Effectiveness of Primary and Comprehensive Stroke Centers
PERFECT Stroke: A Nationwide Observational Study From Finland

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Background and Purpose—Previous studies show better outcomes for patients with stroke receiving care in stroke units, but many different stroke unit criteria have been published. In this study, we explored whether stroke centers fulfilling standardized Brain Attack Coalition criteria produce better patient outcomes than hospitals without stroke centers.

Methods—We did an observational register–linkage study of all patients with ischemic stroke treated in Finland between 1999 and 2006. After exclusion of recurrent strokes and nonanalyzable patients, we included 61 685 consecutive patients treated in 333 hospitals classified in national audits either as Comprehensive Stroke Centers, Primary Stroke Centers, or General Hospitals according to Brain Attack Coalition criteria. Primary outcome measures were case-fatality and being in institutional care 1 year after stroke.

Results—Care in stroke centers was associated with lower 1-year case-fatality and reduced institutional care compared with General Hospitals. The number-needed-to-treat to prevent 1 death or institutional care at 1 year was 29 for Comprehensive Stroke Centers and 40 for Primary Stroke Centers versus General Hospitals. Patients treated in stroke centers had lower mortality during the entire follow-up of up to 9 years and their median survival was increased by 1 year.

Conclusions—This study shows a clear association between the level of acute stroke care and patient outcome and supports use of published criteria for primary and comprehensive stroke centers. (Stroke, 2010;41:00-00.)

Key Words: acute stroke ■ organized stroke care ■ stroke units

All patients with stroke can benefit from treatment in a stroke unit and, according to US and European guidelines and the Helsingborg Declaration, should be treated in one.1–3 Many trials4 and observational studies5 have shown that patients treated in an organized stroke setting are more likely to be alive, independent, and living at home than those treated in any other setting, a benefit that lasts at least for a decade.6,7

The problem with the stroke unit trials was that they had no uniform criteria for a stroke unit; many were rehabilitation units instead of acute units.4 Implementing trial results into practice was therefore challenging. To overcome this problem and standardize practice, the Brain Attack Coalition published criteria for primary8 and comprehensive9 stroke centers. This has led to widespread standardization through stroke center certification in the United States. The chosen criteria, however, are the result of expert consensus and their effect on patient outcome has not been tested.

This study was conducted to determine whether care in stroke centers fulfilling published criteria will lead to improved patient outcome as compared with hospitals not fulfilling these criteria.

Methods

Design and Setting
Finland (population 5.2 million in 2002) has excellent registries that cover medical care of all inhabitants. We conducted a national registry-based observational follow-up study (PERFOrmance, Effectiveness, and Cost of Treatment episodes in Stroke [PERFECT Stroke]) linking several administrational registries. All patients with first-ever ischemic stroke treated in any Finnish hospitals or institutions between January 1, 1999, and December 31, 2006, were included. All patients were followed-up until December 31, 2007.

Study Population
The patients for this study were selected from the National Hospital Discharge Register. This government-based administrative registry includes all acute and long-term hospital and institutional care admittances in Finland. Ischemic stroke was selected with the International Classification of Diseases, 10th Revision diagnosis code 163 or the same code as the etiologic cause in stroke syndromes.
starting with the code G46. The validity of stroke diagnoses in the register has been previously established.10

Hospitalization rate for stroke in Finland was 96% in 1997.11 Patients with stroke treated outside of hospitals are not systematically registered and could not be included in this study. Patients with a history of previous stroke in the National Hospital Discharge Register (checked backward up to year 1986), those already in institutional care (defined as continuous institutional care for 90 days before stroke), those with whom follow-up was not possible (nonresidents and citizens of the archipelago of Åland, population 26,766), and children aged <18 years were excluded from the present study. Previous transient ischemic attack was not an exclusion criterion.

Ethical committee approval was not required by Finnish law because none of the patients was contacted or identifiable by the authors.

Register Linkage
Information was collected from the following sources: The Hospital Discharge Register, the Register of Prescribed Medicines, the Regi-
ister of Common Reimbursed Diseases, and the Causes of Death Register. These government-based nationwide administrative registers were linked on individual patient level with the Social Security identification number. This number uniquely identifies a person in all Finnish government registers. The linkage method allows for 100% day-to-day follow-up of all hospital and nursing home visits, case-fatality, and purchase of prescription medication.

