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Risk factors and outcome of subtypes of ischemic stroke. Data from a multicenter multinational hospital-based registry. The European Community Stroke Project

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Abstract

Background: Information on determinants and prognosis of ischemic stroke subtypes is scarce. We aimed at evaluating risk factors, pathogenesis, treatment and outcome of different ischemic stroke subtypes.
Methods: In a European Concerted Action involving seven countries, ischemic stroke subtypes defined according to the Oxfordshire Community Stroke Project (OCSP) were evaluated for demographics, baseline risk factors, resource use, 3-month survival, disability (Barthel Index) and handicap (Rankin Scale).
Results: During the 12-month study period, cerebral infarction was diagnosed in 2740 patients with first-in-a-lifetime stroke (mean age 70.5 ± 12.4 years, 53.4% males). OCSP classification was achieved in 2472 (90.2%). Of these, 26.7% were total anterior circulation infarctions (TACI), 29.9% partial anterior circulation infarctions (PACI), 16.7% posterior circulation infarctions (POCI) and 26.7% lacunar infarctions (LACI). In multivariate analysis, atrial fibrillation was predictive of TACI (odds ratio [OR], 1.61; 95% CI, 1.28–2.03), hypertension (OR, 1.38; 95% CI, 1.16–1.65) and myocardial infarction (OR, 1.42; 95% CI, 1.08–1.86) predictive of PACI, hypertension (OR, 1.25; 95% CI, 1.04–1.50) predictive of LACI. A negative association was observed between TACI and hypertension (OR, 0.51; 95% CI, 0.42–0.61). Discharge home was 50% less probable in TACI and PACI than in LACI patients. As compared to LACI, TACI significantly increased the risk of 3-month death (OR, 5.73; 95% CI, 3.91–8.41), disability (OR, 3.27; 95% CI, 2.30–4.66) and handicap (OR, 2.71; 95% CI, 1.91–3.85).
Conclusions: Ischemic stroke subtypes have different risk factors profile, with consequences on pathogenesis and prognosis. Information on determinants of the clinical syndromes may impact on prevention and acute-phase interventions.

Keywords: Risk factors; Stroke classification; Stroke prevention; Stroke outcome

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1. Introduction

Stroke is a highly heterogeneous disorder with distinct subtypes, each presenting specific clinical and epidemiological aspects [1]. In developed countries, cerebral infarction represents the most common type of stroke and may be further differentiated in subtypes. Subtype characterization of ischemic stroke may improve knowledge of risk factors and pathogenesis, with a positive impact on prevention, acute-phase treatment and, possibly, outcome [2].

The Oxfordshire Community Stroke Project (OCSP) classification defined four clinically identifiable subgroups of cerebral infarction: total anterior circulation infarction (TACI), partial anterior circulation infarction (PACI), posterior circulation infarction (POCI) and lacunar infarction (LACI) [3]. This classification showed a moderate to good interobserver reliability [4,5], could predict size and site of infarction seen on computed tomography or magnetic resonance imaging in about 75% of cases [6], and was proposed for clinical–epidemiological purposes, but little is known about possible determinants and prognosis of the single subtypes.

The objective of the present study was to evaluate differences in risk factors, resource use and 3-month outcome of different ischemic stroke subtypes, defined according to the OCSP classification, in a large European setting of patients hospitalized for acute stroke.

2. Patients and methods

A European Union Concerted Action was initiated to establish the relationships between resource use, costs and outcome of packages of care for stroke in Europe. The specific objectives have been outlined previously [7]. The study was prospective and involved 12 centers (22 hospitals) in 7 countries: England, France, Germany, Hungary, Italy, Portugal and Spain. The hospitals were chosen because they contained staff interested in stroke research. They provide general acute care to the local population; most are community hospitals, serving up to 150,000 inhabitants. Patient-based data collection began in September 1993 and related to all first-ever stroke admissions for the subsequent year.

