In-Hospital Medical Complications, Length of Stay, and Mortality Among Stroke Unit Patients

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Background and Purpose—The relationship between in-hospital stroke-related medical complications and clinical outcome remains unclear. We examined whether medical complications were associated with length of stay (LOS) and mortality among stroke unit patients.

Methods—Using population-based Danish medical registries, we performed a follow-up study among all patients with acute stroke admitted to stroke units in 2 counties between 2003 and 2009 (n=13 721). Data regarding in-hospital medical complications, including pneumonia, urinary tract infection, pressure ulcer, falls, deep venous thrombosis, pulmonary embolism, and severe constipation together with LOS and mortality were prospectively registered.

Results—Overall, 25.2% of patients (n=3453) experienced 1 or more medical complications during hospitalization. The most common complications were urinary tract infection (15.4%), pneumonia (9.0%), and constipation (6.8%). Median LOS was 13 days (25th and 75th quartiles, 5 and 33). All medical complications were associated with longer LOS. The adjusted relative LOS extension ranged from 1.80 (95% CI, 1.54–2.11) for pneumonia to 3.06 (95% CI, 2.67–3.52) for falls. Patients with 1 or more complications had an increased 1-year mortality rate (adjusted mortality rate ratio [MRR], 1.20; 95% CI, 1.04–1.39). The association was mainly because of pneumonia, which was associated with higher mortality both after 30 days (adjusted MRR, 1.59; 95% CI, 1.31–1.93) and 1 year (adjusted MRR, 1.76; 95% CI, 1.45–2.14).

Conclusions—In-hospital medical complications were associated with longer LOS and some, in particular pneumonia, also with an increased mortality among patients with acute stroke. **(*Stroke*. 2011;42:3214-3218.)**

Key Words: medical complications ■ length of stay ■ mortality

Although prevention, early recognition, and management of poststroke medical complications are considered to be essential aspects of modern stroke care, patients with stroke remain at high risk of medical complications including pneumonia, urinary tract infection (UTI), pressure ulcer, falls, venous thromboembolism (VTE), and severe constipation.[1–3] Medical complications may possibly directly and indirectly (eg, by hindering optimal rehabilitation) affect clinical outcome, including extended LOS[4,5] and increased mortality.[3,6–14] However, reported findings have been inconsistent, and most studies are small and have primarily focused on short-term outcomes.[9,11,14,15] Further, existing studies have often been conducted either in rehabilitation units[12] or in clinical trial settings.[9] There is consequently a need for large-scale studies with long-term follow-up on unselected patients to comprehend better the impact of medical complications in current, real-life, acute stroke care settings. We therefore aimed to examine the association of in-hospital medical complications and LOS and the 30-day and 1-year mortality in patients with stroke in a population-based, follow-up study.

Methods

We conducted this study using Danish medical registries. All Danish citizens are assigned a unique 10-digit civil registration number, which is used in all registries, enabling unambiguous linkage between them.[16] The Danish National Health Service provides tax-supported healthcare to all residents, including free access to hospital care and general practitioners.

Study Population

Patients were identified from the Danish National Indicator Project (DNIP), a nationwide initiative to improve the quality of care for specific diseases, including for stroke.[17] DNIP monitors the implementation of central elements of the national clinical guidelines on acute stroke care issued by the Danish Society of Stroke. Participation is mandatory for all hospitals treating patients for acute stroke. Staff members responsible for data collection have been appointed at all participating departments. Detailed written instructions are available to the staff to ensure validity of the data collected and completeness of patient registration in the DNIP. Completeness of

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the data collection is continuously monitored and regular feedback is given to the participating departments. To ensure completeness of patient registration in DNIP, its enrollees are compared with local hospital discharge registries. A structured audit process is performed every year on a national, regional, and local basis to assess critically the quality of the data set and the results. After the audit process is completed, data are released publicly, including comments on the results from the audit groups.

