Stroke in the Very Old
Clinical Presentation and Determinants of 3-Month Functional Outcome:
A European Perspective

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Background and Purpose—The oldest old represent the fastest-growing segment of the elderly population in developed countries. Knowledge of age-specific aspects of stroke is essential to establish diagnostic and therapeutic pathways and to set up prevention and rehabilitation programs. We sought to evaluate stroke features and functional outcome in patients aged ≥80 years compared with the younger age groups.

Methods—In a European Union Concerted Action involving 7 countries, 4499 patients hospitalized for first-in-a-lifetime stroke were evaluated for demographics, risk factors, clinical presentation, resource use, and 3-month disability (Barthel Index) and handicap (Rankin Scale).

Results—Overall, 3141 patients (69.8%) were aged <80 years, and 1358 (30.2%) were aged ≥80 years. At baseline, female sex, prestroke institutionalization, and a worse prestroke Rankin score were significantly more frequent in the older patients, as were coma, paralysis, swallowing problems, and urinary incontinence in the acute phase (all P values <0.001). Brain imaging and other diagnostic tools were significantly less used in the older patients. Paralysis, swallowing problems, and incontinence during hospitalization independently predicted 3-month disability or handicap in both groups. For the older patients, prestroke institutionalization proved a further strong and independent determinant of 3-month disability (odds ratio, 2.33; 95% CI, 1.22 to 4.45) and handicap (odds ratio, 7.04; 95% CI, 1.62 to 30.69).

Conclusions—In the very old, both medical and sociodemographic factors may significantly influence stroke outcome, showing peculiar characteristics. Knowledge of these determinants may reduce the burden on health systems, improving quality of care.

Key Words: disability evaluation ▪ elderly ▪ stroke outcome

Cost-effective approaches to the assessment and management of patients with stroke require accurate data on specific mechanisms and outcomes of the disease in different age groups. This information appears essential to establish appropriate in-hospital diagnostic and therapeutic pathways and to set up prevention and rehabilitation programs able to reduce the burden of the disease. Age independently influences stroke outcome,1 and well-organized management of elderly stroke patients has been associated with improvement in both clinical outcome and resource use.2

Given the strong relationship of stroke with advanced age,3–5 the burden of stroke-related disability is expected to increase together with life expectancy.6 The decline in stroke mortality achieved in the past few decades, only in part explained by improved control of risk factors and more effective therapeutic interventions, may result in a longer period of disability before death,7,8 with huge costs for individuals and society overall.9,10

Since the oldest old represent the fastest-growing segment of the elderly population in developed countries11 and, in proportion, the major consumers of healthcare resources, the availability of accurate data on specific characteristics of stroke in this age group is of relevance for planning healthcare systems and for allocation of resources. The objective of the present study is to examine differences in demographics, risk factors, clinical presentation, resource use, and 3-month outcome in stroke patients aged ≥80 years compared with the younger age group in a large sample of patients hospitalized for acute stroke in several European countries.

Subjects and Methods
A European Union BIOMED Concerted Action was initiated to establish the relationships between resource use, costs, and outcome

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of packages of care for stroke in Europe. The specific objectives have been outlined previously.12,13 The study involved 12 centers (22 hospitals) in 7 European countries: England, France, Germany, Hungary, Italy, Portugal, and Spain. The hospitals were chosen because they contained staff interested in stroke research and with the ability of providing the resources necessary for the data collection. All the hospitals provide general acute care to the local population; most are community hospitals, serving up to 150 000 inhabitants, and overall they cover urban, suburban, and rural areas. Some centers, located in the United Kingdom, Germany, and Hungary, are teaching hospitals. One UK center has a stroke rehabilitation ward, and the centers in France, Germany, Hungary, and Italy have acute stroke-monitoring facilities. Patient-based data collection began in the majority of the centers in September 1993 and related to all first-ever stroke admissions for the subsequent year. Informed consent was given according to institutional guidelines. Stroke was defined according to the World Health Organization.14

Pathological subtypes of stroke were defined as cerebral infarct (TACI), partial anterior circulation infarct (PACI), or previous smoking, and alcohol consumption were significant differences.