Stroke was defined according to the World Health Organization [8]. Patients were evaluated in the acute phase and at 3 months. Informed consent was given according to institutional rules. Variables germane to this article include:

1. Baseline characteristics: age, sex, living conditions, prestroke medications and level of handicap (modified Rankin Scale) [9].
2. Vascular risk factors and comorbid conditions: hypertension (previous diagnosis, current treatment or values $\geq$160/95 mm Hg in at least two subsequent measurements; during admission, only measurements taken after 1 week from the index stroke were considered valid for diagnosis), atrial fibrillation ([AF] history of chronic AF, supported by past electrocardiogram [ECG] and positive ECG during hospitalization, or past medical history with positive ECG), previous myocardial infarction (previous diagnosis based on documented transient elevation of biochemical markers of myocardial necrosis with typical ECG signs), transient ischemic attack ([TIA] acute neurological deficit of vascular origin, lasting <24 h), diabetes mellitus (previous diagnosis, concurrent treatment with insulin or oral hypoglycemic medications, or fasting plasma glucose level $\geq$7.8 mmol/L [$\geq$140 mg/dL]), smoking (current or former practice) and alcohol consumption (specified as average units of alcohol per day: a unit was a glass, bottle or can of beer, a 125-ml glass of wine or a shot of liquor).
3. Clinical state at time of maximum impairment, use of major diagnostic tests (brain imaging, conventional angiography, Doppler sonography, echocardiogram) and therapeutic interventions (neurosurgery, carotid surgery, other vascular surgery) and amount of inpatient rehabilitation (formal therapy sessions).
4. Hospital stay: the length of hospital stay by ward type was recorded for each patient; the total length of stay was calculated by summing the length of stay in each hospital ward, including inpatient rehabilitation provided in the acute hospital setting.
5. Destination from acute hospital: home, rehabilitation hospital and institution.

Pathological types of stroke were defined as cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage or unclassifiable stroke according to the presence and results of brain imaging. Using the clinical criteria from the OCSP, cases of definite cerebral infarction were further classified into TACI, PACI, POCI and LACI [3]. Final diagnosis was reached according to a consensus by participating neurologists in each centre. Following the original definition by Bamford et al., final allocation of OCSP subtype was based on the clinical pattern at the time of maximum deficit, and brain imaging was used only to identify definite cerebral infarction and not to classify patients in the different OCSP subgroups [3].

Outcome data were collected 3 months after stroke. These included information on vital status, activities of daily living measured by the Barthel Index [10] and handicap assessed by the Rankin Scale [9]. These assessments were usually made through a direct or a proxy face-to-face interview.

To minimize across centers and interobserver variability, a manual was produced with definitions for each data item. The study team visited centers to oversee data collection. Issues regarding collection, interpretation and quality of data were discussed at site visits and at six monthly meetings.

2.1. Statistical analysis

Categorical variables were analyzed using the χ^2 test. Comparisons of means were made using analysis of variance (ANOVA) and Tukey's post-hoc test. In univariate analysis, frequencies of baseline and acute-phase variables of each ischemic stroke subtype were compared against all other subtypes combined, and significance of these differences was also evaluated with a direct comparison between individual stroke subtypes. The role of baseline variables as predictors of OCSP subtype and of all variables, including OCSP subtypes, as predictors of destination at discharge and 3-month death, disability and handicap, was evaluated in a series of forward stepwise logistic regression analyses, controlling for age and sex. In multivariate models including OCSP subtypes, LACI was the reference category against which individual subtypes were compared. Results were expressed as odds ratios (ORs). The 95% confidence intervals (CIs) were calculated.

Disability and handicap were evaluated in univariate analysis using the Mann–Whitney nonparametric test and dichotomizing the scales in logistic regression models. The selected categories were 0–14 and 15–20 for the Barthel Index, and 0–1 and 2–5 for the Rankin Scale. Statistical levels are two-tailed. The α level was set at $p<0.05$. Data were analyzed using the SPSS software.

3. Results

During the 12-month study period, cerebral infarction was diagnosed in 2740 patients with first-in-a-lifetime stroke (mean age 70.5±12.4 years, range 13.7–100.4). Overall, 1463 patients were males (53.4%, mean age 68.2±11.9 years) and 1277 females (46.6%, mean age 73.1±12.4 years). A definition of OCSP subtypes was achieved in 2472 (90.2%) of the 2740 events diagnosed as ischemic strokes. A total of 659 events (26.7%) were TACI, 740 (29.9%) PACI, 413 (16.7%) POCI and 660 (26.7%) LACI.

