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Prognosis of stroke patients undergoing mechanical ventilation

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Abstract. *Objective:* to determine the outcome of stroke patients undergoing mechanical ventilation.
Design: retrospective chart review and follow-up telephone interview.
Setting: medical ICU in a multidisciplinary university hospital.
Patients and participants: 199 stroke patients from 1984–1989 where the final diagnosis was stroke.
Interventions: all patients were admitted for the need of mechanical ventilation.
Measurements and results: demographic information, previous relevant diseases, stroke type, general clinical and neurological data, biochemical variables, severity of illness were recorded for the first 24 h following ICU admission. A 1-year follow-up was performed, including mortality and functional status of survivors. Of 170 eventually analyzable patients, 123 (72.4%) died during their ICU stay and 156 (91.8%) during the first year. Three variables were independently associated with one-year mortality: Glasgow score <10 ($p < 0.03$), bradycardia ($p < 0.001$), absence of brainstem reflexes ($p < 0.0004$).
Conclusion: overall prognosis of stroke needing mechanical ventilation is poor, strongly linked to symptoms of neurological impairment.

Key words: Cerebrovascular disease – Coma – Mechanical ventilation – Multivariate analysis

During the 70s several studies tried to assess to role and benefit of stroke intensive care units (SICU) in the management of acute stroke [1–7]. Subsequent to the success of coronary intensive care units, a reduction in overall mortality was expected. Some studies attempted to compare the outcome of stroke in SICU and in general medical wards. Despite selection bias, some authors concluded in favour of the beneficial role played by the SICU management in acute stroke; this has been confirmed by a more recent study [8]. However, most studies showed that there was no striking effect on overall mortality but that intensive care management of stroke patients reduced functional disability and the need for long-term hospital care [9, 10]. Nevertheless, those studies could not assess beneficial effect of SICU management in some sub-groups of stroke patients like comatose or patients with poor neurological scores. Few studies are available that attempted to assess prognosis of these patients. Nouailhat [11] demonstrated that in spite of an overall mortality reaching 87%, long-term outcome in comatose patients did not result in poor quality of life in survivors. Beside coma, respiratory failure leading to mechanical ventilation is another cause of ICU admission and there is currently no available data on outcome of those patients needing respiratory support after acute stroke. To assess prognosis of these patients and determine factors influencing survival or death, we designed a retrospective study over a 5-year period.

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Patients and methods

During a 5 year period from 01/01/84 to 31/12/88, 199 patients were referred to our intensive care unit (ICU) for mechanical ventilation during the course of an acute stroke. The diagnosis of stroke was confirmed by CT scan, cerebral angiography, lumbar puncture or autopsy. Clinical and biological data were recorded according to a standardized way. According to the diagnosis, the following subgroups were considered: ischemic strokes were divided into carotid ischemic stroke, vertebro-basilar ischemic stroke, undetermined ischemic stroke; hemorrhagic strokes were divided into lobar cerebral hemorrhage, sub-arachnoid hemorrhage, infra-tentorial hemorrhage and intraventricular hemorrhage (either isolated or associated to other form of stroke).

The following data were recorded for each patient: age, sex, previous history of cardiac ischemic disease or other cardiac disease, previous history of stroke, of hypertension, of diabetes or alcoholism. Clinical data were recorded for the first 24 h following ICU admission: heart rate, blood pressure, temperature, diuresis and cause of mechanical ventilation. Neurological data included status epilepticus defined as two or more crisis without normal consciousness between two crisis, Babinski sign, brainstem reflexes (pupillary light and corneal reflexes). Biological data recorded were hematocrit, white blood cell count, urea, sodium, potassium, bicarbonates and blood glucose. Glasgow coma score (GCS) and simplified acute physiological score (SAPS) were recorded. Coma was defined as a GCS <10 thus including coma and stupor. Follow-up data were established according to the medical files of the medical units in which patients were hospitalized after ICU discharge. Long-term follow-up information was obtained by mail questionaire or phone calls to the family or to the patient's physician. The cause of death was obtained according to medical files. Survivors neurological status was defined according to a 4-class scale:

- Class 1: no sequelae; could return to previous occupation
- Class 2: functional sequelae; autonomic but slightly impaired.
- Class 3: important sequelae; severely impaired.
- Class 4: bed-ridden.

