Epidemiology of Aphasia Attributable to First Ischemic Stroke
Incidence, Severity, Fluency, Etiology, and Thrombolysis

Stefan T. Engelter, MD; Michal Gostynski, MD, MPH; Susanna Papa; Maya Frei; Claudia Born; Vladeta Ajdacic-Gross DrSc; Felix Gutzwiller, MD, DrPH; Phillipe A. Lyrer, MD

Background and Purpose—In a geographically defined population, we assessed incidence and determinants of aphasia attributable to first-ever ischemic stroke (FEIS).

Methods—A 1-year prospective, population-based study among the permanent residents of the canton Basle City, Switzerland, was performed using multiple overlapping sources of information.

Results—Among 188 015 inhabitants, 269 patients had FEIS, of whom 80 (30%; 95% CI, 24 to 36) had aphasia. The overall incidence rate of aphasia attributable to FEIS amounted to 43 per 100 000 inhabitants (95% CI, 33 to 52). Aphasic stroke patients were older than nonaphasic patients. The risk of aphasia attributable to FEIS increased by 4% (95% CI, 1% to 7%), and after controlling for atrial fibrillation, by 3% (95% CI, 1% to 7%) with each year of patients’ age. Gender had no effect on incidence, severity, or fluency of aphasia. Cardioembolism was more frequent in aphasic stroke patients than in nonaphasic ones (odds ratio [OR], 1.85; 95% CI, 1.07 to 3.20). Aphasic patients sought medical help earlier than nonaphasic stroke patients. Still, after controlling for stroke onset–assessment interval, aphasic stroke patients were more likely to receive thrombolysis than nonaphasics (OR, 3.5; 95% CI, 1.12 to 10.96).

Conclusion—Annually, 43 of 100 000 inhabitants had aphasia resulting from first ischemic stroke. Advancing age and cardioembolism were associated with an increased risk for aphasia. Severity and fluency of aphasia were not affected by demographic variables. (Stroke. 2006;37:1379-1384.)

Key Words: aphasia ■ epidemiology ■ stroke ■ thrombolysis

A phasia in stroke patients is associated with increased mortality,1 decreased rates of functional recovery,2,3 and reduced probability to return to work4 compared with nonaphasic stroke patients. High-intensity speech therapy has been shown recently to improve outcome5 but requires the availability of a sufficient number of qualified therapists. Thus, for planning stroke rehabilitation processes and resource allocation, epidemiological data about frequency and severity of aphasia in stroke patients are crucial. The frequency of aphasics among stroke patients ranged from 21% to 38%.6–10 However, these numbers are based on studies with different methodological approaches entailing specific limitations. Some used a retrospective design.11 Some were based on surveys,7 in-hospital stroke registries,9 stroke unit cohorts,1,12 or patients of neurological departments.10,13 Most of these studies assessed only patients admitted to a hospital,1,6,9,12,14 thus introducing a potential bias because the presence of aphasic symptoms may increase the probability of admission.7,15 Furthermore, aphasia studies meeting current standards for epidemiological studies16 are lacking to the best of our knowledge.

Some groups reported that demographic factors like age and gender influence the occurrence,10,17 severity,18 and fluency9,18,19 of aphasia, whereas other studies could not confirm these findings.6,20–22

Aphasia was predominantly attributed to cardioembolic stroke etiology,23 whereas other case series reported multiple underlying stroke mechanisms.24 Population-based studies about stroke etiology stratified to the presence or absence of aphasia are lacking. Furthermore, it had yet to be studied whether there is an association between aphasia as stroke symptom and treatment with thrombolysis. With these considerations in mind, we designed a 1-year prospective, population-based study to determine the incidence and the determinants of aphasia resulting from first-ever ischemic stroke (FEIS), including an adjustment to European standard population.25

Patients and Methods

Study Population and Data Acquisition

As a joint initiative of the Stroke Unit Basel, the Institute of Social and Preventive Medicine, Zurich, and the Swiss Aphasia Society, we...
designed a prospective bipartite study about the epidemiology of: FEIS\textsuperscript{26} and of aphasia attributable to FEIS. The canton Basle City, Switzerland, was considered an appropriate model for such a study because of its geographically well-defined catchment area and the advanced degree of organized stroke care available for all inhabitants. After ethical approval, we prospectively recorded all FEIS patients among the residents of the canton Basle City in between June 1, 2002, and May 31, 2003 (188 015 inhabitants, census 2002).