Statistical Analysis
Analysis of differences in the frequency of categorical variables was performed with the χ² test. Student’s t test for independent samples was used for the continuous variables. To assess disability and handicap, we used the Barthel Index and the Rankin Scale, which consist of categories forming an ordinal scale in which the intervals among points are not necessarily equal. We therefore decided not to analyze them as continuous variables. The other options were to use nonparametric tests or to categorize patients into 2 groups, dichotomizing the scales, and expressing results as odds ratios (OR) estimated by logistic regression analysis. This procedure has been considered the most appropriate in a previous report evaluating the validity of statistical methods used to analyze stroke outcome. Consequently, the Barthel Index and the Rankin Scale were evaluated, at univariate analysis, by the Mann-Whitney nonparametric test, while logistic regression analysis, with the forward stepwise method for selection of variables, was used to identify, among baseline and clinical variables, the best independent predictors of 3-month disability and 3-month handicap. We controlled for age and sex in the first model and for age, sex, and prestroke level of handicap in the second model. By dichotomizing both scales, we were able to better estimate the net effect of the predictive variables on the transition from total, or nearly total, independence to limitation in daily functioning. The selected categories were 0 to 14, 15 to 20 for the Barthel Index and 0 to 1, 2 to 5 for the Rankin Scale. All statistical levels quoted (P values) are 2-tailed. The 95% CIs were calculated to describe the precision of the estimates. Data were analyzed with SPSS (release 6.1.3) statistical software.25

Results
During the 12-month study period, 4534 consecutive patients with first-in-a-lifetime stroke were registered in the participating hospitals, and 4499 (50.2% females; mean age, 71.8±12.6 years; range, 13.7 to 102.1 years) completed the data set. Overall, 3141 patients (69.8%; 42.9% females) were aged <80 years (mean age, 66.2±10.6 years; range, 13.7 to 79.9), and 1358 (30.2%; 66.9% females) were aged ≥80 years (mean age, 85.0±3.7 years; range, 80.0 to 102.1). Compared with the younger age group, the older patients were more often female and more often lived in an institution before stroke. They showed higher level of handicap, as defined by prestroke Rankin Scale, and a higher frequency of atrial fibrillation, history of transient ischemic attack, and antplatelet therapy. History of hypertension, diabetes, current or previous smoking, and alcohol consumption were significantly more frequent in the younger age group (Table 1).

Table 2 reports the clinical state at time of maximum impairment and in-hospital use of diagnostic facilities and surgical procedures. Clinical conditions were more severely compromised in the older patients, who, at the neurological evaluation, were more often confused or in a coma. These patients presented with paralysis, language deficits, swallowing problems, and urinary incontinence more frequently than the younger patients. The use of investigation was far less frequent among the older patients for all the resources considered: brain imaging, Doppler examination, echocardiogram, and angiography. Surgical interventions were also performed more frequently in the younger patients, with a significant difference for neurosurgery and carotid surgery.
Table 3 shows that a definition of pathological subtype was obtained significantly more often in the younger patients. This was mostly explained by the lower proportion of brain imaging performed in the older patients (66.9% versus 87.7%; \( P < 0.001 \)), with a subsequent higher number of pathologically unclassified stroke in this age group (41.3% versus 20.8%; \( P < 0.001 \)). A definition of clinical subtype following the Oxfordshire Community Stroke Project classification was achieved in 2472 (90.2%) of the 2740 events \( (n = 1358) \), with a subsequent higher number of POCI was significantly more frequent in the older subjects, while TACI and PACI were significantly more common in the younger age group. The frequency of LACI was similar in the 2 groups.

Table 4 reports the results of the age- and sex-adjusted logistic regression analysis for predictors of 3-month disabil-
ity (Barthel Index <15) in the overall study sample and in the 2 age groups evaluated separately. When all the study patients were considered, significant predictors of 3-month disability were paralysis, swallowing problems, and urinary incontinence among the variables related to the clinical status in the acute phase. History of hypertension showed a protective effect. When the 2 age groups were examined separately, atrial fibrillation and diabetes were positive predictors of 3-month handicap among the younger patients, while for the older ones prestroke institutionalization was the most significant baseline predictor of disability (OR, 2.33; 95% CI, 1.22 to 4.45). Paralysis, swallowing problems, and urinary incontinence in the acute phase were significantly related to disability in both groups. History of hypertension in the younger group showed a protective effect.