Mean values are given with SEM. Numerical variables were analyzed with Fisher's exact test. Follow-up ranged from 1 to 5 years. Survival curves were generated by the Kaplan-Meier modified life table method that related survival to the onset of stroke [12]. Survival curves were constructed until the end of the first year of follow-up. Comparisons between sub-groups were made using the log-rank test. Variables related to risk factors or stroke-related factors were analyzed by univariate analysis. Fifteen variables: Diabetes melitus, hypertension, hyperglycemia, urea, GCS, seizures, pupillary or corneal reflexes (entered as a single variable), hemorrhagic stroke, SAPS, hyperkalemia, Babinski sign, bradycardia, tachycardia, age, were analyzed through a Cox multivariate analysis model [13]. A p value of less than 0.05 was considered significant.

Results

The main end-point of the study was to assess the prognosis of stroke at one-year follow-up. A total of 170 patients could eventually be included since 13 patients were excluded because they presented with transient ischemic stroke or cerebral venous thrombosis, 13 patients were excluded because of unreliable diagnosis and 3 more patients were lost during follow-up.

On admission, mean age was 63 ± 1 (sex ratio men/women 1.25), mean SAPS 18.5 ± 1 and mean Glasgow score 6 ± 1. Most of the patients ($n = 131$) were admitted in the ICU within 24 h following the onset of stroke; others ($n = 39$), were admitted secondarily after initial treatment in medical or neurological wards. There was 143 (84%) patients who presented with coma. CT scan was performed in 140 patients (82.4%). Ischemic strokes represented 79 (46.5%) cases and hemorrhagic strokes 91 (53.5%). Table 1 summarizes the relation to outcome of the different stroke types. Overall prognosis was poor: 72.4% of the patients died during the critical care unit stay, 91.8% died during the first year and only 8.2% could regain home. Mechanical ventilation was indicated due to coma (43%), respiratory failure (alveolar hypoventilation, pneumonia, pulmonary embolism, airway obstruction or aspiration) (27%), status epilepticus (10%) or circulatory failure (cardiogenic, septic or hypovolemic shock) (8%). Death was related to coma with cerebral herniation or brain death (60%), respiratory failure including pneumonia and pulmonary embolism (15.3%) or circulatory failure (11.8%). Among the deaths, 65.4% occurred during the first seven days following ICU admission and there was no secondary "mortality peak" in our population. Mean delays between admission and death were different according to the cause of death: 4.5 ± 2.3 days (extreme $1-105$ days) for coma, 34 ± 11 days (extreme $1-300$ days) for circulatory failure and 102 ± 18 days (extreme $9-360$ days) for respiratory failure. At the end of the first year of follow-up, 13 patients had survived their stroke (Table 2) of whom 10 presented initially with ischemic stroke and 3 with hemorrhagic stroke. Seven one-year survivors initially presented with coma. Two patients were in functional class 1 (mean age 73). Five patients were in functional class 2 (mean age 55); 2 of them could return to work. Lastly, 6 patients were in functional class 3 (mean age 57). There was no bedridden patient at 1 year follow-up.

Previous diseases had no effect on outcome except diabetes mellitus that developed limited significance ($p = 0.035$) and was associated with better survival. This effect disappeared after multivariate analysis. Age had no effect on outcome; there was no significant difference for age between the "survivors" and "non-survivors" subgroups (survivors 62.2 ± 4; non-survivors 64.4 ± 1.5; $p = 0.8$) although patients with ischemic stroke were significantly older than patients with hemorrhagic stroke (Isch:65, Hem:61.5, $p < 0.01$). Survival was significantly affected by the stroke type: ischemic strokes (17.3% survival) did much better than hemorrhagic strokes (3.3% survival) at the end of the first year ($p < 0.0002$). In the ischemic group, vertebro-basilar strokes had the worse prognosis with only 4.8% of survivors at one year. In the hemorrhagic group, infra-tentorial hemorrhage and SAH had the worse prognosis with no survivors at one-year

Table 1. Prognosis according to stroke type

	n	%	1-year survival (%)
Ischemic strokes			
Carotid	45	26.4	7 (15)
Vertebro-basilar	20	14.7	1 (5)
Undetermined	14	10.5	2 (14)
Hemorrhagic strokes			
Lobar	45	26.4	2 (4.5)
Infra-tentorial	38	22.5	1 (6)
SAH[a]	35	20.5	0
Ventricular	17	10	0

[a] SAH: Subarachnoïd hemorrhage. The total number of hemorrhagic strokes exceeds 91 due to the associated forms

Table 2. Functional outcome of survivors

Functional class	Ischemic (n)	Hemorrhagic (n)		Total (n)
1	2	0	2	7 Good outcome
2	4	1	5	
3	4	2	6	6 Poor outcome
4	0	0	0	

