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ORIGINAL CONTRIBUTIONS

# Functional Outcome After Common Poststroke Complications Occurring in the First 90 Days

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The aim of this study was to explore the associations of common medical complications with functional outcome at 90 days post stroke.

Patients with unselected acute stroke were included and observed for 16 predefined complications during the first week. Fifty percent (244 patients) were allocated to follow-up of 13 complications until 90 days and then assessed with the modified Rankin Scale 90. Common complications were defined as complications with frequencies of ≥5%. Ordinal logistic regression (worsened outcome), as well as binary logistic regression for severe dependency and death (modified Rankin Scale score>3) was performed.

Seven of the 13 complications occurred at a frequency ≥5%. Recurrent stroke and chest infection were found to have an odds ratio for worsened outcome of 7.45 (95% confidence interval, 2.83–20.96; $P<0.0001$) and 3.28 (95% confidence interval, 1.16–9.29; $P=0.025$), respectively. Infections other than chest infections and urinary tract infections had an odds ratio for worsened outcome of 1.59 (95% confidence interval, 1.12–2.24; $P=0.009$) and falls an odds ratio of 1.43 (95% confidence interval, 1.06 to 1.93; $P=0.021$). Myocardial infarction, urinary tract infections, and pain were not associated with a worsened outcome in terms of modified Rankin Scale 90.

Recurrent stroke and chest infections were strongly associated with a worsened outcome. Other infections and falls were associated with less worsening. For myocardial infarction, urinary tract infections, and pain no association with functional outcome was found. Active strategies for prevention and early treatment of the first 2 complications seem advisable; patient monitoring as part of comprehensive stroke unit care should ensure timely identification and treatment of all complications.

**Key Words**: complications ■ patient outcome assessment ■ stroke ■ stroke unit



Stroke is a serious global public health problem with an annual incidence varying from 100 to 400 cases in 100 000 inhabitants, and a leading cause of death and disability, both in high- and low-income countries.[1] The crude annual incidence of stroke in Central Norway is known to be 300 in 100 000 inhabitants.[2] The reported 1-month case-fatality rate from different

countries varies between 14% and 34%.[1] Although the majority of deaths are accounted for by neurological sequellae of the stroke, a significant proportion has been judged to be caused by immobility and cardiac disease.[3] Stroke unit (SU) care reduces the case-fatality by 18%, and it has been suggested that the prevention and timely treatment of medical complications may account for most of the survival benefits related to SUs.[4,5]

Poststroke complications have been studied both in the acute phase and in the rehabilitation phase.[6–8] They can be categorized into 3 groups: (1) neurological complications (cerebral edema, stroke progression, stroke recurrence, seizures, anxiety, and depression), (2) cardiovascular complications, and (3) complications of immobility (chest infection, urinary tract infection [UTI], other infections, dehydration, venous thromboembolism, falls, pressure sores, and pain).[3,5] The percentage of patients experiencing ≥1 complication within the first month post stroke is reported with great variation at 24%,[9] 59%,[6] 85%,[8] and 95%.[7] In our comprehensive SU, the frequencies of common complications were 64% within the first week and 82% during the first 3 months.[10] Studies relating stroke complications to parameters of functional outcome are scarce, yet suggest that the majority of complications are associated with a reduction in functional outcome.[7,9]

The aim of the present study was to examine the association between complications and functional outcome at 90 days for patients treated in an SU, followed by an early supported discharge service, which both have been evaluated in randomized trials and have shown beneficial effects on functional outcome.[11,12]

## SUBJECTS AND METHODS

The SU, Department of Medicine at the University Hospital of Trondheim, serves as the primary hospital for ≈200 000 inhabitants of South Trondelag and as the tertiary hospital for Central Norway. All patients, admitted consecutively between January 1, 2002, and May 15, 2003, and presenting with symptoms consistent with acute stroke (n=664), were included in the study if the following criteria were fulfilled: (1) a diagnosis of acute stroke according to the World Health Organization's definition, (2) computerized tomographic scan exclusion of alternative pathologies (eg, tumor, trauma, infection, and vasculitis; n=110), and (3) admission to the SU within 24 hours of stroke onset (n=54). Screening for inclusion was halted after completed inclusion of 500 patients. Of the 500 patients thus eligible for inclusion, 11 did not wish to participate during follow-up. A total of 489 patients were included in the analysis of complications during the first week.[10]

Fifty percent of these patients were randomly allocated to 90-day follow-up, and these 244 patients are the contributors to this study (Figure 1).