We identified all patients admitted with acute stroke to the stroke units (n=10) in the former Copenhagen Hospital Corporation and Aarhus County between January 13, 2003 and December 31, 2009. The stroke units serve a well-defined population of approximately 1.3 million. All patients ≥18 years old were eligible for inclusion in the DNIP. We only included the first stroke event registered in the study period (n=13 721). A flow chart of the identification of the patient population is presented in Supplemental Figure I (http://stroke.ahajournals.org).

Medical Complications

The following in-hospital medical complications were prospectively registered: pneumonia, UTI, pressure ulcer, falls, VTE, and severe constipation. Only complications that developed after hospital admission were registered. Definitions (Supplemental Table I) of the complications were in general in accordance with definitions used in other studies.[3,11] The included medical complications were chosen as they are relatively frequent, amenable for clinical intervention,[18] and at least some of them have previously been linked with adverse clinical outcome.[8,10,13,19,20,21] Fever was only included as a complication when occurring together with other symptoms, indications of pneumonia, or UTI.

LOS

LOS was defined as the time from admission to discharge. Admission date was defined as the date the patient was admitted to the hospital with stroke, or the date of stroke occurrence if the patient was already hospitalized with another diagnosis. Discharge date was defined differently in the 2 study areas: in the former Copenhagen Hospital Corporation, the date was defined as the date of discharge from the stroke unit. In the former Aarhus County, LOS also included transfers to rehabilitation wards, and therefore covered the entire hospital stay.

Mortality

Information on changes in vital status during the follow-up period was obtained from the Danish Civil Registration System, which, since 1968 has maintained electronic records of the population.[16] For all practical purposes, follow-up on mortality using the Civil Registration system can be considered fully complete. Information on the immediate cause of death was obtained from the Danish National Registry of Causes of Death.[22]

Patient Characteristics

The following characteristics were registered on admission: age, sex, marital status (living with partner, family, or friend; or living alone), housing (own home, nursing home, or other institution), profession at admission (employed, unemployed, or pensioner), Scandinavian Stroke Scale score, Charlson comorbidity index (0, no comorbidity; 1–2, low comorbidity; ≥3, high comorbidity), previous stroke, previous and/or current atrial fibrillation, hypertension (yes/no), preadmission modified Rankin score, smoking habits (current, former [>0.5 years], or never), and alcohol intake (≤21 versus >21 drinks per week for men and ≤14 versus >14 drinks per week for women; cut-off was defined according to recommendations on maximum alcohol consumption from The Danish National Board of Health). The Charlson Comorbidity Index score was computed based on the entire previous hospitalization history.[23] We used an adapted version of the index that utilizes International Classification of Diseases codes by identifying all hospital diagnoses for each patient in the Danish National Registry of Patients.[24] This registry contains data for all discharges from all nonpsychiatric hospitals in Denmark since 1977.[25]

Information on processes of in-hospital care during the acute phase, which have been linked with mortality and LOS,[18,26] included: early admission to a specialized stroke unit, early administration of antiplatelet or anticoagulant therapy, early examination with computed tomography or magnetic resonance imaging scan, and early assessment by a physiotherapist and occupational therapist, assessment of nutritional status and swallowing function, and early mobilization. We computed a variable containing the percentage of received processes of care for each patient as a measure for the quality of in-hospital stroke care. The study was approved by The Danish Data Protection Agency (J.no.2007-41-0563).

Statistical Analysis

First, we examined the association between individual complications and LOS by linear regression. A natural log (ln) transformation was used to correct for the right skew of LOS.

When reporting the findings of the analyses, we transformed the regression estimates back into the original units by exponentiating the estimates, and thereby obtained the ratios of the geometric means of LOS.

Follow-up started on the admission date and ended after 30 days (or 1 year), date of death or emigration, or end of the study period. Cox proportional hazard regression analyses were used to obtain MRRs and 95% CI 30 days or 1 year after stroke adjusted for all afore-mentioned patient characteristics. Age and Scandinavian Stroke Scale score were included as natural cubic splines. We used a random-effects model to correct for possible clustering by stroke unit in all analyses.

