

J. F. Varona  
F. Bermejo  
J. M. Guerra  
J. A. Molina

## Long-term prognosis of ischemic stroke in young adults

### Study of 272 cases

**Abstract** *Background* There have been few studies of the long-term prognosis of young adults with ischemic stroke. The present study aimed to evaluate the long-term clinical outcome in a large series of young adults with ischemic stroke admitted to a tertiary medical center over the last 27 years, and to identify possible predictors for mortality, stroke recurrence and poor functional recovery. *Methods* We retrospectively reviewed 272 young adults (15–45

years) with a first-ever ischemic stroke admitted to the Neurology Department of University Hospital “12 de Octubre” between 1974 and 2001. Follow-up assessments were performed by review of medical records and telephone interviews. *Results* Nine patients (3%) died as the result of their initial stroke and follow-up information about the status of 23 (8%) patients was not available. The remaining 240 patients (89%) were followed. Two hundred and ten of them (88%) were alive with a mean follow-up of 12.3 years and 30 (12%) died during follow-up. The average annual mortality rate was 1.4%, being notably higher during the first (4.9%) than in the subsequent years (0.9%) after the initial stroke. Ninety per cent of the followed patients were independent and 53% returned to work, although adjustments were necessary for 23% of them. The annual stroke recurrence rate during the first year was 3.6% dropping to 1.7% in subse-

quent years. Age over 35 years, male gender, the presence of cardiovascular risk factors and large-artery atherosclerosis in the carotid territory were predictors of negative long-term outcome after the initial stroke. *Conclusions* The long-term prognosis for the ischemic stroke in the young is better than in the elderly, but the risk of mortality in young adults with ischemic stroke is much higher than in the general population of the same age. A bad prognosis is associated with an atherosclerotic risk profile, with a higher mortality and recurrent stroke rates and poorer functional recovery. The main functional limitation in the young survivors of their initial ischemic stroke occurs in work activity, since most patients are independent but almost half of them do not return to work.

**Key words** ischemic stroke · prognosis · young adult

Received: 24 March 2004  
Received in revised form: 8 June 2004  
Accepted: 14 June 2004

J. F. Varona, MD (✉) · F. Bermejo, MD ·  
J. M. Guerra, MD · J. A. Molina, MD  
Department of Internal Medicine  
University Hospital “12 de Octubre”  
Avda. Andalucía, km 5.4  
28041-Madrid, Spain.  
Tel.: +34-91/390-8286  
Fax: +34-91/390-8103  
E-Mail: jfva\_varona@yahoo.com

### Introduction

Stroke in young adults is not exceptional. Up to 12% of first strokes occur in patients under 45 years of age [1–6]. However, only the short-term prognosis has been widely evaluated and there have been few investigations about long-term functional recovery of young adults who experience ischemic stroke. Previous studies have

described good functional recovery in young adults with ischemic stroke, since most patients become independent and at least 50% return to work [6–9]. The objective of the present study was to evaluate the long-term outcome of a large series of young adult patients with ischemic stroke, paying special attention to identifying predictive factors for mortality, recurrence and good/poor functional recovery.

## Patients and methods

### ■ Patients

We collected from the Stroke Registry of the Neurology Department all patients aged 15 to 45 years with a first-ever ischemic stroke admitted between March, 1974, and March, 2001, to the Neurology Department of the University Hospital "12 de Octubre", Madrid, Spain. The reference population of this Hospital was not constant over this period, but between 1990 and 2000 the mean reference population numbered 550,000, 250,000 of whom were aged between 15 and 45 years.

### ■ Methods

#### Follow-up

Patients' medical records were exhaustively reviewed and follow-up was performed by means of one or more of the following: a) periodic reviews in the outpatient clinic after the initial admission (a detailed chart review of recovery from the stroke is available in the medical record for most of the patients); b) complete telephone interview with either the patient or a relative, completing a detailed and validated questionnaire with several items about the recovery from and the evolution after stroke (functional status, recurrence, ...). In the telephone questionnaire, we specifically collected the following data: events as death, recurrent stroke and other cardiovascular events; functional disability, evaluated by completing the modified Rankin Scale (mRS) [13] and the Barthel Index (BI) [14]; and occupational status; and c) information obtained from other admissions in our centre. Efforts to determinate the status of all patients at the period 1999–2001 were made by consulting the database of the Health Area and the registry of the Hospital.