Similar results were obtained when handicap was evaluated as measured by the Rankin Scale. Table 5 reports the results of logistic regression analysis of predictors of 3-month handicap. When the entire sample was considered, prestroke institutionalization, history of myocardial infarction and diabetes were significant predictors of 3-month handicap among the elderly patients. In the younger group, prestroke institutionalization was again confirmed as the best baseline predictor of handicap (OR, 7.04; 95% CI, 1.62 to 30.69). Paralysis and urinary incontinence in the acute phase were significant predictors of handicap in both age groups. Only in the younger patients were aphasia and swallowing problems in the acute phase positively associated with handicap, and a previous diagnosis of hypertension confirmed a protective effect.

**Discussion**

The main purpose of this study was to evaluate prestroke risk factors, clinical presentation, use of diagnostic tools and rehabilitation, and determinants of outcome in very old subjects (>80 years), using as source of data a large sample of elderly stroke patients hospitalized in a European context. In the comparison with younger (<80 years) patients, there were significant differences in baseline living conditions, risk factor profile, and stroke severity at onset and during hospitalization. No major differences were found in the use of in-hospital rehabilitation services, but diagnostic tools were

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Sample</th>
<th>&lt;80 y</th>
<th>≥80 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prestroke institutionalization</td>
<td>NS</td>
<td>NS</td>
<td>2.33 (1.22–4.45)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.69 (0.54–0.87)</td>
<td>0.69 (0.52–0.91)</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>NS</td>
<td>1.46 (1.01–2.13)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>NS</td>
<td>1.48 (1.08–2.04)</td>
<td>NS</td>
</tr>
<tr>
<td>Paralysis</td>
<td>2.87 (2.25–3.68)</td>
<td>2.47 (1.85–3.31)</td>
<td>3.71 (2.37–5.81)</td>
</tr>
<tr>
<td>Swallowing problems</td>
<td>2.37 (1.72–3.26)</td>
<td>2.40 (1.64–3.51)</td>
<td>1.91 (1.09–3.34)</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>4.16 (3.21–5.39)</td>
<td>4.55 (3.35–6.20)</td>
<td>3.94 (2.48–6.24)</td>
</tr>
</tbody>
</table>

NS indicates nonselected in the final model.
used rather sparingly in the older patients. In terms of outcome, advanced age was associated with a higher 28-day case-fatality rate, higher in-hospital and 3-month mortality, and a longer in-hospital stay. Older patients were more likely to be discharged to an institution than home and were more disabled and more severely handicapped as assessed at 3 months after stroke. In both age groups, disability or handicap was mainly predicted by selective clinical features of the acute phase, such as paralysis, swallowing problems, and urinary incontinence, which are well known as ominous predictors of functional outcome. For the older patients, prestroke institutionalization proved a further strong independent determinant of poststroke disability and handicap.

Our results come from a multicenter collaborative study examining patients admitted for stroke in several hospitals throughout many European countries, and this might have reduced the homogeneity of our data set. Published data from this Concerted Action showed that differences exist among the participating centers, according to demographic characteristics, length of in-hospital stay, packages of care, and destination at discharge. For instance, mean age ranged from 65.0 ± 12.5 years in Hungary to 75.2 ± 11.2 years in the United Kingdom. The percentage of females varied between 45.1% in France and 53.5% in the United Kingdom. The proportion of patients receiving brain imaging was 64.2% in Hungary and 96.7% in France. Patients discharged home were 49.4% of the total sample in the United Kingdom and 80.8% in Portugal.

However, when we analyzed the single variables separately for each country, the major findings of the present study, for the 2 age groups, were essentially confirmed. Female sex was significantly overrepresented in each country in the older age group. In all the states, older patients showed higher rates of prestroke institutionalization (difference with younger patients was significant in the United Kingdom, France, Germany, and Italy) and higher level of handicap before stroke (difference significant in all countries except Hungary). Paralysis, swallowing problems, and urinary incontinence in the acute phase were more frequent in the older patients in all countries. Differences were always significant apart from paralysis in France and Hungary and swallowing problems in Hungary. Brain imaging was significantly less frequently performed in older patients in all the states. Older patients were less often discharged home in every country except Spain, where figures in the 2 age groups were similar, while difference with younger patients was significant in the United Kingdom, France, Germany, and Italy. The addition of country to the multivariate models analyzing the predictors of functional outcome did not alter the findings for the entire sample and for both the age groups considered.