A total of 7032 patients (51.25%) had missing data on 1 or more of the patient characteristics. We therefore used multiple imputation to impute missing values of patient characteristics, assuming that data were missing at random.[27,28] We imputed 5 data sets using patient characteristics, stroke unit identifier, and the proportion of relevant processes of care received. In addition, we included the event indicator and the Nelson-Aalen estimator of the cumulative hazard to the survival time in the imputation model. Finally, we performed additional analyses to evaluate the robustness of our findings. First, we replicated the analyses of LOS stratified by discharge status (dead/alive) and second according to geographic area (Copenhagen, Aarhus). Third, we stratified analyses according to age, sex, and Scandinavian Stroke Scale score to assess whether these acted as effect modifiers on the association between medical complications and LOS or mortality. Fourth, a complete case analysis was performed including only patients with available information on all covariates. Finally, we compared the distribution of causes of death among patients with and without medical complications. For all estimates, 95% CI was calculated. STATA version 11.0 (StataCorp, LLP) was used to perform the analyses.

Results

A total of 25.2% of the patients (n=3453) experienced at least 1 medical complication during their hospitalization. The most frequent complications were UTI (15.4%), pneumonia (9.0%), and constipation (6.8%). Median LOS was 13 days (25th and 75th quartiles, 5 and 33). Descriptive data are presented in Supplemental Table II.

Table 1 presents relative LOS according to individual medical complications. All complications were associated with longer LOS, and these associations remained after adjusting for possible confounding factors. Adjusted relative LOS extension ranged from 1.80 (95% CI, 1.54–2.11) for pneumonia to 3.06 (95% CI, 2.67–3.52) for falls.

Overall 30-day mortality rate was 8.9%, and overall 1-year mortality rate was 21.0%. Among the patients who died within 30 days, 35.0% had experienced at least 1 in-hospital

Table 1. Medical Complications and Length of Stay

Medical Complication	N	%	Median LOS (25th and 75th Quartiles), n	Median LOS (25th and 75th Quartiles), Complications Present	Crude Ratio of LOS (95% CI)	Adjusted Ratio of LOS* (95% CI)
Pneumonia	1,235	9.0	11 (4, 28)	31 (14, 60)	2.41 (1.91–3.05)	1.80 (1.54–2.11)
Urinary tract infection	2,107	15.4	10 (4, 25)	36 (16, 64)	3.12 (2.25–4.32)	2.29 (1.88–2.80)
Pressure ulcer	163	1.2	13 (5, 32)	48 (26, 74)	3.34 (2.20–5.06)	1.98 (1.53–2.55)
Falls after stroke	288	2.1	12 (5, 31)	56 (31, 86)	4.33 (3.24–5.78)	3.06 (2.67–3.52)
Venous thromboembolism	86	0.6	13 (5, 32)	56 (25, 99)	3.73 (2.65–5.25)	2.40 (1.96–2.95)
Constipation	935	6.8	11 (5, 28)	45 (25, 73)	3.80 (2.82–5.11)	2.66 (2.23–3.16)
Any complication	3,453	25.2	9 (4, 21)	33 (15, 62)	3.29 (2.45–4.14)	2.48 (2.01–3.06)

LOS indicates length of stay; CI, confidence interval.

*All analyses are corrected for clustering of patients by stroke unit and age, sex, marital status, housing, profession, alcohol intake, smoking habits, atrial fibrillation, previous stroke, hypertension, Charlson comorbidity index, Scandinavian stroke scale score on admission, type of stroke, and relevant processes of care received.

complication; the corresponding proportion among patients dying within the first year was 41.6%.