Table 1 reports baseline variables by OCSP subtype. POCI patients were the youngest and PACI patients the oldest ones. TACI patients lived more often at home alone and showed the highest level of prior handicap. AF was significantly more common in TACI and PACI patients, while the frequency of hypertension was significantly lower in TACI patients, who were also less often diabetic. PACI patients were those with the highest frequency of hypertension and myocardial infarction. No difference was found in smoking habits, but alcohol consumption was significantly more common in LACI patients, that also showed the lowest percentage of AF and myocardial infarction. Only 3.3% of TACI patients were on anticoagulants before stroke, compared with 5.8% of PACI patients.

Significance of these differences was also evaluated with multiple comparisons between individual stroke subtypes. In this analysis, POCI patients were significantly younger than TACI and PACI patients, and PACI patients were significantly older when compared with POCI and LACI patients (ANOVA, Tukey's test, all p-values <0.05). TACI patients lived significantly more often at home alone compared with PACI, POCI and LACI patients (all p-values <0.05). Their level of prestroke handicap was significantly higher than in POCI and LACI patients (Mann–Whitney, both p-values <0.05). The frequency of AF was significantly higher in TACI than in POCI and LACI patients, while hypertension was significantly less frequent in TACI than in PACI, POCI and LACI patients (all p-values <0.05).

Table 1
Baseline variables by OCSP subtype

Variable	TACI, $n=659$	PACI, $n=740$	POCI, $n=413$	LACI, $n=660$	Total sample, $n=2472$
Mean±S.D. age, years[a]	71.6±12.5	72.0±12.3	68.7±13.1	70.3±11.8	70.9±12.4
Sex (males)	53.6%	49.7%*	53.8%	55.9%	53.1%
Home alone	37.9%***	26.8%*	28.0%	28.7%	30.5%
Home with companion	58.2%***	69.8%*	70.0%	67.3%	66.1%
Institutionalized	3.9%	3.4%	2.0%	4.0%	3.4%
Atrial fibrillation	24.2%***	22.3%**	17.7%	11.4%***	19.1%
Hypertension	37.3%***	53.9%**	52.2%	51.6%	48.6%
Diabetes	19.0%*	21.7%	22.8%	24.1%	21.8%
Current or previous smoking	41.5%	42.8%	41.5%	43.2%	42.3%
Alcohol intake	29.0%	30.9%	31.1%	36.1%**	31.8%
Previous myocardial infarction	13.1%	13.7%*	8.7%	8.2%**	11.2%
Previous TIA	11.1%	13.6%	11.1%	13.2%	12.4%
Anticoagulant therapy	3.3%	5.8%**	2.7%	2.9%	3.9%
Antiplatelet therapy	18.9%	22.1%	17.9%	21.8%	20.5%
Prestroke Rankin Score (2–5)	27.8%*,b	23.7%**,b	16.9%*,b	18.1%**,b	22.1%

[a] ANOVA $p<0.001$.
[b] Mann–Whitney test.
* $p<0.05$.
** $p<0.01$.
*** $p<0.001$.

The lower frequency of diabetes in TACI patients was significant only in the comparison with LACI patients ($p<0.05$). The frequency of TACI patients on anticoagulants was significantly lower than in PACI patients ($p<0.05$). PACI patients had more frequently AF than LACI patients ($p<0.05$). They had more frequently myocardial infarction and were more often on anticoagulants compared with POCI and LACI patients (all p-values <0.05). The higher level of prestroke handicap in PACI patients was significant in the comparison with POCI and LACI patients (Mann–Whitney, both p-values <0.05). Alcohol consumption was significantly more common in LACI patients compared with both TACI and PACI patients (both p-values <0.05).

Multivariate analyses, age- and sex-adjusted, considering baseline variables as possible predictors of single OCSP subtypes, confirmed AF as independent predictor of TACI (OR, 1.61; 95% CI, 1.28–2.03), hypertension (OR, 1.38; 95% CI, 1.16–1.65) and myocardial infarction (OR, 1.42; 95% CI, 1.08–1.86) as independent predictors of PACI, hypertension (OR, 1.25; 95% CI, 1.04–1.50) and alcohol intake (OR, 1.25; 95% CI, 1.02–1.54) as independent predictors of LACI. Considering non-drinkers as the reference category, light to moderate drinkers (<1 to 2 alcohol units daily) had a multivariate-adjusted OR of 1.27 (95% CI, 1.02–1.59) and heavier drinkers (>2 alcohol units daily) of 1.41 (95% CI, 1.04–1.91). Negative associations were observed between TACI and hypertension (OR, 0.51; 95% CI, 0.42–0.61), LACI and AF (OR, 0.48; 95% CI, 0.37–0.63), and LACI and myocardial infarction (OR, 0.58; 95% CI, 0.42–0.80).