The participating hospitals contained physicians and researchers with an interest in stroke and might be considered not necessarily representative of their country. However, since 22 units in 12 centers in 7 European states were included, with urban and rural population coverage and predictable variations of services between hospitals, we believe that overall our study may reflect the types of stroke care practiced in western and central Europe. To increase the homogeneity of data collection, a manual was provided to each research unit, and frequent meetings were organized to discuss and standardize data collection, both in the preparation phase and throughout the study progression. In the meantime, this type of data set has the advantages of including a wide range of premorbid, clinical, and service use variables and of providing adequate numbers of patients in the age groups considered, allowing statistically meaningful results. The problem of a reduced sample size is common in studies focusing on stroke in patients of advanced age. Previous surveys evaluating the influence of age on stroke outcome were based on study samples encompassing between 300 and 500 patients,1,25,26 and most included <200 patients.

Our rate of patients lost to follow-up (21.4%) is similar to those previously reported in studies on stroke outcome.25,30 The chance of being lost to follow-up was higher among younger than older patients (mean age, 72.6 ± 12.1 years in followed versus 69.2 ± 13.8 in lost patients; P<0.001) and in those without major neurological deficits after stroke such as coma or paralysis. This may have affected the precision of our estimates, but probably not enough to determine a distortion in the trends of differences observed between the 2 age groups.

The distribution of baseline variables confirms epidemiological data on the relative frequency of stroke-related risk

### TABLE 5. Predictors of 3-Month Handicap, Defined as Rankin Score Between 2 and 5: Logistic Regression Analysis With Stepwise Selection of Variables Adjusted for Age, Sex, and Prestroke Level of Handicap

<table>
<thead>
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<th>≥80 y</th>
</tr>
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<tbody>
<tr>
<td>Prestroke institutionalization</td>
<td>2.16 (1.03-4.57)</td>
<td>NS</td>
<td>7.04 (1.62-30.69)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.67 (0.54-0.83)</td>
<td>0.62 (0.49-0.79)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.40 (1.08-1.83)</td>
<td>1.37 (1.03-1.83)</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.46 (1.01-2.11)</td>
<td>1.82 (1.19-2.79)</td>
<td>NS</td>
</tr>
<tr>
<td>Paralysis</td>
<td>2.28 (1.75-2.98)</td>
<td>2.05 (1.53-2.75)</td>
<td>4.33 (2.15-8.72)</td>
</tr>
<tr>
<td>Aphasia</td>
<td>1.51 (1.16-1.96)</td>
<td>1.60 (1.19-2.16)</td>
<td>NS</td>
</tr>
<tr>
<td>Swallowing problems</td>
<td>1.82 (1.25-2.67)</td>
<td>1.65 (1.07-2.54)</td>
<td>NS</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>2.55 (1.85-3.53)</td>
<td>2.90 (2.01-4.21)</td>
<td>2.32 (1.22-4.41)</td>
</tr>
</tbody>
</table>

NS indicates nonselected in the final model.
Factors and comorbid conditions selectively detectable at advanced age. Atrial fibrillation is well established to be an age-related pathological condition, and therefore the fact that it was significantly more frequent among our older stroke patients is not surprising, while major vascular risk factors, such as hypertension, smoking, and diabetes, were more common in the younger patients.

Age, and not stroke severity, seemed to be a major discriminating factor for the use of diagnostic resources. Despite more severely compromised clinical conditions, in the older patients brain imaging, Doppler examination, echocardiogram, and angiography were performed significantly less often. The limited investigation, and hence intervention, received by older patients might contribute to their worse prognosis. Whether different investigations and associated interventions influence outcome in older stroke patients will be the subject of future analyses. The high rate of unclassifiable strokes, a consequence of the reduced use of brain imaging in the elderly patients, was a major limitation for drawing inferences from the relative frequency of stroke subtypes. When the analysis was limited to patients with clearly defined ischemic stroke, TACI and PACI, known as the clinical syndromes with a more severe prognosis, were significantly more frequent in the elderly patients. The effect of age on acute and short-term mortality is consistent with previous reports.