#### Endpoints

The study protocol collected the following data from all patients: 1. Type and etiological subtype of stroke. We applied criteria which have been described elsewhere [10, 12]. We used the data available in the clinical record for patients collected before 1993 to carefully re-classify the etiological category, according to these criteria, if necessary; 2. Risk factors present before the onset of the stroke; 3. Data of the follow-up after the initial stroke, including: time and type (outpatient clinic, clinical record, telephone interview) of follow-up; mortality (due to initial stroke, in the first 30 days, or after); residual disability, rated by the modified Rankin Scale (mRS) [13] and Barthel Index (BI) [14], occupational status (returning to work, professional adjustments in occupation, retirement due to illness), recurrent episodes of stroke and other non-cerebral vascular events.

### ■ Statistical Analysis

We performed Statistical analyses using the package SAS 12.1. Cary. NC. USA. Survival and survival free of recurrent stroke were analysed using Kaplan-Meier survival curves. To predict the category outcomes of mortality, vascular mortality, good functional recovery (mRS < 3 and BI > 90), bad functional recovery (mRS > 2 and BI < 90), return to work, retirement, recurrence and development of other vascular events, we performed univariate and multivariate logistic regression analyses with age, sex, risk factors, initial stroke severity, treatment and etiology as possible predictors.

## Results

Two hundred and seventy-two young adults (aged 15–45 years) with a first ischemic stroke were admitted to the Neurology Department of our Hospital during the 27-year period. These were 9.2% of all patients admitted to the Neurology Department with an ischemic stroke. The mean age was 36.6 years (standard deviation (SD): 7.2). Two hundred and thirty patients (85%) had a completed ischemic stroke and 42 (15%) an ischemic transient attack. Baseline characteristics and the etiological diagnoses are summarized in Table 1. Nine patients (3%) died as the result of their initial stroke and follow-up information was not available for 23 patients (8%). The

**Table 1** Baseline characteristics, vascular risk factors and etiological subtypes of initial ischemic stroke in the 272 patients included in the study

Characteristic	n (%)
Age	–
15–20 years	6 (2)
21–25 years	24 (9)
26–30 years	23 (8)
31–35 years	38 (14)
36–40 years	71 (26)
41–45 years	110 (41)
Sex	–
Men	177 (65)
Women	95 (35)
Positive family history of stroke	22 (8)
Medium-to-high risk cardiac source for emboli <sup>a</sup>	26 (10)
Classical migraine	29 (11)
Human immunodeficiency virus infection	7 (3)
Drugs abuse	11 (4)
Cardiovascular risk factors	176 (65)
Arterial Hypertension	59 (22)
Hypercholesterolemia	46 (17)
Diabetes mellitus	21 (8)
Cigarette Smoking	133 (49)
Oral contraceptives <sup>b</sup>	17 (18)
High alcohol intake	84 (31)
Stroke subtype	
Atherothrombotic	67 (25)
Cardioembolic <sup>c</sup>	47 (17)
Non-atherosclerotic vasculopathy	45 (17)
Migraine	13 (29)
Dissection of extracranial arteries	9 (20)
Others	23 (51)
Hypercoagulable state	11 (4)
Cerebral venous thrombosis	4 (1)
Undetermined	98 (36)
Complete evaluation (unknown etiology)	17 (17)
Incomplete evaluation	62 (63)
Multiple possible etiologies	19 (20)

<sup>a</sup> In 21 cases a medium-to-high risk cardiac source for emboli was identified as the result of the diagnostic workup and had not been diagnosed before the stroke.

<sup>b</sup> percentage of the total of the number of female patients (95)

remaining 240 (89%) were followed after their initial ischemic stroke, with a mean time of follow-up of 11.7 years (range, 0.2 to 27 years; median: 10 years; SD: 7.9 years).