Table 2 shows the use of resources during hospitalization by OCSP subtype. LACI patients received the highest and PACI patients the lowest number of Doppler examinations. POCI patients had the highest frequency of conventional angiographic evaluations and LACI patients the lowest. As expected, no neurosurgical intervention was performed in LACI patients. TACI patients received the highest amount of physiotherapy, speech and occupational therapy, both in terms of frequency and number of sessions.

Differences were again evaluated in a direct comparison between individual stroke subtypes. In this analysis, the number of Doppler examinations was significantly lower in PACI than in TACI, POCI and LACI patients, while conventional angiographic evaluations were significantly more often performed in POCI than in TACI, PACI and LACI patients (all p-values <0.05). Differences in amount of physiotherapy, speech and occupational therapy of TACI patients were significant when compared, respectively, with PACI, POCI and LACI patients, while in LACI patients speech therapy was significantly less often performed also in comparison with PACI and POCI patients (all p-values <0.05). Considering mean number of sessions, physiotherapy was more often performed in TACI compared, respectively, with PACI, POCI and LACI patients (ANOVA, Tukey's test, all p-values <0.05). Speech therapy sessions were significantly more common in TACI than in PACI and LACI patients (ANOVA, Tukey's test, both p-values <0.05). Occupational therapy sessions were also significantly more frequent in TACI compared, respectively, with PACI, POCI and LACI patients (ANOVA, Tukey's test, all p-values <0.05).

The 28-day case-fatality was 15.8% in TACI ($p<0.05$), 6.8% in PACI ($p>0.05$), 6.8% in POCI ($p>0.05$) and 3.8% in LACI patients ($p<0.05$). Hospital stay was 29.3±27.2 days in TACI, 21.3±27.4 days in PACI, 19.8±17.2 days in POCI and 17.6±18.8 days in LACI patients (ANOVA $p<0.05$). Destination at discharge was home for 68.1% of TACI, 72.4% of PACI, 82.7% of POCI and 82.8% of LACI patients (all p-values <0.05); were referred to an institution 8.6% of TACI ($p<0.05$), 6.5% of PACI ($p>0.05$), 2.8% of POCI ($p<0.05$) and 5.3% of LACI patients ($p>0.05$); were referred to a rehabilitation hospital 10.2% of TACI ($p>0.05$), 11.5% of PACI ($p<0.05$), 5.9% of POCI ($p<0.05$) and 6.4% of LACI patients ($p<0.05$). Nine

Table 2
Resource use during hospitalization by OCSP subtype

Variable	TACI, $n=659$	PACI, $n=740$	POCI, $n=413$	LACI, $n=660$	Total sample, $n=2472$
Doppler	52.1%	39.7%***	53.8%	56.7%***	49.9%
Echocardiogram	39.7%	34.0%	39.8%	35.4%	36.9%
Conventional angiography	9.0%	6.5%*	14.5%***	6.2%*	8.5%
Neurosurgery	0.7%	0.3%	0.3%	0	0.3%
Carotid surgery	1.4%	1.1%	1.7%	1.1%	1.3%
Other vascular surgery	0.3%	1.5%**	1.2%	0.2%*	0.8%
Physiotherapy	79.8%***	64.1%	59.5%**	61.7%**	66.6%
Mean±S.D. physiotherapy sessions, n[a]	16.7±15.0	12.0±14.3	12.6±14.7	10.4±10.1	13.1±13.9
Speech therapy	43.3%***	22.3%	20.0%	14.3%***	24.4%
Mean±S.D. speech therapy sessions, n[a]	12.7±10.4	8.3±9.8	9.2±10.3	6.0±4.1	9.8±9.7
Occupational therapy	37.6%***	22.5%*	23.2%	21.7%*	25.6%
Mean±S.D. occupational therapy sessions, n[a]	15.0±11.6	9.6±10.5	9.9±8.8	8.7±8.6	11.1±10.5

[a] ANOVA $p<0.001$.
* $p<0.05$.
** $p<0.01$.
*** $p<0.001$.