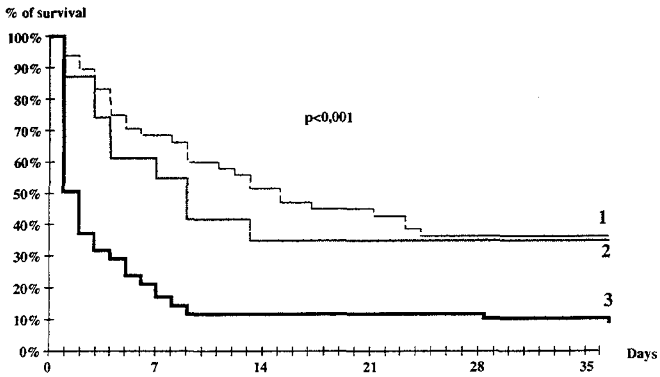

Fig. 1. Survival curves at 1-year follow-up according to the cause of mechanical ventilation ($p < 0.001$). The curves has been constructed until the end of the first month but statistical significance was achieved until the third month. *1*, ventilatory support for status epilepticus ($n = 15$); *2*, ventilatory support for respiratory failure ($n = 38$); *3*, ventilatory support for coma ($n = 77$)

follow-up. The cause of mechanical ventilation had a significant effect on outcome until the third month. Patients intubated for the management of coma had an overmortality when compared to patients intubated for respiratory failure or for status epilepticus ($p < 0.001$) (Fig. 1). Univariate analysis could isolate ten factors significantly related to worse prognosis (Table 3): coma (Glasgow score < 10), absence of pupillary light reflexes, absence of corneal reflexes, absence of status epilepticus, previous history of diabetes mellitus, hemorrhagic stroke, absence or bilateral Babinski sign (as opposed to unilateral Babinski sign wich was associated to better prognosis), SAPS > 15, bradycardia (heart rate < 55/mn) and hyperkalemia ($K^+ > 5{,}5$ meq/l). Fifteen factors were reevaluated through a Cox multivariate analysis model. Among these, coma, bradycardia and absence of brainstem reflexes were independant predictors of death (Table 3).

Discussion

As previously shown in the studies of Nouailhat et al. [11, 14] the present results provide evidence that overall prognosis in stroke patients admitted to ICU is poor despite unlimited support of vital functions including mechanical ventilation, careful monitoring of cardio-vascular parameters as well as fluid and electrolyte balance and symptomatic therapy of brain edema. Criteria of entry in our ICU – the need for mechanical ventilation – generated a selection bias responsible for the high proportion of comatose patients that also may explain the unusual ratio between hemorrhagic and ischemic strokes in this population.

Table 3. Univariate and multivariate analysis of risk factors

	n	% of survivors	*p* univariate	*p* multivariate
Age			0.21	0.06
Previous disease				
Ischemic cardiopathy	23	10	0.6	
Other cardiopathy	29	8.5	0.3	
Stroke	30	10.5	0.5	
Hypertension	75	8	0.7	
Diabetes melitus	26	11.5	0.02 S	0.06
Alcoholism	26	10.3	0.4	
Clinical factors				
Hypertension (BP > 190 mmHg)	38	8	0.3	0.73
Shock (BP < 80 mmHg)	17	12	0.1	0.8
Fever (T° > 38° 5)	20	15	0.3	
Tachycardia	33	8	0.3	0.054
Bradycardia	24	4	0.03 S	0.001 S
Biological factors				
Hematocrit < 30% or > 50%	20	13.5	0.3	
Sodium < 130 or > 150 meq/l	32	6.2	0.4	
Potassium > 5.5 meq/l	16	0	0.02 S	0.39
Blood Glucose > 14 mmol/l	68	4.4	0.19	0.32
Urea > 21 mmol/l	10	0	0.14	0.27
Acidosis (HCO3 – < 20 meq/l)	25	6	0.3	
Leucocytes > 15000/mm^3	65	7.8	0.5	
Neurological factors				
Coma (GCS < 10)	143	4.2	0.0001 S	0.03 S
Loss of brainstem reflexes	104	1	0.00001 S	0.00004 S
Absence of status epilepticus	155	5.2	0.02 S	0.13
Hemorrhagic stroke	91	3.5	0.0002 S	0.09
No or bilateral BBK sign	120	5	0.0009 S	0.49
Ventricular hemorrhage	38	5.4	0.6	
Others				
SAPS < 15	63	15.8	0.0004 S	0.56

Mean age of our patients was similar to previous studies but does not have any prognostic significance. Some authors showed that older stroke patients were at particular risk of early death [15, 16]. In these studies overall gravity of patients was less than in the present population whose early death was strongly related to coma as shown in Fig. 1. In the present study, neurological impairement very likely outweighed age-related gravity. This issue is of practical importance since it means that older patients with limited neurological impairment could more benefit from ICU admission than younger comatose patients. Presumably, neurological severity also explains that previous diseases or associated illness did not demonstrate an influence on outcome.