Among these 240 followed surviving patients, 30 (12%) died during the follow-up with a mean survival of 9.3 years and 210 (88%) were alive after a mean follow-up of 12.3 years (range, 0.2 to 27 years; median: 10.3 years; SD: 7.7 years). One hundred and ninety-nine patients (83%) were followed for more than 3 years. Follow-up information about the status of the patients was obtained by a combination of data from the clinical record and telephone interview in 121 cases (51%), only the clinical record in 70 (29%) and only the telephone interview in 49 (20%).

During the period 1999–2001, we could determinate the status of 217 patients (80% of the 272 included patients). The status of the remaining 55 patients was determined from information from medical record obtained prior to 1999.

### ■ Mortality

Thirty patients (12%) died during follow-up. Fourteen (47%) died from a vascular cause (10 from recurrent fatal stroke, 4 from myocardial infarct) and 16 (53%) from non-vascular causes (10 of these from cancer).

The average annual mortality rate from all causes (vascular and non-vascular) was 1.4%. The mortality rates for periods after the initial stroke are summarized in Table 2. The calculated annual mortality from vascular death was 0.8%, and was higher in the first year after the stroke (4.1%) than in successive years (0.3% per year). Furthermore, the annual vascular mortality was higher in patients with atherothrombotic (0.9%) and with multiple possible etiologies (1.4%) than in those with unknown etiology (0%).

In the statistical analyses, male gender (with relative risk [RR] of 1.9;  $p=0.05$ ), age over 35 years (RR: 2.0;  $p=0.02$ ) and unfavorable initial course (with severe handicaps at discharge) (RR: 5.1;  $p<0.01$ ) were identified as risk factors for mortality, while the following were associated with lower mortality: dissection of the extracranial arteries (RR: no events;  $p<0.01$ ), stroke associated with classical migraine (RR: no events;  $p<0.01$ ), hypercholesterolemia (RR: 0.3;  $p=0.03$ ), the

presence of normal life at discharge (RR: 0.2;  $p<0.01$ ) and the use of adjusted-dose oral anticoagulation after stroke (RR: 0.3;  $p=0.05$ ) (the last only for vascular mortality, but not for global mortality).

### ■ Long-term functional handicaps (Fig.1)

Among the 240 patients followed during a mean period of 11.7 years, 215 (90%) were independent in spite of the previous stroke. Sixty-two (26%) had no handicap, while 27 (11%) had severe deficits. The independent status was more frequent in patients without recurrent stroke (93%) than in those with recurrence/s (64%). Ninety-five per cent could walk without any assistance from another person. The Barthel Index (BI) was 100 (completely independent) in 74% of patients, more than 90 (the patient needs mild assistance) in 83% and less than 90 (at least, mild-to-moderately dependent) in only 10%. The modified Rankin Scale (mRS) was 0 (free of any handicap) in 27%, less than 3 (the handicap, if it exists, does not prevent daily activities) in 85% and more than 2 (at least, moderate incapacity with, at least, some assistance needed) in 15%. Factors associated with a good long-term functional outcome (mRS = 0 to 2 and BI > 90) on the bivariate analysis were: transient ischemic stroke (RR: 1.3;  $p=0.01$ ), favorable initial course (without moderate-to-severe handicaps at discharge) (RR: 1.6;  $p<0.01$ ) and normal life at discharge (RR: 2.8;  $p<0.01$ ). Age over 35 years (RR: 2.5;  $p=0.01$ ), unfavorable initial course (RR: 3.4;  $p<0.01$ ) and severe handicaps at discharge (RR: 7.2;  $p<0.01$ ) were identified as factors associated with poor long-term functional recovery.

### ■ Other sequelae

Twenty-three patients (10%) had seizures during the follow-up, and most needed pharmacological prophylaxis for them. Fifty-two (22%) had depressive symptoms, assessed by a psychiatrist.