Table 3
Predictors of destination at discharge

Variable	OR (95% CI)		
	Home	Institution	Rehabilitation hospital
Home with companion	1.78 (1.39–2.28)	0.43 (0.27–0.68)	0.65 (0.47–0.90)
Prestroke institutionalization	0.10 (0.05–0.21)	8.38 (4.25–16.55)	NS
Hypertension	0.75 (0.59–0.95)	NS	1.39 (1.01–1.91)
Previous TIA	0.68 (0.49–0.95)	NS	1.67 (1.10–2.54)
Anticoagulant therapy	NS	NS	2.20 (1.13–4.28)
OCSP subtypes:			
LACI (reference)	1	1	1
TACI	0.50 (0.36–0.69)	1.77 (1.02–3.06)	1.50 (0.95–2.37)
PACI	0.51 (0.37–0.69)	1.28 (0.74–2.22)	1.90 (1.26–2.85)
POCI	1.05 (0.70–1.57)	0.54 (0.23–1.29)	0.97 (0.56–1.68)

Age- and sex-adjusted logistic regression with stepwise selection of variables.
NS: nonselected in the final model.

percent of patients were discharged to other or unspecified destinations.

The direct comparison between individual stroke subtypes showed that the 28-day case-fatality was significantly higher in TACI compared, respectively, with PACI, POCI and LACI patients, and in both PACI and POCI compared with LACI patients (all p-values <0.05). Hospital stay was significantly longer in TACI than in PACI, POCI and LACI patients, and in PACI compared with LACI patients (ANOVA, Tukey's test, all p-values <0.05). Differences for destination home were significant when TACI and PACI where compared with POCI and LACI patients (all p-values <0.05). TACI patients were referred to an institution significantly more frequently than POCI and LACI patients, as were PACI compared with POCI patients (all p-values <0.05). Were referred to a rehabilitation hospital significantly more TACI and PACI patients compared with POCI and LACI patients (all p-values <0.05).

Table 3 reports the results of three (age- and sex-adjusted) models of logistic regression evaluating predictors of destination at discharge. While living with companion was strongly associated with returning home after stroke and poorly associated with institutionalization, patients institutionalized at baseline were almost certain to return in institution. Hypertensive patients and those with previous TIA also had a reduced probability to be discharged home and increased chances of admission to rehabilitation hospitals. Discharge home was 50% less probable in TACI and PACI as compared with LACI patients. As a consequence, TACI patients had significantly increased odds of institutionalization and PACI of admission to rehabilitation hospitals than LACI patients.

Follow-up information was completed for 1983 of the 2472 patients (80.2%), without major differences among subtypes (range from 76.5% of TACI to 83.4% of PACI). At 3 months, 35.1% of TACI were dead ($p<0.05$), as compared with 15.7% of PACI ($p<0.05$), 16.1% of POCI ($p>0.05$) and 9.1% of LACI patients ($p<0.05$). Among survivors at 3 months, mean scores for the Barthel Index were 13.8 ± 6.9 in TACI, 15.4 ± 5.5 in PACI, 17.5 ± 4.4 in POCI and 17.1 ± 4.7 in LACI patients (Mann–Whitney, all p-values <0.05). The respective values for the Rankin Scale were 2.9 ± 1.6 in TACI (Mann–Whitney $p<0.05$), 2.4 ± 1.5 in PACI (Mann–Whitney $p>0.05$), 1.9 ± 1.4 in POCI (Mann–Whitney $p<0.05$) and 2.0 ± 1.3 in LACI patients (Mann–Whitney $p<0.05$).

Table 4 shows the results of three (age- and sex-adjusted) models of logistic regression evaluating predictors of 3-month death, disability (Barthel Index <15) and handicap (Rankin Score >1). Among baseline variables, prestroke Rankin and AF were significant predictors of 3-month death, disability and handicap. As compared to LACI, considered the reference category, TACI significantly increased the risk of 3-month death (OR, 5.73; 95% CI,

Table 4
Predictors of 3-month death, disability (Barthel Index 0–14) and handicap (Rankin Scale 2–5)