Finnish Healthcare System
The public health system of Finland covers 100% of the population. Finnish public hospitals are owned and politically controlled by groups of municipalities and funded by tax payers. Management of stroke is variable, depending on political resource allocation decisions. Geographical variations in the level of resources and processes of stroke care make it possible to evaluate their effect on patient outcome. Choice of acute treating hospital is determined by the patient’s home address only. In case of acute stroke, the emergency medical service takes patients to the hospital determined by their home address. If patients are very far from their own hospital, they will first be brought to the nearest hospital and are transferred to their own hospital when their clinical status allows it. Patients with stroke are usually treated in neurological departments. In rural regions, hospitals are smaller and do not have neurological wards. Patients with stroke are therefore taken to larger hospitals, but with older patients, this is not always the case. Private hospitals do not treat patients with acute stroke but may be involved in rehabilitation.

Hospital Classification
Acute stroke care resources and practices were evaluated in 2003. The evaluation included on-site visits by a stroke neurologist (S.R.) of all the hospitals that treated annually >20 patients with stroke (n=56) and mailed questionnaires or conducted over-the-phone interviews with 94% response rate of the hospitals with less patients with stroke. A re-evaluation using mailed questionnaires or over-the-phone interviews was performed in 2006. According to data from these evaluations, all hospitals (n=333) were classified into 3 categories. Primary Stroke Centers (PSC, n=5 in 1999 to 2003, n=6 in 2004 to 2005, n=7 in 2006) and Comprehensive Stroke Centers (CSC, n=4 in 1999 to 2003, n=5 in 2004 to 2006) were classified according to Brain Attack Coalition criteria (Table 1).8,9 The visited hospitals included all the PSC and CSC hospitals. Hospitals that did not meet CSC or PSC criteria were classified as General Hospitals (GH). Due to the Finnish geography, many GHs were acute medical wards incorporated as part of health centers, and many had only a few stroke admissions each year.

Outcome Measures
The a priori set primary outcome measures were case-fatality and being in institutional care at 1 year, which together were also used by the Stroke Unit Trialists’ Collaboration.12 Both outcomes were adjusted for all available patient demographics (age, sex, previous comorbidities, previous use of prescription medication, year of stroke, and hospital days 1 year before stroke). Stroke severity at baseline is not included in Finnish registers and could not be adjusted for.

Case-fatality was evaluated by merging the Hospital Discharge Register with the Causes of Death Register, a method that has been previously validated for patients with stroke in Finland.11 Institutional care was determined from the Hospital Discharge Register, which, in addition to hospitals, includes all long-term care facilities and ongoing care. The secondary outcome measure was case-fatality by the end of follow-up adjusted for patient demographics. Dependency is not included in the national registers and could not be analyzed.

Statistical Analysis
To test for differences between hospital categories (CSC, PSC, GH) in baseline characteristics and given care, the Kruskal–Wallis and 1-way analysis of variance tests were used where appropriate.

To evaluate hospital categories’ effect on 1-year case-fatality and being in institutional care, a multivariate logistic regression model adjusting for demographics was used to calculate OR and 95% CIs. To evaluate absolute risk of death or institutional care at 1 year, a logistic regression with the preceding covariates was estimated. Parameter estimates were used to estimate the expected risk for each individual patient. For hospital categories, the adjusted rates were calculated as national average of the whole patient population multiplied by observed/expected ratio of patients treated in that hospital category.13 CIs were calculated as described by Ash and coworkers.14

Cox proportional hazards regression model was used to compare survival between classified hospitals adjusting for the same patient characteristics as in the logistic regression model. These Cox model estimates were used to plot the probability of survival for an average patient, and hazard ratios with 95% CIs were calculated. Censoring was done by death or end of follow-up.

Cox modeling was done on R 2.8.1 software package (The R Foundation for Statistical Computing, Vienna, Austria), and the other statistical analyses were done on SAS 9.1 (SAS Institute Inc, Cary, NC).

Results
Baseline Characteristics and Care
For 1999 to 2006, there were 93 514 ischemic stroke cases treated in Finnish hospitals of which 27 250 had an earlier stroke and 4570 had ≥1 other exclusion criteria (4254 in chronic institutional care before stroke, 258 patients from the archipelago of Åland, and 79 children) leaving a study population of 61 685 patients.

Thirty-two percent of the patients were treated in CSC, 17% in PSC, and 50% in GH classified hospitals (Table 2). Patients treated in GHs were older, more often females, and had more comorbidities than patients treated in stroke centers. The CSCs treated more patients each year than PSCs or GHs.

Median length of stay was 7 days in CSCs, 5 days in PSCs, and 8 days in GHs. Patients treated in stroke centers were more likely to receive thrombolytic therapy or undergo carotid endarterectomy (Table 3).

Patient Outcome
Unadjusted all-cause 1-year case-fatality after incident ischemic stroke was 16.6% in CSCs, 19.1% in PSCs, and 27.3% in GHs (Table 4). Portion of patients in institutional care at 1 year was 8.8%, 9.6%, and 13.2%, respectively. Stroke centers produced better results also after adjusting for confounders (age, sex, previous comorbidities, previous use of prescription medication, year of stroke, and hospital days 1 year before stroke).