Neurological impairment was of major prognosis significance in our patients. Of the 10 factors related to survival or death 1, after univariate analysis, were neurological (Table 3). Multivariate analysis showed an independent effect on outcome for 2 of them: coma and loss of brainstem reflexes. The loss of conscioussness is unanimously recognized as the major prognosis determinant in acute stroke patients [17–19]. The severity of coma is usually assessed by associated signs such as brainstem reflexes impairment or severity of motor dysfunction [14]. In the present study, the loss of pupillary and corneal reflexes could not be considered as consequences of severe coma since it has an independant predictive value on outcome. The positive effect on outcome of status epilepticus is one of the more unexpected results of our study. Seizures have been related to worsened prognosis or to prolonged comatose state after acute stroke [20]. In our study, status epilepticus was mainly associated with ischemic stroke (11 cases) and particularly with carotid ischemic stroke (7 cases) which were of better prognosis. Seizures or status epilepticus were unusual in extensive cerebral infarction or in hemorrhagic strokes with brainstem impairment. The low GCS in the group of patients with seizures witnessed more the loss of conscioussness during or immediately after the critical episod rather than the extent of cerebral damage. Thus in our study, status epilepticus -and unilateral Babinski sign- presumably witnessed for limited cerebral impairment due to distal vascular lesions and reflected the better prognosis of the constituted ischemic stroke type. However, neither seizures nor Babinski sign were significant after multivariate analysis thus failing to be independant factors of outcome.

After univariate analysis, 4 non-neurologic parameters had significant effect on outcome: SAPS, bradycardia, hyperkalemia and previous history of diabetes melitus. SAPS score is of limited value in cerebro-vascular diseases since it was designed to express extra-neurologic severity [21]. Our study confirms these data, showing that SAPS has no independent effect on outcome after multivariate analysis. This result is explained by the fact that signs of major cerebral impairment are occulted in the SAPS construction, leading to underestimation of neurologic severity.

Bradycardia was found in 24 patients of whom only one survived at one year follow-up. A first analysis was to relate this fact to intra-cranial hypertension, thus making bradycardia a neurologic-like prognosis factor. However, multivariate analysis demonstrated significance independently of coma. Moreover, the time-interval to death in the bradycardia sub-group was different from that of the coma sub-group (49 days, extreme 1 and 720 days, versus 4.5 days extreme 1 and 105 days). Bradycardia could then represent the role of acute cardiac complications in early stroke mortality, irrespective of neurological impairment. This hypothesis could be reinforced by the borderline significance developped by tachycardia in the multivariate analysis which may confirm the role of cardiac-related death in acute stroke.

Hyperkalemia is an unexpected prognosis factor after univariate analysis, although this effect disappeared after multivariate analysis. This biochemical abnormality was found in 16 patients in whom there was no survivors at 30-days follow-up. Although altered in most of these hyperkalemic patients, renal function could not account for death and did not achieve by itself a significant prognosis value. Since death could not be related to a direct complication of hyperkalemia, at least in 14 out of the 16 patients, the relevance of hyperkalemia as a prognosis factor remains unclear.

The present study confirms the major weight of coma in predicting death. As shown in Fig. 1, almost all patients in whom coma solely imposed mechanical ventilation died within 10 days, regardless of stroke type. These data suggest that ICU management was unable to have a beneficial effect on the natural history of stroke. Despite symptomatic correction of factors that could clearly worsen brain damage – hypoxia, hypercapnia, acidosis, fluid and electrolyte disturbances – no improvement of clinical relevance was observed in these patients. Nevertheless, some stroke patients who underwent mechanical ventilation for respiratory failure or seizures which otherwise would probably have died could benefit from ICU management.

Despite high mortality, functional outcome analysis provides some hopeful results. Thirteen patients survived at one year follow-up with mild disability or no disablement at all. Unlike anoxic encephalopathy, ICU management of acute stroke does not lead to persistent vegetative state.