Variable	OR (95% CI)		
	Death	Disability	Handicap
Atrial fibrillation	1.54 (1.14–2.08)	1.41 (1.03–1.93)	1.43 (1.02–2.01)
Prestroke Rankin Score (2–5)	2.51 (1.88–3.35)	2.80 (2.05–3.82)	2.98 (2.05–4.33)
OCSP subtypes			
LACI (reference)	1	1	1
TACI	5.73 (3.91–8.41)	3.27 (2.30–4.66)	2.71 (1.91–3.85)
PACI	1.65 (1.10–2.46)	1.73 (1.25–2.38)	1.52 (1.13–2.03)
POCI	2.22 (1.40–3.52)	0.88 (0.57–1.35)	1.06 (0.76–1.49)

Age- and sex-adjusted logistic regression with stepwise selection of variables.
NS: nonselected in the final model.

3.91–8.41), disability (OR, 3.27; 95% CI, 2.30–4.66) and handicap (OR, 2.71; 95% CI, 1.91–3.85), PACI increased by more than 50% the risk of 3-month death, disability and handicap, and POCI more than doubled the risk of 3-month death.

4. Discussion

This study evaluated differences in risk factors, management and outcome of subtypes of ischemic stroke, defined according to the OCSP classification, in a large sample of European patients. There were differences in baseline living conditions, risk factor profile and stroke outcome. Different subtypes required different use of in-hospital rehabilitation services and diagnostic tools. Also, separate patterns were observed for in-hospital stay, 28-day case-fatality rate and 3-month mortality. TACI and PACI patients were more likely to be discharged to an institution or rehabilitation hospital than home, and were more disabled and more severely handicapped as assessed 3 months after stroke. These data may be useful for planning interventions in the acute phase and facilities for long-term care and rehabilitation.

One of potential shortcomings of this report is that, although participating hospitals contained physicians and researchers with an interest in stroke, they might be considered not necessarily representative of their country. However, including 22 units in 12 centers in seven European states, with urban and rural population coverage and predictable variations of services between hospitals, the information may reflect characteristics of stroke and 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 standardize procedures. This type of data set had the advantage of providing the so far wider sample of patients with the OCSP classification, increasing statistical power. The relative proportions of patients in each OCSP subtype were in line with previously reported figures [3,11–14]. In all studies, PACI was the most common subtype, with frequencies ranging from 30% to 56%. Frequencies for other subtypes varied between 15% and 27% for TACI, 8% and 24% for POCI, and 20% and 28% for LACI.

Our rate of lost to follow-up (19.8%) is similar to those previously reported in studies on stroke outcome [15,16]. While gender did not influence follow-up rates (were followed 80.0% of males and 80.4% of females; $p > 0.05$), the chance of being lost to follow-up was higher among younger patients (mean age 71.8 ± 11.8 years in followed versus 67.1 ± 13.8 in lost patients; $p < 0.05$). This may have affected the precision of our estimates, but probably not enough to determine a distortion in the observed trends.

This is one of the first studies and the largest one evaluating the impact of vascular risk factors and comorbid conditions on the probability of developing the different OCSP subtypes. The knowledge of distribution of risk factors in stroke subtypes is essential for understanding potential pathogenic mechanisms and targeting preventive treatments. TACI patients showed the highest frequency of AF and the lowest frequency of hypertension and diabetes. Data on the frequency of risk factors in ischemic stroke subtypes are scarce [17]. Assuming a major role of cardioembolism in TACI, our data are in line with the few available analyses on stroke subtypes defined according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification [18], showing that both hypertension and diabetes are significantly less frequent in cardioembolic stroke as compared with stroke due to large-artery atherosclerosis or small vessels arteriopathy linked with lacunar infarct [19–22].

The evaluation of risk factors in stroke subtypes defined according to the OCSP might be less biased towards cardioembolic stroke, considering that AF is among factors influencing subtype diagnosis in the TOAST classification, while it is irrelevant for the attribution of clinical syndromes following the OCSP classification. The hypothesis of a major pathogenic role for cardioembolism in TACI was at first proposed by Bamford et al., although they wrote "satisfactory data are lacking" [3]. Despite the significantly higher frequency of AF, only 3.3% of TACI patients were on anticoagulant therapy before stroke, a negligible proportion, not different from that observed in patients with the other syndromes but with a lower frequency of AF. This study is a further confirmation of the poor prognosis of stroke associated with AF [23], explained by the significant association with the most severe OCSP subtype.