Multiple, overlapping sources of information were used, as suggested by Sudlow and Warlow\textsuperscript{16} (1). The stroke register of the local university hospital, which is the only hospital providing stroke unit care not only in Basle City but in the whole region, enabled us to ascertain all stroke patients on a daily basis (2). The register of the only neurorehabilitation unit of Basle City, which is located outside the university hospital, was used to identify all patients with in-hospital neurorehabilitation, regardless of the place of acute stroke treatment (3). The records of speech therapists within all hospitals in Basle City were used to identify all stroke patients with aphasia (4). All hospitals in Basle City received mailings every 3 months to provide data about their stroke patients treated (5). All physicians practicing in Basle City, taking care of nursing home residents, or filling in death certificates were contacted by mail every 3 months, to report on all stroke patients they have encountered. This approach was chosen to retrieve patients who were managed outside hospitals or who died because of stroke before hospitalization (6). The records of a stroke neurologist who made stroke ward rounds in a nearby hospital outside Basle City were checked on a weekly basis for possible study patients (7). For identification of pediatric strokes, only pediatric hospital was contacted. The distribution of data sources and the manner in which our study population was assembled are shown in the Figure.

Diagnosis and Assessment of Aphasia

In all stroke patients hospitalized in the university hospital, the diagnosis of aphasia was made by a stroke unit neurologist on admission. A bedside language examination\textsuperscript{27} was done. It includes the use of the standardized items for language testing of the National Institutes of Health Stroke Scale,\textsuperscript{28} which have a good inter-rater reliability ($\kappa$ value 0.68 to 0.71).\textsuperscript{28} Additionally, within the next 3 days, evaluation by a speech therapist started in all patients with abnormalities of speech, language, or swallowing, and the Basel–Minnesota Test for the differential diagnosis of aphasia\textsuperscript{29,30} was applied by the speech therapist to confirm or disapprove of the diagnosis of aphasia. In cases of disagreement between initial neurologist ratings and speech therapist assessments, consensus was reached by comparing the source data of both raters.

In patients hospitalized in primary care hospitals lacking stroke unit treatment, diagnosis of aphasia was made by a speech therapist. In patients not hospitalized, presence or absence of aphasia relied on the assessment of the treating primary care physician and a speech therapist, if such a therapy was implemented.

Patients with pre-existing aphasia caused by a nonstroke etiology were excluded, as were all patients who had aphasia resulting from ischemic stroke but in whom this event was a recurrent rather than the first ischemic stroke ($n=9$). Native languages other than German were no exclusion criterion.

Severity of aphasia was graded into 3 categories (ie, 1 mild, 2 moderate, and 3 severe) applying the aphasia subscale of the Scandinavian Stroke Scale.\textsuperscript{31} This scale was used in a previous community-based aphasia study\textsuperscript{6} and was shown to have a high inter-rater reliability ($\kappa$ value 0.86). Aphasia was dichotomized as fluent or nonfluent aphasia based on the initial bedside language assessment.\textsuperscript{27} In cases of $>1$ severity or fluency ratings, the earliest assessment was used for further analysis.

Verification of Diagnosis and Determination of Stroke Etiology

Diagnoses “FEIS” and “aphasia” were verified by a single, experienced stroke neurologist (S.T.E.), who reviewed all available source data of reported patients. Source data check was performed for all patients who were either treated in the university hospital or in the rehabilitation unit, or both, and in selected cases for those assessed or treated elsewhere. For nonhospitalized patients, diagnoses of FEIS and aphasia were solely based on the information provided by the physicians in charge. Stroke etiology was determined by the same stroke neurologist according to the Trial of Org 10172 in Acute Stroke Treatment TOAST.\textsuperscript{32} Data about the risk factor profile, clinical symptoms and syndromes, and the findings of etiological investigations were reviewed. The latter comprised extracranial and transcranial Doppler/duplex sonography ($n=189$), computed tomography scan ($n=228$), MRI with magnetic resonance angiogram ($n=128$), digital subtraction angiogram ($n=11$), 24-hour ECG
(n = 130), and echocardiography (n = 162). High-risk or medium-risk sources for cardiac embolism had to be present for cardioembolic stroke etiology. Patients with 2 possible stroke pathomechanisms (eg, high-grade carotid stenosis and atrial fibrillation) were classified as having undetermined stroke etiology, as were those with incomplete workup. Patients with missing data were excluded from this part of the study (ie, comparison between stroke etiology and presence versus absence of aphasia). These were 23 of 269 patients (8.6%) of the entire population or 11 of 80 (13.8%) of the aphasic subgroup, respectively.

