findings support the proposal of Oppenheimer and Hachinski[10] that continuous cardiac rhythm monitoring should be an integral part of acute stroke management.

In summary, the results of this pilot study suggest that intensive monitoring of physiological variables during at least the first 48 hours after admission for acute ischemic stroke may reduce poor outcome and death. A larger trial is required to confirm these findings.

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