In conclusion, this study provides some evidence that ICU management of acute stroke does not greatly affect natural history of stroke. Early mortality is still dependent on direct neurological impairment and extent of cerebral lesions for which ICU therapy is probably of very limited impact. Level of consciousness, type of stroke, limited cerebral lesions even when expressed by status epilepticus are the major determinants of survival. Nevertheless, stroke patients who display acute respiratory failure in relation to aspiration pneumonia, airway obstruction, repeated seizures can clearly benefit of ICU stay regardless of age, provided that underlying cerebral lesions are relatively limited.

This rather pessimistic conclusion may not support the view the ICU is futile for the care of acute stroke patients. Indeed, the new approaches of stroke therapy including early thrombolysis will probably allow ICU management to be the cornerstone of stroke therapy.

References

1. Kennedy FB, Pozen TJ, Gabelman EH, Tuthill JE, Zaentz SD (1970) Stroke intensive care. An appraisal. Am Heart J 80:188–196
2. Pitner SE, Mance CJ (1973) An evaluation of stroke intensive care: results in a municipal hospital. Stroke 4:737–741
3. Silver FL, Norris JW, Lewis AJ, Hachinski VC (1984) Early mortality following stroke: a prospective review. Stroke 15:492–496
4. Woimant F, de Liège P, Dupuy M, Haguenau M, Pépin B (1984) Traitement des accidents vasculaires cérébraux dans une unité de soins intensifs. Presse Méd. 13:2121–2124
5. Chambers BR, Norris JW, Shurvell BL, Hachinski VC (1987) Prognosis of acute stroke. Neurology 37:221–225
6. Drake WE, Hamilton MJ, Carlsson M (1973) Acute stroke management and patient outcome: the value of neurovascular care units. Stroke 4:933–945
7. Norris JW, Hachinski VC (1976) Intensive care management of stroke patients. Stroke 7:573–577
8. Indredavik B, Bakke F, Solberg R, Rokseth R, Haaheim LL, Holme I (1991) Benefit of a stroke unit: a randomized controlled trial. Stroke 22:1026–1031
9. Strand T, Asplund K, Eriksson S, Hägg E, Lithner F, Wester PO (1986) Stroke unit care-who benefits? Stroke 17:377–381
10. Norris JW, Hachinski VC (1986) Stroke units or stroke centres? Stroke 17:360–362
11. Nouailhat F, Outin HD, Merrer J (1989) Devenir des AVC admis dans le coma en réanimation. Réan Soins Intens Med Urg 5:447 (abstract)
12. Kaplan EL, Meier P (1958) Non parametric estimation from incomplete observations. J Am Stat Assoc 53:457–481
13. Cox DR (1972) Regression models and life tables. J R Soc Stat 34:187–220
14. Caronna JJ, Levy DE (1983) Clinical predictors of outcome in ischemic stroke. Neurol Clin 1:103–117
15. Bonita R, Ford MA, Stewart AW (1988) Predicting survival after stroke: a three-year follow-up. Stroke 19:669–673
16. Howard J, Walker MD, Becker C, Coull B, Feibel J, McLeroy K, Toole JF, Yatsu F (1986) Community hospital-based stroke programs: North Carolina, Oregon, New-York. III-Factors influencing survival after stroke. Stroke 17:294–299
17. Oxbury JM, Greenhall RCD, Grainger KMR (1975) Predicting outcome of stroke: acute stage after cerebral infarction. Br Med J 3:125–127
18. Levy DE, Bates D, Caronna JJ, Cartlidge NEF, Knill-Jones RP, Lapinski RH, Singer BH, Shaw DA, Plum F (1981) Prognosis in non traumatic coma. Ann Intern Med 94:293–301
19. Nouailhat F, Simon N, Outin H, Merrer J, Casciani D, Mollo JL, Lemoine E (1987) Histoire naturelle et pronostic des accidents vasculaires cérébraux. Place des soins intensifs. In: Réanimation et médecine d'urgence. Expansion Scientifique Française, Paris, pp 166–190
20. Goulon M, Gajdos P, Margent P, Raphaël JC, Barois A, Combes A, Grobuis S, Levy-Alcover M, Gastinne H (1977) Neurological problems in intensive care. Proceedings 11th World Congress Neurol. Excerpta Medica, Amsterdam, pp 283–298
21. Le Gall JR, Loirat P, Alperovitch A, Glaser P, Granthil C, Mathieu D, Mercier P, Thomas R, Villers D (1984) A simplified acute physiologic score for ICU patients. Crit Care Med 12:975–977