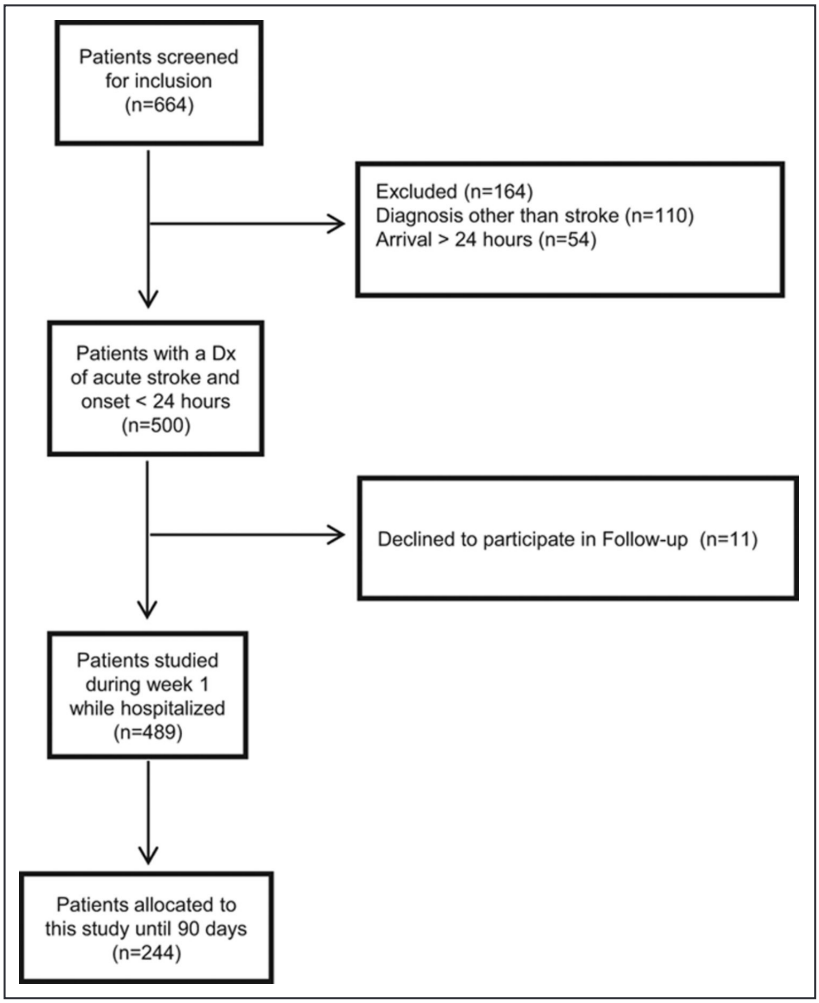


**Figure 1**. Patient flow.

All patients received initial diagnostic evaluation and treatment in accordance with our SU protocol.[13,14] It stresses physiological homeostasis, a strategy for early mobilization and integration of medical and nursing care, and rehabilitation via a multidisciplinary team. There was a strong focus on prevention of complications, including routine swallowing evaluation before any oral-intake, frequent ultrasound assessment for urinary retention and the use of intermittent urinary catheterization as necessary.

After discharge from the SU, the patients were followed up by an early supported discharge service, previously described.[11] As part of this service, all patients received an outpatient follow-up medical evaluation 4 weeks after discharge. At 90 days, a home-visit and functional assessment using modified Rankin Scale (mRS) scores[15] were performed by a staff-member unfamiliar with the patient.