The risk of death by 1 year adjusted for baseline characteristics was 20.8% (95% CI, 20.2% to 21.5%) for CSCs, 21.7% (20.9% to 22.5%) for PSCs, and 23.2% (22.8% to 23.6%) for GHs. The adjusted risks of institutional care at 1 year were 10.5% (10.0% to 10.9%) for CSCs, 10.6% (10.0% to 11.3%) for PSCs, and 11.6% (11.3% to 12.0%) for GHs. Number-needed-to-treat to allow 1 more patient to live at home 1 year after stroke was 29 for CSCs and 40 for PSCs when compared with GHs.

Stroke center care reduced mortality for the whole follow-up, up to 9 years. Median survival was increased by 1 year in CSC- compared with GH-treated patients (Figure).
Discussion

Stroke centers reduced the risk of death and institutional care. This was true also after adjustment for differences in baseline characteristics. Patients treated in a PSC were 11% less likely to die, 11% less likely to be in institutional care, and 16% more likely to live at home 1 year after their stroke than patients treated in GHs. CSCs further improved patient outcome. The criteria for stroke centers as suggested by the Brain Attack Coalition thus seem valid. Level of care is associated with patient outcome.

The many randomized controlled trials on stroke unit care were mostly single-center and ran decades ago, after which the treatment of stroke has profoundly changed. Our number-needed-to-treat values to prevent 1 death or institutional care, 29 to 40, were higher than reported in trials of stroke unit versus alternative service (number-needed-to-treat 21), which could be due to improvement of stroke care in all hospitals, including GHs. Modern care facilities or the acute care model has not been comprehensively studied in trials. Stroke units in clinical practice have been studied in 3 previous studies with similar methodology as ours. In the Swedish Riks-Stroke study, hospitals registered 70% to 75% of national patients (n = 11005) treated on either stroke units or general wards to show 3-month relative risk reductions for death (9%) and being in institutional care (6%) in favor of stroke units, but only for a subgroup of patients who had normal consciousness on arrival. Reduction in mortality was maintained for 2 years only with patients independent in activities of daily living before their stroke. A stroke unit was defined as “a service provided by a designated stroke ward or stroke team working exclusively in the care of stroke patients.” In the UK Sentinel Audit Study, hospitals reported on routine treatment of up to 40 consecutive stroke cases (n = 7352). After adjustment for patient characteristics, stroke units reduced 30-day case-fatality by 25%. Stroke unit was defined as “any unit or ward within the hospital/trust that is designated by local agreement as a stroke unit either for the...

Table 3. Characteristics of Care

<table>
<thead>
<tr>
<th></th>
<th>CSC (n=20 045)</th>
<th>PSC (n=10 749)</th>
<th>GH (n=30 891)</th>
<th>Total (n=61 685)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay in days at CSC/PSC/GH, median (IQR)</td>
<td>7 (4–11)</td>
<td>5 (2–8)</td>
<td>8 (4–18)</td>
<td>7 (4–14)*</td>
</tr>
<tr>
<td>Total length of stay, median (IQR)</td>
<td>11 (6–35)</td>
<td>10 (4–30)</td>
<td>13 (5–39)</td>
<td>12 (5–36)*</td>
</tr>
<tr>
<td>CEA performed, n (%)</td>
<td>712 (3.6)</td>
<td>251 (2.3)</td>
<td>472 (1.5)</td>
<td>1285 (2.4)*</td>
</tr>
<tr>
<td>Thrombolytic therapy, n (%)</td>
<td>437 (2.2)</td>
<td>79 (0.7)</td>
<td>34 (0.1)</td>
<td>550 (0.9)*</td>
</tr>
</tbody>
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Difference between hospital categories, *P<0.001. IQR indicates interquartile range; CEA, carotid endarterectomy.
acute care or rehabilitation of stroke or both. In the Italian Project on Stroke Services in Italy (PROSIT) study, consecutive patients treated in stroke units were compared with a sample of patients treated in other settings (n = 11,572) to show a 14% reduction in mortality by the end of follow-up (mean, 20 months). A stroke unit was defined as “a hospital ward with dedicated beds (at least 80% stroke admission) and with a dedicated stroke staff (at least 1 physician and 1 nurse) who work exclusively in the care of stroke patients.”

All of these studies used widely differing criteria for a stroke unit and did not cover all national patients with stroke. One study on patient outcome has tested the Brain Attack Coalition PSC criteria. This US multicenter study based on university hospital discharge registries (n = 16,853) showed an association with PSC criteria and increased rate of thrombolysis, but no association with in-hospital mortality was observed, possibly due to a short median follow-up of 5 days. Other studies have associated stroke center designation with better process indicators of stroke care and increased rate of thrombolysis, but no correlation with patient outcome and Brain Attack Coalition stroke center criteria has been demonstrated before our study.