Aphasic Versus Nonaphasic Stroke Patients

We compared aphasic with nonaphasic stroke patients in respect of stroke etiology, demographic characteristics, stroke risk factors according to criteria used by other epidemiological studies, type of stroke care provider (ie, stroke unit, other hospital, or primary care physician), and stroke onset–assessment interval. The latter was defined as the time delay between first stroke symptoms (or the time the patient was last seen without symptoms if exact onset was unknown) and the clinical assessment of stroke and aphasia. In addition, we compared the rates of thrombolysis between both groups based on the Basle thrombolysis databank, in which data of all thrombolyzed stroke patients have been prospectively ascertained since 1997.

Data Analysis

All ages were included in the analysis. Overall, gender- and age-specific incidence rates of aphasia attributable to FEIS were calculated per 100,000 population with 95% CI. In addition, a direct standardization to the European standard population was performed. Furthermore, we assessed the frequency of aphasia in FEIS patients across ages and gender. Bivariate analysis was performed with the test for dichotomous/polytomous variables. Analyses of continuous variables were done with the test. The associations between aphasia and age (unadjusted and adjusted for atrial fibrillation), aphasia and gender (adjusted for age), aphasia and smoking (adjusted for age), and aphasia and thrombolysis (controlling for stroke onset–assessment interval and age) were examined using logistic regres-

<table>
<thead>
<tr>
<th>TABLE 1. Clinical Characteristics, Stroke Etiology, and Treatment With Thrombolysis Among Aphasic Vs Nonaphasic Stroke Patients</th>
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<tbody>
<tr>
<td>Clinical Characteristics</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Demographic data</td>
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<tr>
<td>Age, mean (range)</td>
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<tr>
<td>Median, y</td>
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<tr>
<td>Female gender % (n)</td>
</tr>
<tr>
<td>Stroke onset–assessment interval</td>
</tr>
<tr>
<td>Type of stroke care provider, % (n)</td>
</tr>
<tr>
<td>Stroke unit</td>
</tr>
<tr>
<td>Other hospital</td>
</tr>
<tr>
<td>Primary care physician</td>
</tr>
<tr>
<td>Treatment with thrombolysis, % (n)</td>
</tr>
<tr>
<td>Stroke risk factors, % (No.)†‡</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Smoking (current)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>Stroke etiology, % (No.)†‡†‡</td>
</tr>
<tr>
<td>Cardioembolism</td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
</tr>
<tr>
<td>Small artery occlusion</td>
</tr>
<tr>
<td>Other determined etiologies$</td>
</tr>
<tr>
<td>Undetermined etiology*</td>
</tr>
</tbody>
</table>

†Stroke onset–assessment interval was defined as time interval between stroke onset (or time patient was last seen without symptoms) until clinical stroke assessment took place. In 5 patients (1.9%), data were missing. They were excluded from this part of the study.

‡In 23 (8.6%) patients, data about risk factor profile and etiological workup were missing. They were excluded from this part of the study.

†Stroke etiology according to TOAST. This category includes dissection, vasculitis, and other uncommon causes of stroke.

Adjusted for atrial fibrillation, age, or stroke onset–assessment interval.
sion analyses. To examine the relationship between severity or fluency of aphasia and age or gender, nonparametric tests (Kruskall–Wallis H test and Mann–Whitney U test) were performed. Values of P<0.05 (2-sided test) were considered statistically significant. Descriptive and inferential analyses were performed using the SPSS statistical package (SPSS for Windows; version 9).34 Data were presented as odds ratios (ORs) or percentages with 95% CIs unless otherwise stated.

Results

Study Population
Among 269 FEIS patients, 80 patients had aphasia, yielding an overall 30% (95% CI, 24% to 36%) prevalence of aphasia in FEIS. Clinical stroke assessment took place after a median of 20 hours (range 30 minutes to 6 weeks). The 25/50/75 percentiles of the stroke onset–assessment interval were 5/20/60 hours. Aphasic FEIS patients had a shorter median onset–assessment interval (13 hours) than their nonaphasic peers (22 hours). Atrial fibrillation was more common in aphasic (42%) than in nonaphasic (23%) FEIS patients, yielding an OR of 2.41 (95% CI, 1.33 to 4.35). Other stroke risk factors and the type of stroke care did not differ significantly between both groups (Table 1).