## Assessment of Complications

During the first week after admission, patients were screened daily for 16 prespecified complications by specially trained physicians, nurses, and physical therapists.[10] Two-hundred forty four patients were allocated to weekly follow-up via telephone to the patient or the primary caregiver for 3 months and with assessment of the following complications: stroke recurrence, seizure, chest infection, UTI, other infections, falls (serious and nonserious), pressure sores, pulmonary embolism, deep vein thrombosis, myocardial infarction, and pain (shoulder and other). All complications were based on a clinical diagnosis, and their definitions were similar to the

definitions used in previous studies.[6,8] The definitions and the frequencies of these complications have been published previously.[10]

### Data Analysis

Complications occurring in 5% of patients or more over the entire 3-month period were defined as common complications and were analyzed for their association with functional outcome at 90 days. Ordinal logistic regression was performed to calculate an odds ratio (OR) for worsened outcome and binary logistic regression with a cutoff between mRS 3 and 4 was performed to calculate an OR for bad outcome. Both were adjusted for the potential confounders: age, sex, prestroke mRS and Scandinavian stroke scale (SSS) day 1; the latter represents stroke severity. Ordinal logistic regression analysis is judged to provide a more sensitive estimate than analysis of a dichotomized-outcome and it was, therefore, chosen as a primary end point.[16,17] A cutoff between mRS 3 and 4 was used, when the conditions of the parallel line-test for proportionality were not met. The calculations were performed in SPSS and Stata.

### Ethics

This study was part of a larger investigation on recovery after stroke and was approved by the regional ethics committee.

## RESULTS

The patients baseline characteristics are shown in Table 1. A total of 56% of patients were women and the mean age was 76.5 years (SD±9.8). Ninety percent had an ischemic stroke and 10% had a hemorrhagic stroke. Mean SSS day 1 was 40.3 (SD±16.6). Mean estimated prestroke mRS was 1.6 (SD±1.1) and mean mRS day 1 was 3.47 (SD±1.3).

**Table 1**. Baseline Characteristics of the Patients (n=244) (Table view)

| Characteristics | n | % |
|---|---|---|
| Women | 137 | 56 |
| Age, y, mean±SD | 76.5±9.8 | |
| Risk factors | | |
| Hypertension | 93 | 38 |
| Previous stroke | 47 | 19 |
| Atrial fibrillation | 46 | 19 |
| Diabetes mellitus | 30 | 12 |
| Previous myocardial infarction | 35 | 14 |
| Smoking | 48 | 20 |
| TIA | 24 | 10 |
| Diagnosis | | |
| Ischemic stroke | 219 | 90 |
| Hemorrhagic stroke | 25 | 10 |

TIA indicates transient ischemic attack.

As presented in Table 2, the following 7 complications occurred in ≥5% of patients: recurrent stroke 5%, myocardial infarction (MI) 7%, chest infection 17%, UTI 28%, other infections 13%, falls (combined-serious and nonserious falls) 29%, and pain (combined-shoulder and diffuse pain)

57%. The following complications seizures, pressure sores, pulmonary embolism, and deep vein thrombosis occurred at a frequency of 2.5, 2.9, 1.2, and 2.5%, respectively and were not analyzed further. mRS at day 90 (mRS90) varied greatly between the complications. In unadjusted analysis, recurrent stroke, MI, and chest infection were associated with a worsening of survival and function (mRS≥3) at 90 days; pain and falls were to a lesser degree (Figure 2).

**Table 2**. Frequency of Complications and Distribution of Outcomes in Terms of mRS90 (Table view)

| Complication | n | % of Cohort | Age, y | Earlier mRS, Mean±SD | mRS90, Mean±SD | mRS90, 0–3, % | mRS90, 4–6, % | mRS90, 6, % |
|---|---|---|---|---|---|---|---|---|
| Whole cohort | 244 | 100 | 77±9 | 1.6±1.1 | 3.0±1.8 | 66 | 34 | 17 |
| Recurrent stroke | 12 | 5 | 78±6 | 1.6±1.2 | 4.7±1.6 | 25 | 75 | 42 |
| MI | 17 | 7 | 84±6 | 2.1±1.4 | 4.8±1.6 | 23 | 77 | 53 |
| Chest infection | 42 | 17 | 82±7 | 2.0±1.2 | 4.7±1.6 | 19 | 81 | 45 |
| UTI | 68 | 28 | 81±9 | 2.0±1.1 | 3.9±1.5 | 40 | 60 | 19 |
| Other infection | 31 | 13 | 78±9 | 1.4±0.9 | 3.4±1.6 | 48 | 52 | 13 |
| Falls | 70 | 29 | 76±10 | 1.4±0.9 | 3.1±1.2 | 69 | 31 | 4 |
| Pain | 140 | 57 | 77±10 | 1.5±1.1 | 3.9±1.6 | 66 | 34 | 12 |