The European Stroke Initiative has also suggested criteria for stroke centers, which are practically the same as the Brain Attack Coalition criteria. Validated criteria are warranted, because <15% of European patients with stroke are treated in stroke centers. Incorrect coding of stroke is a potential bias, but this rarely occurs in Finland. Population-based verification rate (CT, MRI, angiography, or autopsy) for stroke is high (>98%). Emigration in Finland is so rare in these age groups that probably 20 (<0.05%) of our patients may have moved abroad after their stroke and could potentially be lost to follow-up for institutional care. Losses to follow-up for case-fatality are practically 0% because deaths abroad are included in official statistics. Observational studies run a risk of hospital and patient selection. Registries with voluntary participation for hospitals are likely to overrepresent those with special interest in stroke care, but our study includes all hospitals and virtually all eligible patients in Finland. Selection bias seems unlikely. Patients treated in GHs were older and had more comorbidities than those treated in stroke centers. The difference could be due to geographic variation, that is, younger general population in the major cities with the universities and stroke centers. It is possible that elderly patients admitted to small rural hospitals may have been transferred less to stroke centers. In the analyses, baseline differences were adjusted for. One of the confounding factors we were unable to control for was the baseline stroke severity, which is not included in national registers. This source of potential bias would overestimate the treatment effect if only patients with the mildest stroke were referred to the stroke centers, but the practice probably is the opposite. Functional status of patients discharged home would be of interest, but this information is not included in Finnish registers.

Thrombolytic therapy was and still is mainly administered at the stroke centers and the treatment was uncommon over the study period (Table 3). Alteplase for stroke was licensed in 2003, and it took several years before the treatment was available in all parts of the country. Stroke centers were larger and treated more patients each year than general hospitals. The interaction between hospital size and resourcing is difficult to interpret, because the requirements of CSC and PSC are such that smaller hospitals are unlikely to meet them. The results of our study seem to support centralized acute care of stroke at

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<th>Table 4. Outcome of Finnish Patients With Ischemic Stroke</th>
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<td>Unadjusted outcome, no. (%)</td>
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<tr>
<td>Case-fatality by 1 year</td>
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<tr>
<td>Institutional care at 1 year</td>
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<td>Home at 1 year</td>
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<td>Outcome adjusted for patient demographics, OR (95% CI)</td>
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<td>Case-fatality by 1 year</td>
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<td>Institutional care at 1 year</td>
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<td>Home at 1 year</td>
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Figure. Survival probability based on acute treating hospital facilities adjusted with a Cox model for age, sex, comorbidities, previous medication and hospital use, and year of stroke. The hazard ratios were 0.87 (95% CI, 0.84 to 0.89) for CSC and 0.90 (0.87 to 0.93) for PSC when compared with GH.
stroke centers, where expertise translates to better patient outcomes, in line with recent German observations.\(^28\)

Use of routine administrative registries in research causes limitations on data detail, but full nationwide coverage of all hospital-treated patients with stroke and their indefinite follow-up is not economically feasible in any other study setting. Nationwide universal healthcare, linkable patient Social Security numbers, and high-quality comprehensive national registers in Finland make this study design possible.

**Summary**

This study, which includes all patients with first-ever ischemic stroke and all hospitals and institutions in Finland from 1999 to 2006, shows an association between the level of acute stroke care and patient outcome. Patients treated at stroke centers had better outcomes than those treated at GHs. The results support the use of Brain Attack Coalition criteria for PSCs and CSCs and validate the criteria in a healthcare system different from the one where they were originally developed. Large and well-equipped dedicated stroke centers produce better patient outcomes in acute stroke care than less well-organized care in GHs.

**Sources of Funding**

This study was supported by the Finnish Academy, Finnish Neurological Foundation, Finnish Innovation Fund STIRRA, Aarne Koskela Foundation, Orion-Farmos Research Foundation, Maire Taponen Foundation, Paavo Ahvenainen Foundation, Instrumentarium Science Foundation, Helsinki University Central Hospital EVO Funding, Marja Virmio Memorial Fund, Bayer Schering Pharma Research Foundation, Finnish Medical Foundation, and Yrjö Jahnsson Foundation.

**Disclosures**

None.

**References**


Effectiveness of Primary and Comprehensive Stroke Centers. PERFECT Stroke: A Nationwide Observational Study From Finland
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Stroke. published online April 15, 2010;
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

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/early/2010/04/15/STROKEAHA.109.577718.citation