Disability indicates any restriction or lack resulting from an impairment of ability to perform an activity in the manner or within the range considered normal for a human being, while handicap is related to the disadvantage resulting from an impairment or a disability that limits or prevents the fulfillment of a role that is normal (depending on age, sex, and social and cultural factors) for a given individual. To assess disability and handicap, we used the Barthel Index and the Rankin Scale, which are reliable and widely used tools to evaluate outcome in stroke patients. The predictive effect of motor symptoms and urinary incontinence on disability and handicap was evident in both the age groups and consistent with previously reported data on clinical features of the acute phase predicting disability in stroke survivors. Prestroke institutionalization proved a determinant of 3 months’ disability and handicap only in the older patients. Its effect was independent of prestroke level of handicap and of variables expressing the severity of the stroke event. Since rehabilitation referral and treatment were not significantly different between younger and older patients, other factors, such as comorbidity, are likely to explain the effect of previous institutionalization on the 3-month outcome.

Both medical and social factors are recognized as increasing the risk of being institutionalized. In particular, it has been shown that frailty, defined as a vulnerable state resulting from the balance and interplay of medical and social factors, is strongly associated with institutionalization. Comorbidity, cognitive impairment, marital status, absence of caregivers, and lack of motivation are all potential contributors to frailty in the elderly. These factors are also well known for reducing effectiveness of rehabilitation and for negatively influencing the recovery after stroke. Since some degree of functional dependence may be induced by institutional care per se, we are cautious in generalizing these results. However, our findings point out the need to pay particular attention to the limited recovery from stroke in institutionalized patients. An extension of the present study is currently evaluating the levels of support available from family members in the different countries and the impact this may have on outcome, demands of, and expectations from healthcare services.

In conclusion, our data relate to >4000 hospital admissions for stroke across 22 hospitals in 7 European countries, with complete follow-up information available for approximately 79% of the study sample. We cannot completely exclude that the probability of being missed at follow-up might depend on the actual outcome, and this may limit the precision of our estimates. Our findings suggest a complex interplay of sociodemographic factors, preexisting frailty, and stroke severity in determining the outcome in elderly patients. While other interventions may require a long-term perspective, the achievement of a diagnostic accuracy similar to that reached in younger patients and aimed at a better definition of pathogenic features, together with particular attention to the acute-phase predictors of functional outcome, seem affordable objectives, with possible positive consequences on general management and prognosis. When the impact of stroke in terms of disability and resource use in an aging population is considered, accurate information on stroke patterns in the very old may improve the overall quality and cost-effectiveness of stroke care in Europe.

Appendix

Study Participants

O. Tofani, A. Rosselli, F. Cordopatri, G. Giuntoli, M. Magherini, P. Pennati, S. Tatini, F. Trucco, E. Pieragnoli, F. Manetti, C. Mugnaini, L. Bagnoli, O. Marrazza, G.P. Meneguzzo, I. Meucci, G. Landini, A. Ghetti, Ospedale S.M. Annunziata, Health Area 10, Florence, Italy; C. Cappelletti, M.C. Baraffi, S. Spolveri, M. Ricca, P. Adriani, C. Bianco, Nuovo Ospedale S. Giovanni di Dio, Health Area 10, Florence, Italy; R. Beech, Department of Public Health Sciences, The Guy’s, Kings College, and St Thomas’ Hospital Medical and Dental School, Guy’s Campus, London, England; A.G. Rudd, Department of Care of the Elderly, St Thomas’ Hospital, London, England; D.H. Barer, Y. Ellul, Department of Medicine for the Elderly, Newcastle General Hospital (England); M. Ayana, P. Gompertz, R. Harwood, P. Pound, Department of Primary Care and Population Sciences, Royal Free Hospital School of Medicine, London, England; H. Rogers, Center for Health Service Research, University of Newcastle (England); M. Giroud, M. Menassa, M. Lemesle, Service de Neurologie, Centre Hospitalier Regional et Universitaire de Dijon (France); K. Kunze, Neurologischen Universitaetsklinik, Hamburg-Eppendorf, Germany; J. Berger, Institute of Mathematics and Computer Science in Medicine, University Hospital Eppendorf (Germany); B. Haussler, W. Mall, H. Nolting, Institut fur Gesundheits und Sozialforschung GmbH (IGES), Berlin, Germany; Z. Nagy, C. Ovary, Z. Vokog, National Stroke Center, Budapest, Hungary; M. Carrageta, J. Namora, I. Remidios, A. Santos, J. Coisinha, Hospital Garcia de Orta, Almada, Portugal; J. Dias, Divisao de Epidemiologia, Direccao Geral de Saude, Lisboa, Portugal; A. Arias, P. Casquero, S. Montserrat, M. Torrent, Division Proincional INSALUD, Gabinete de Estudios, Palma de Mallorca, Spain.

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