Table 2 shows adjusted MRRs for the individual medical complications. Pneumonia (adjusted MRR, 1.59; 95% CI, 1.31–1.93) and VTE (adjusted MRR, 1.49; 95% CI, 0.75–2.96) were associated with higher 30-day mortality rate, although the association did not reach statistical significance in the case of VTE. UTI, falls, and constipation were all associated with significant lower 30-day mortality rate with adjusted MRRs ranging from 0.21 to 0.74, whereas no clear association with 30-day mortality rate was found for pressure ulcer.

The highest 1-year mortality rate was found among patients with pneumonia (adjusted MRR, 1.76; 95% CI, 1.45–2.14) and pressure ulcer (adjusted MRR, 1.47; 95% CI, 1.17–1.85).

In contrast, patients experiencing falls after stroke and constipation had a lower 1-year mortality compared with patients without complications. We found no substantial differences when stratifying analyses according to age, sex, and Scandinavian Stroke Scale score. Furthermore, overall analyses were confirmed by a complete case analysis (Supplemental Table III).

When comparing the distribution of causes of death among patients dying with and without in-hospital medical complications, we found increased risk of dying from infections among patients with medical complications both within 30 days (unadjusted relative risk [RR], 2.39; 95% CI, 1.88–3.02) and 1 year (unadjusted RR, 1.50; 95%CI, 1.31–1.74) compared with patients who died without having medical complications. Increased RR estimates (although not all statistically significant) of dying from infections were also found when focusing on patients with specific complications, except for patients who experienced falls after stroke (Supplemental Tables IV and V).

Discussion

Despite differences in study design, sample sizes, study settings, definition of medical complications, and length of follow-up, our finding of an overall association between medical complications and a higher risk of adverse outcome supports results from a number of previous studies.[4,5,13,29–31] Regarding LOS, previous studies have particularly focused on infections,[19,29,31–33] whereas data are limited on other types of medical complications. However, increased LOS found in our study for patients experiencing falls is in line with a study

Table 2. Medical Complications and 30-Day and 1-Year All-Cause Mortality

	30-D Mortality Rates			1-Y Mortality Rates		
Medical Complication	30-D Mortality, n/N (%)	Unadjusted MRR (95% CI)	Adjusted MRR* (95% CI)	1-Y Mortality, n/N (%)	Unadjusted MRR (95% CI)	Adjusted MRR* (95% CI)
Pneumonia	307/1,235 (24.9)	4.43 (3.57–5.50)	1.59 (1.31–1.93)	628/1,235 (50.9)	4.07 (3.43–4.80)	1.76 (1.45–2.14)
Urinary tract infection	153/2,107 (7.3)	0.88 (0.69–1.12)	0.45 (0.38–0.54)	669/2,107 (31.8)	1.91 (1.73–2.11)	0.94 (0.84–1.05)
Pressure ulcer	22/163 (13.5)	1.64 (1.03–2.62)	0.74 (0.42–1.30)	88/163 (54.0)	3.20 (2.62–3.90)	1.47 (1.17–1.85)
Falls after stroke	7/288 (2.4)	0.27 (0.13–0.56)	0.21 (0.10–0.47)	68/288 (23.6)	1.11 (0.99–1.25)	0.82 (0.68–0.99)
Venous thromboembolism	15/86 (17.4)	2.24 (1.30–3.84)	1.49 (0.75–2.96)	30/86 (34.9)	1.93 (1.14–3.29)	1.28 (0.71–2.29)
Constipation	45/935 (4.8)	0.54 (0.35–0.83)	0.38 (0.28–0.50)	260/935 (27.8)	1.41 (1.18–1.69)	0.87 (0.76–0.99)
Any complication	426/3,453 (12.3)	1.79 (1.40–2.29)	0.78 (0.65–0.95)	1,201/3,453 (34.8)	2.53 (2.18–2.95)	1.20 (1.04–1.39)

MRR indicates mortality rate ratio; CI, confidence interval.