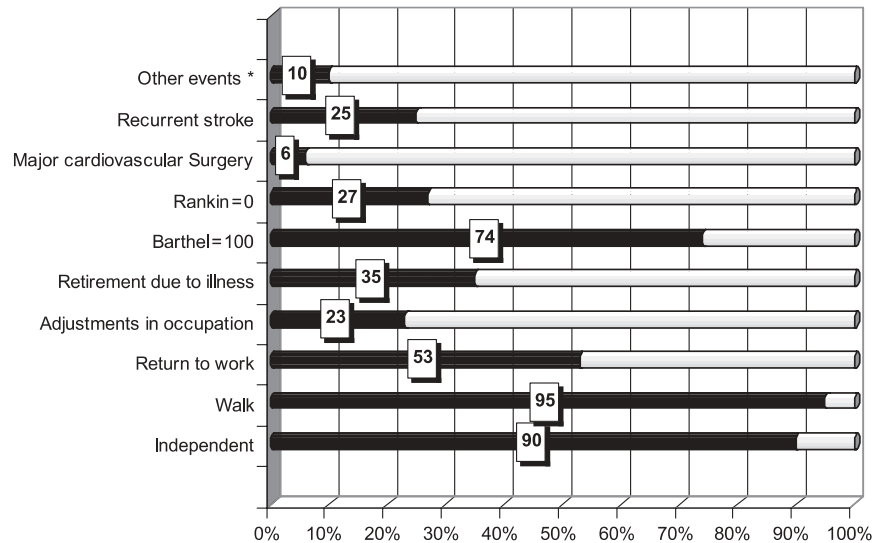
### ■ Occupational status

One hundred and twenty-eight patients (53%) returned to work after the stroke. Of these, thirty (23%) needed to

**Table 2** Annual and cumulative rates of mortality and recurrent stroke in young adults after a first-ever ischemic stroke

	0–1 year	2–5 years	2–10 years	2–20 years
Mean Annual Mortality (%)	4.9	1.0	0.8	0.9
Cumulative Mortality (%)	4.9	9.0	12.1	21.7
Mean Annual Recurrence (%)	3.6	3.0	2.3	1.7
Cumulative Recurrence (%)	3.6	15.4	24.2	36.4

**Fig. 1** Long-term outcome after a mean follow-up of 11.7 years in the 240 young adult patients with ischemic stroke in whom follow-up could be completed. \* Other non-cerebral cardiovascular events



make occupational adjustments (another job or part-time employment). Eighty-four patients (35%) were considered to be unable to work for medical reasons by the social security department and received a permanent retirement pension, although only 77 patients were found not to be performing any work activity after stroke. The 28 remaining patients (12%) were in a situation in which they did not work, but they did not leave work as the result of the stroke (because they had not worked before or their labor activity was not legally recognized: student, house-wife...) and were therefore ineligible for a pension.

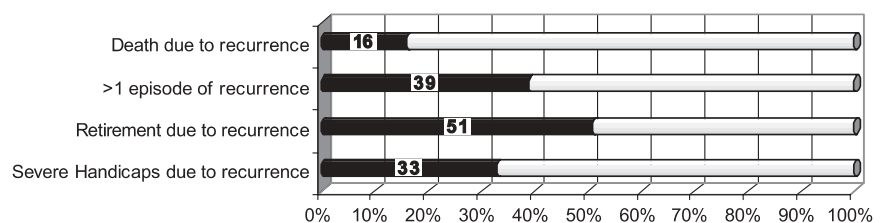
The percentage returning to work was higher in patients with non-atherosclerotic vasculopathy (64%) and unknown etiology (69%). Being able to return to work was less frequent in patients with cardioembolic stroke (34%) and those with multiple possible etiologies (40%) and these patients had also to make more adjustments in their occupation (38% and 37%, respectively). The statistical analyses showed that being able to return to work was associated with the following: age lower than 36 years (RR: 1.3;  $p = 0.01$ ), classical migraine (RR: 1.5;  $p = 0.02$ ), oral contraceptives use (RR: 1.7;  $p < 0.01$ ), transient ischemic attack (RR: 1.5;  $p < 0.01$ ) and normal life at discharge (RR: 3.9;  $p < 0.01$ ). The following were associated with not returning to work: unfavorable ini-

tial course (RR: 1.6;  $p = 0.05$ ), severe handicaps at discharge (RR: 3.3;  $p < 0.01$ ), major cardiovascular surgery (RR: 1.8;  $p = 0.02$ ) and cardioembolic stroke (RR: 1.6;  $p = 0.02$ ).