Descriptive data. MI indicates myocardial infraction; mRS, modified Rankin Scale; and UTI, urinary tract infection.

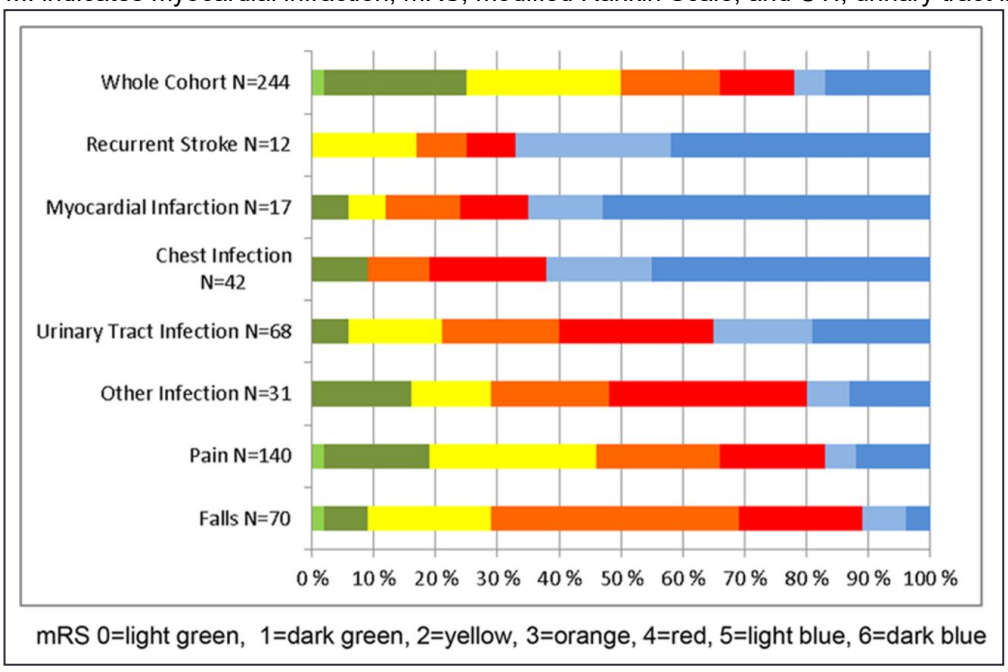


**Figure 2**. Distribution of modified Rankin Scale (mRS) scores at 90 days.

Table 3 shows the results of the outcome analysis adjusted for age, sex, prestroke mRS and SSS day 1. According to both the shift and the dichotomized analyses recurrent stroke and chest infection had an OR for worsened outcome of 7.45 (95% confidence interval [CI], 2.83–20.96; *P*<0.0001) and 3.28 (95% CI, 1.16–9.29; *P*=0.025), respectively, and an OR for bad outcome (mRS>3) of 10.45 (95% CI, 1.03–38.93; *P*<0.0001) and 2.52 (95% CI, 1.14–8.53; *P*=0.022). Infections other than chest and UTI, as well as falls, had ORs for worsened outcome of 1.59 (95% CI, 1.12–2.24; *P*=0.009) and 1.43 (95% CI, 1.06–1.93; *P*=0.021), respectively. The ORs for bad outcome (mRS>3) were 2.09 (95% CI, 1.15–3.80; *P*=0.015) and 1.41 (95% CI, 1.06–1.88;

*P*=0.019). Myocardial infarction, as well as UTI and pain, was not associated with a reduction in functional outcome.