*All analyses are corrected for clustering of patients by stroke unit and age, sex, marital status, housing, profession, alcohol intake, smoking habits, atrial fibrillation, previous stroke, hypertension, Charlson comorbidity index, Scandinavian stroke scale score on admission, type of stroke, and proportion of relevant processes of care received.

by Czernuszenko et al, who found that the probability of experiencing a first fall increases with LOS.[34] Furthermore, in accordance with a Chinese study, we found that patients with constipation stayed longer in the hospital than those without constipation.[35]

Interpretation of observational data regarding complications and LOS is in general a challenge, as pointed out in earlier studies,[30,4] as it is difficult with certainty to determine whether longer LOS is caused by medical complications or whether longer LOS caused the complications. This challenge is also present in our study and should be kept in mind when interpreting the findings. However, the fact that most of the medical complications seem to develop early after hospital admission supports the hypothesis that medical complications may increase LOS.[11,31]

A number of studies have examined the association between medical complications and mortality. Variation in lengths of follow-up and levels of confounding control (several studies have only reported unadjusted risk estimates) between the studies makes direct comparisons difficult.

Medical and neurological complications have in previous studies been linked with at least 50% of deaths in the early phase following stroke.[8,10,13,19–21] We found that pneumonia was particularly associated with increased risk of both short- and long-term mortality, which is in accordance with previous studies.[8,10,13,20,21] Thus, both Katzan at al[10] and Heuschmann et al[8] have reported that approximately 1 of 3 early deaths among stroke patients are related to pneumonia, and Vermeij et al[13] estimated that 1-year mortality in patients with poststroke pneumonia was doubled compared with those without.

Data on UTI are more sparse. Interestingly, we found lower adjusted MRRs after UTI than did some previous studies.[20,36] However, in line with our findings, a lower risk of in-hospital mortality among patients with UTI has also previously been reported.[29,31]

VTE was associated with higher mortality in our study, although it did not reach statistical significance. This result is partly in agreement with previous studies that have identified VTE as an important contributor to mortality in patients with stroke.[8,37]

Our findings of a lower 30-day mortality rate in stroke unit patients with falls and constipation may at first seem somewhat unexpected. However, the findings are partly in accordance with a systematic review that indicated that stroke unit care appeared to reduce the risk of death attributable to complications of immobility.[2] It is not entirely clear how some medical complications can be associated with lower mortality. However, patients with complications might receive closer monitoring during their stay, which could contribute to lower mortality compared with patients without the aforementioned medical complications. The lower proportion of patients with falls dying from infections found in our study may at least partly support this hypothesis.

Overall, our findings together with the existing literature strongly underline the need for effective preventive measures and careful treatment of medical complications, in particular pneumonia, among patients with stroke. Early mobilization and careful monitoring of clinical parameters seem to be key elements.[7,38]

The strengths of our study include the population-based design, availability of prospectively collected detailed data, and large number of patients included. The study focused on some common medical complications; however, it remains important to realize that patients with stroke may experience a long list of medical and neurological complications. Several of these complications not included in our study (eg, brain edema and epilepsy) are also known to be of major importance for clinical outcome. As always is the case in observational studies, confounding is a concern. However, several measures were taken to minimize the impact of possible confounding, including control for a wide range of well-established prognostic factors (eg, stroke severity), as well as correction for clustering at the individual stroke units. It is well known that misclassification can occur during data collection in routine clinical settings. Still, thorough efforts are made to ensure data validity in the DNIP.[17] Regular structured audits are conducted nationally, regionally, and locally, which include validation of the completeness of patient registration against hospital discharge registries. Furthermore, we have examined the validity of medical complications registered in the DNIP and found a high specificity (ie, 97.3% [95% CI, 96.7–97.8]) and reasonable overall positive predictive value (ie, 71.7% [95% CI, 67.4–75.8]).[39]

In conclusion, we found that patients hospitalized with medical complications had significantly longer LOS than did patients without complications. Furthermore, medical complications, in particular pneumonia, were associated with increased 30-day and 1-year mortality.

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Disclosures

None.

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