PACI patients were older and also showed a high frequency of AF, with 5.8% of them on anticoagulants before stroke. They were those carrying the highest frequency of hypertension and previous myocardial infarction. Overall, these findings seem to suggest that, while cardioembolism play a major role in TACI, the picture for PACI is more complex, and may in part be explained by large-artery atherosclerosis and diffuse vasculopathy. A portion of PACI might also be due to cardioembolic infarct, considering the high frequency of AF that these patients share with the TACI group.

POCI patients were the youngest ones and those with the lowest frequency of prestroke handicap. We failed to find any significant association between POCI and baseline variables in multivariate analysis. LACI patients showed the lowest frequency of previous myocardial infarction and AF, and a significant association with hypertension in the multivariate analysis. The role of hypertension as predictor of LACI confirms previous findings on hypertensive changes of small penetrating arteries in the pathogenesis of lacunar infarction [19–22]. Although the frequency of diabetes was slightly higher in LACI patients, the association was not significant in the multivariate analysis. The role of diabetes in the pathogenesis of lacunar stroke remains controversial, with opposite findings in different surveys [2,21]. There are very few studies evaluating the

relationship between alcohol intake and lacunar stroke, and they failed to show any clear association [21,24–27]. However, where given, definitions of alcohol consumption varied considerably among studies. The role of alcohol in the pathogenesis of lacunar stroke remains uncertain. The alcohol-induced hypertension, believed to be one of mechanisms involved in the relationship between alcohol consumption and stroke [28–31], might offer a possible explanation, but further studies are warranted.

The occurrence of TACI significantly increased hospital stay and use of rehabilitation services. The 28-day case-fatality showed more than twice the rate found in PACI and POCI. Compared with LACI, and controlling for baseline variables, TACI and PACI patients had a significantly lower probability of returning home and an almost two-fold increased chance of being institutionalized or admitted to a rehabilitation hospital.

In previous studies, TACI showed the highest and LACI the lowest case-fatality, with intermediate values for PACI and POCI [3,11,12,14]. TACI and PACI patients were those with the highest levels of disability and handicap 3–6 months after stroke, followed by LACI and POCI patients [3,14]. Our study is the first providing results on the net effect of OCSP subtypes on survival and function. As compared with LACI, and controlling for demographics, risk factors and comorbidity, TACI increased by six times the risk of death and by three times the risk of disability and handicap 3 months after stroke. In the same analysis, POCI patients had a doubled risk of death and PACI patients a 50% to 70% increased probability of death, disability and handicap.

In conclusion, different subtypes of ischemic stroke showed differences in risk factors profile, pathogenesis, acute-phase requirements, destination and prognosis. Information on determinants of the clinical syndromes may affect prevention, planning of clinical trials and acute-phase practice. Cost-effectiveness of interventions in stroke patients requires an early definition of clinical syndromes to address resource use and to define pathways of care.

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Appendix A

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Appendix B

The Oxfordshire Community Stroke Classification [3].

TACI (total anterior circulation infarcts): patients presenting with a combination of new higher cerebral dysfunction (e.g. dysphasia, dyscalculia, visuospatial disorder), homonymous visual field defect and ipsilateral motor and/or sensory deficit of at least two areas of the face, arm and leg. If the conscious level was impaired and formal testing of higher cerebral function or the visual fields was not possible, a deficit was assumed.

PACI (partial anterior circulation infarcts): patients presenting with only two of the three components of the TACI syndrome, with higher cerebral dysfunction alone or motor/sensory deficit more restricted than those classified as LACI (e.g. confined to one limb, or to face and hand but not to the whole arm).

POCI (posterior circulation infarcts): patients presenting with any of the following: ipsilateral cranial nerve palsy with contralateral motor and/or sensory deficit; bilateral motor and/or sensory deficit; disorder of conjugate eye movement; cerebellar dysfunction without ipsilateral long-tract deficit (i.e. not ataxic hemiparesis); isolated homonymous visual field defect.

LACI (lacunar infarcts): patients presenting with a pure motor stroke, pure sensory stroke, sensori-motor stroke or ataxic hemiparesis. Two of three areas (face, arm, leg) must be involved with involvement of the whole of any affected limb. Absence of cortical signs as defined for TACI and PACI and absence of brainstem signs as defined for POCI.

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