**Table 3**. OR for Worsened Outcome (Ordinal Logistic Regression) and Bad Outcome (mRS>3 at Day 90) (Table view)

| Complication | OR (95% CI) for Worsened Outcome | *P* Value | OR (95% CI) for mRS>3 | *P* Value |
|---|---|---|---|---|
| Recurrent stroke | 7.45 (2.83–20.96) | <0.0001 | 10.45 (1.03–38.93) | <0.0001 |
| MI | 1.83 (0.62–5.36) | 0.272 | 1.89 (0.42–8.53) | 0.408 |
| Chest infection | 3.28 (1.16–9.29) | 0.025 | 2.52 (1.14–5.54) | 0.022 |
| UTI | 1.19 (0.63–1.74) | 0.323 | 1.33 (0.91–1.93) | 0.137 |
| Other infection | 1.59 (1.12–2.24) | 0.009 | 2.09 (1.15–3.80) | 0.015 |
| Falls | 1.43 (1.06–1.93) | 0.021 | 1.41 (1.06–1.88) | 0.019 |
| Pain | 1.00 (0.92–1.09) | 0.961 | 0.94 (0.80–1.10) | 0.439 |

Ordinal logistic regression was performed, correcting for age, sex, prestroke mRS, and SSS day 1 (worsened outcome). Binary logistic regression for severe dependency or death (mRS>3) was performed correcting for the same confounders (bad outcome). CI indicates confidence interval; MI, myocardial infraction; mRS, modified Rankin Scale; OR, odds ratio; SSS, Scandinavian stroke scale; and UTI, surinary tract infection.

## DISCUSSION

Functional outcome after a stroke is in large part determined by the nature of the incident stroke. Other established factors associated with reduced functional outcome are advanced age and a reduced level of premorbid function.[18,19] In this study, we were able to show that recurrent stroke and chest infection were strongly associated with reduced functional outcome at 90 days. Falls and other infections had a much weaker association with reduced functional outcome. No other complication assessed was associated with a reduction in function.

Five percent of our patients were found to have a recurrent stroke. Other studies reported a frequency of 2% to 18%.[7–9] In our study, this complication had an OR of 7.5 for a worsened outcome and an OR of 10.5 for major disability or death. Early work-up for transient ischemic attack or minor stroke reduced the 90-day recurrent stroke rate from 10.3% to 2.1% in the Oxford Vascular Study.[20] Analogously, recurrent stroke can be considered a likely failure of prevention, justifying a repeated work-up with an aim to improve prophylaxis. Large artery disease, previous MI, and atrial fibrillation seem to be the factors predisposing toward early recurrence and should be actively sought after.[21–23]

A total of 17% of our patients had a chest infection, with an adjusted OR of 3.3 and 2.5 for worsened outcome and for dependency and death, respectively. This complication is reported at a frequency of 10% to 22% in other studies and known to be associated with high-mortality.[6–9] In a study of 14 293 US Medicare patients admitted for stroke, pneumonia was identified in 6.9% of patients and conferred a 3-fold increase in 30-day mortality.[24] The stroke-related causes are judged to be multifactorial: reduced swallowing ability, reduced mobility and thereby lung-mechanics, and central nervous system injury-induced immune depression.[25–27] Performing a swallowing evaluation before any oral-intake has been shown to decrease the incidence of aspiration pneumonia 3-fold.[28] Preventive use of antibiotics is under investigation as a possible strategy in high-risk patients.[29] Early initiation of antibiotic therapy is generally recommended and seems to be one of the interventions that make SU care so effective.[5] Greater emphasis on patient-mobilization is likely another important preventive aspect of SU care. Although it is

established that mobilization within 7 days reduces the number of serious complications, and too much time spent in bed is detrimental, the optimal timing (within 24, 48, or 72 hours from onset of a stroke) and quantity of mobilization are not clear yet.[30–32] Incentive spirometry, commonly used in the postoperative management of patients, could be an accessory measure in those patients, which cannot be mobilized to a standing position. Its use seems most promising in the context of a multifactorial care program, including oral care and mobilization, which has been shown to reduce postoperative pneumonia by 38%.[33]

Infections other than chest infection and UTI occurred in 13% of patients and represent various causes, mostly skin and intravenous line infections, and also sepsis and cholecystitis. This group of infections was shown to be associated with worsened outcome with an OR of 1.59, and severe disability and death with an OR of 2.09. Scant reports describe a frequency between 7% and 10%.[34,35] No association with a reduction in functional outcome was found in a similar analysis.[34] The variability in the findings likely reflects the variability in the case-mix. Measures to counteract nosocomial infections and routine SU care constitute preventive efforts.