Incidence of Aphasia Attributable to FEIS
The overall crude incidence rate of aphasia attributable to FEIS amounted to 43 per 100 000 population (95% CI, 33 to 52; Table 2). The age-specific incidence rates of FEIS-related aphasia increased steeply with age from 5 per 100 000 population among the <65 years of age group to 441 for those ≥85 years of age. After adjustment for age to the European standard population, the overall incidence rate was 21 per 100 000 population (95% CI, 13 to 28). It was similar in females (22; 95% CI, 15 to 29) and males (20; 95% CI, 12 to 28).

Effect of Age and Gender
Aphasic FEIS patients were older than their nonaphasic peers (mean age 80 years versus 75 years; P=0.002). The risk of experiencing aphasia resulting from FEIS increased by 4% (95% CI, 1% to 7%) and after controlling for atrial fibrillation by 3% (95% CI, 1% to 7%) with each year of stroke patient age. Frequency of aphasia among FEIS patients increased from 15% (95% CI, 5% to 26%) in patients <65 years of age to 43% (95% CI, 30% to 56%) among those ≥85 years of age (P=0.002; Table 3). Female FEIS patients showed a nonsignificant trend toward a higher risk of aphasia compared with males (OR, 1.67 [95% CI, 0.97 to 2.34]). Adjusted for age, the OR was 1.40 (95% CI, 0.80 to 2.46).

Aphasia Severity and Fluency Stratified by Gender and Age
Aphasia was mild in 35 (44%), moderate in 24 (30%), and severe in 21 (26%) patients, respectively. Aphasia was fluent in 23 (29%) and nonfluent in 48 (60%) of the patients (in 9,

TABLE 2. Incidence Rate of Aphasia Attributable to First Ischemic Stroke in Basel, Switzerland

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>IR</td>
<td>n/N</td>
</tr>
<tr>
<td>&lt;64</td>
<td>3/74 444</td>
<td>4</td>
<td>4/74 698</td>
</tr>
<tr>
<td>65–74</td>
<td>7/7958</td>
<td>88</td>
<td>8/10 782</td>
</tr>
<tr>
<td>75–84</td>
<td>8/5059</td>
<td>158</td>
<td>24/9173</td>
</tr>
<tr>
<td>85+</td>
<td>9/1509</td>
<td>596</td>
<td>17/4392</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>27/88 970</td>
<td>30 (19–42)</td>
<td>53/99 045</td>
</tr>
</tbody>
</table>

SR (95% CI) ... 20 (12–28) ... 22 (15–29) ... 21 (13–28)

n indicates No. of patients with aphasia attributable to first-ischemic stroke; N, No. of population at risk; IR, incidence rate (per 100 000 population per year); SR, standardized incidence rate adjusted to the European standard population.25

TABLE 3. Gender and Age Effects on the Frequency of Aphasia Attributable to First Ischemic Stroke

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aphasics†/FEIS‡ %</td>
<td>Aphasics†/FEIS‡ %</td>
<td>Aphasics†/FEIS‡ % (95% CI)</td>
</tr>
<tr>
<td>&lt;65</td>
<td>3/27 11</td>
<td>4/19 21</td>
<td>7/46 15 (5–26)</td>
</tr>
<tr>
<td>65–74</td>
<td>7/33 21</td>
<td>8/29 28</td>
<td>15/62 24 (14–36)</td>
</tr>
<tr>
<td>75–84</td>
<td>8/36 22</td>
<td>24/64 38</td>
<td>32/100 32 (23–42)</td>
</tr>
<tr>
<td>85+</td>
<td>9/18 50</td>
<td>17/43 40</td>
<td>26/61 43 (30–56)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>27/114 24 (16–33)</td>
<td>53/155 35 (27–42)</td>
<td>80/269 30 (24–36)</td>
</tr>
</tbody>
</table>

‡No. of patients with FEIS; †No. of FEIS patients presenting with aphasia.
Stroke Etiology
Cardioembolism was more frequent in aphasic than in nonaphasic FEIS patients (OR, 1.85; 95% CI, 1.07 to 3.20; \( P = 0.03 \)). In aphasic FEIS patients, cardioembolism was the underlying stroke etiology in about one half of the patients (48%), and it represents the main determined stroke etiology for this cohort. In turn, small vessel occlusion accounted for 22% of the strokes among nonaphasic FEIS patients but was not present in the aphasic FEIS cohort (\( P \lt 0.001 \); Table 1).