Falls occurred in 29% of the cohort. This frequency compares with a range of 2.2% to 26% reported.[6,8,9] A minority (3%) of patients sustained a concomitant serious soft tissue injury or fracture. Falls (all combined) conferred an OR of 1.43 for worsened outcome and an OR of 1.41 for disability or death. This association, although statistically significant, was of a lesser magnitude than the association observed between a recurrent stroke or chest infection and reduction in functional outcome. Appropriate interventions to reduce falls should increase the patient's coping ability and concomitantly reduce his/her fear of falling to counteract the downward spiral of fear, less physical activity, decline in physical ability and further increase in the risk of falling.[36,37]

A poststroke MI occurred in 7% of the patients. The literature reported a frequency of MI or cardiac failure of 2% to 4% in patients poststroke.[6,7,9] In our study, despite being associated with a high-rate of disability and mortality in the unadjusted analysis, this serious event, which occurred mainly in older patients, was not independently associated with a reduction in functional outcome.

UTI occurred in 28% of patients. The reported frequency varies between 7% and 27%.[6–9,34,38] This infection was not independently associated with a reduction in 90-day function in our study. A similar result was obtained in a study of 412 patients by Stott et al.[34] Pain, including shoulder-pain and diffuse pain, occurred in 57% of patients. No association with functional outcome at 90 days could be found.

The reported frequency varies widely for most of the complications, and our results are usually at the higher end of this range. Variations in definition of complications, timing and duration of follow-up, and case-mix are probably contributing factors to the variation in complication rates. Although our results could in part imply a failure of prevention, they might, alternatively, reflect thorough screening procedures. We do think that a foremost strength of our study is the fact that it was performed in an SU combined with an organized follow-up service (early supported discharge), which has shown good outcomes previously for patients with stroke, and whose members were actively searching for complications. With this approach, one would expect to best approximate a complete reporting of events. Another strength of the study is the choice of end point, because the functional outcome at 3 months is a predictor for long-term survival.[39]

A potential weakness of our study is the lack of assessment for neuropsychiatric complications: delirium, depression and poststroke fatigue. These could be assessed concomitantly with the assessment of softer end points and patient reported outcomes.

Ten years have passed between the conduction of the study and this analysis. During this time, stroke care may have improved, and this may have lead to a reduction in the frequency of

complications. However, the relative associations with outcome should not have been affected by this process. To our knowledge, an equally comprehensive outcome analysis with regards to complications has not become available in the literature in the intervening years.

Looking to the future, it would be interesting to explore, which of these complications are associated with an increase in morbidity and mortality in the longer term. Especially important is a follow-up in regards to falls, which according to the geriatric literature conveys a serious prognosis and is important in patient safety campaigns.[40] Preventive antibiotics for aspiration pneumonia in high-risk patients and a multifactorial approach to mobilization and chest physical therapy in the context of an SU deserve further study.

## CONCLUSIONS

In our study, 2 complications, recurrent stroke and chest infections, were strongly associated with a worsening of outcome at 90 days post stroke. Other infections and falls were associated with worsening of a lesser magnitude. Pain, although common, seemed not to be associated with a reduction of functional outcome. Cardiovascular assessment and secondary stroke prevention, as well as the prevention and treatment of aspiration pneumonia, seem important in stroke care. Patient monitoring as part of comprehensive SU care should ensure timely identification and treatment of all complications and is applicable in all healthcare settings.[41]

## ARTICLE INFORMATION

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### Disclosures

None.

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