Discussion
This prospective, population-based study about the epidemiology of aphasia attributable to FEIS showed the main findings: 33 to 52 of 100 000 inhabitants are affected per year, and advancing age and cardioembolism are associated with an increased risk for aphasia.

The risk of aphasia increased by 1% to 7% per each year of age of stroke patients. Every seventh FEIS patient \(< 65 \) years of age had aphasia, whereas the proportion nearly tripled for subjects \( \geq 85 \) years of age. So far, an age-dependent increase in the occurrence of aphasia has been noticed only in one among several aphasia studies without such an association.6,9,17 However, our finding is corroborated by data from multicenter, hospital-based stroke registries in which aphasia was significantly more frequent among older than among younger stroke patients.35,36

Female gender was not an independent risk factor for aphasia resulting from FEIS. This finding is in line to the majority of aphasia studies3,13,20,37 but is in contrast to 2 stroke databank studies.17,38

Neither gender nor age had an influence on severity or fluency of aphasia, which is in line with the majority of aphasia studies.6,20–22 Some studies had suggested that nonfluent aphasia is more common in men9 and that severity18,19 and fluency of aphasia11,13 increase with advancing age.

Cardioembolism was present in nearly one half of the aphasic FEIS patients and represents the most important etiology in the aphasic cohort. The impact of atrial fibrillation as major contributor to cardioembolic stroke increases steadily with age.39 The age gradient was also noticed for the likelihood of aphasia as stroke symptom in the current study and may suggest a causal relationship. Thus, cardioembolism may disproportionately frequently cause aphasia. For Wernicke’s aphasia, such a relationship was indeed shown.23 Our results indicate that this association may be extended to ischemic aphasia per se.

Aphasic stroke patients sought medical help earlier than nonaphasic patients, possibly because stroke diagnosis was easier or loss of speech caused more fear than other symptoms in the patients. After controlling for the (shorter) stroke onset–assessment interval, still, the presence of aphasia was associated with a higher likelihood of thrombolysis. However, the small sample size and the wide 95% CI urge toward a cautious interpretation of this observation, which might have occurred by chance. It has been reported recently that patients with right-hemisphere strokes were less likely to receive intravenous thrombolysis than those with left-hemisphere strokes.40 Thus, both observations might support the hypothesis that left-hemispheric symptoms increase the odds for thrombolysis.

As strengths, the present study made incidence estimates based on hospitalized as well as nonhospitalized aphasia patients from a well-defined catchment area. Furthermore, multiple overlapping sources of information were used to ascertain preferably all FEIS regardless of where acute stroke care took place. Such an approach is recommended for epidemiological stroke studies but is novel in aphasia studies to the best of our knowledge.

A weakness of this approach is that the extent of language assessment and the level of expertise of the raters differed across the study population. Thus, the probability of false-positive or false-negative aphasia diagnoses is likely to vary across the data sources. The highest rates of misdiagnosis are expected among nonhospitalized patients for whom aphasia diagnosis is solely based on the assessment of primary care physicians. This subgroup contributes to 4% of FEIS and to 9% of the aphasic FEIS patients, respectively, whereas \( > 90\% \) of the FEIS patients were evaluated by either an experienced neurologist with training and expertise in stroke and aphasia, by a speech therapist, or both. Exclusion of all patients exclusively assessed by primary care physicians would amount to an incidence rate of 39 (95% CI, 30 to 48), which is not substantially different from that of the entire population (43; 95% CI, 33 to 52). Thus, significant alterations of our results resulting from misclassification are unlikely. As another limitation, information about risk factor profile was obtained retrospectively, and etiological investigations were not done thoroughly in all patients. Therefore, the association between presence of aphasia and cardioembolism as underlying stroke etiology requires confirmation. As a caveat, we excluded patients with new aphasia resulting from recurrent stroke and those with aphasia caused by mechanisms other than ischemic stroke. Thus, our data must not be interpreted as an overall estimate of the incidence of aphasia per se.

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References


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