#### ■ Recurrence

Sixty-one patients (25%) had recurrent stroke during follow-up. Atherothrombotic (22 cases) and undetermined (21 cases, 14 of them with incomplete evaluation) were the etiologies most frequently associated with recurrence. The mean time between the initial stroke and the first recurrence was 6.5 years. Thirty-seven patients had just one episode of recurrence and 24 had more than one. Ten patients (16%) died as the result of the recurrence. Thirty-three per cent of the patients with recurrence had severe handicaps and 51% received a permanent incapacity pension because of the stroke as the result of the first recurrence (Fig. 2). The annual rate of recurrence was 3.4% and was higher in patients with atherothrombotic (5.3%) than those with undetermined etiology (2.6%) ( $p < 0.05$ ); and, among those with an undetermined etiology, recurrence was more frequent in those with multiple possible causes (4.3%) than in those with unknown etiology (2.2%) ( $p < 0.05$ ). The

**Fig. 2** Percentages of mortality, recurrence and disability in patients with a first recurrent episode of stroke



annual recurrence rate was 3.6% during the first year and 1.7% between second and twentieth year (table 2).

Age over 35 years (RR: 1.7;  $p = 0.02$ ), the presence of cardiovascular risk factors (RR: 1.6;  $p = 0.03$ ) (especially, diabetes mellitus -RR: 2.5;  $p < 0.01$ -), stroke in the carotid territory (RR: 1.7;  $p = 0.01$ ) and atherothrombotic cause (RR: 1.9;  $p = 0.01$ ) were associated with higher recurrence risk. Dissection of extracranial arteries (RR: 0.4;  $p = 0.02$ ), stroke associated to classical migraine (RR: 0.4;  $p = 0.04$ ) and normal life at discharge (RR: 0.6;  $p = 0.05$ ) were associated with a lower recurrence. Other situations, such as transient ischemic stroke (RR: 1.5;  $p = 0.13$ ) or a cardiac source for emboli (RR: 1.5;  $p = 0.2$ ) were associated with a higher tendency to recurrence, although without statistical signification.

### ■ Other non-cerebral cardiovascular events

Twenty-five patients (10%) had other non-cerebral cardiovascular events (angina/myocardial infarction, cardiac failure and/or arrhythmia) during follow-up. Four patients died as the result of the event. Male gender (RR: 3.0;  $p = 0.01$ ), age over 35 years (RR: 14.0;  $p < 0.01$ ), presence of cardiovascular risk factors (RR: 2.0;  $p = 0.04$ ) (mainly, diabetes -RR: 2.6;  $p = 0.05$ -), atherosclerosis (RR: 3.9;  $p = 0.02$ ) and a cardiac source for emboli (RR: 3.4;  $p = 0.01$ ), major cardiovascular surgery (RR: 2.8;  $p = 0.02$ ), oral anticoagulation after stroke (RR: 2.4;  $p = 0.02$ ) and atherothrombotic (RR: 2.9;  $p < 0.01$ ) and cardioembolic (RR: 4.1;  $p < 0.01$ ) etiologies were associated with a higher risk of non-cerebral cardiovascular events. Dissection (RR: absence of events;  $p = 0.02$ ), Migraine (RR: absence of events;  $p = 0.05$ ) and non-atherosclerotic vasculopathy (RR: absence of events;  $p = 0.03$ ) were associated with lower risk for this kind of events.

## Discussion

The present series of young adults (15–45 years) with ischemic stroke is one of the largest (272 patients) with a longer follow-up after the initial episode (mean follow-up of 11.7 years) reported in the literature. The overwhelming majority of the patients (89%) were followed since their initial stroke, and only 8% were lost to follow-up (the remaining 3% died as the result of their initial stroke). Therefore, mean follow-up time (almost 12 years) of our patients is the longest described to date [7–9, 15–31]. Only the series of Hindfelt and Nilsson had a longer follow-up but their series was much smaller (74 patients) (table 3).

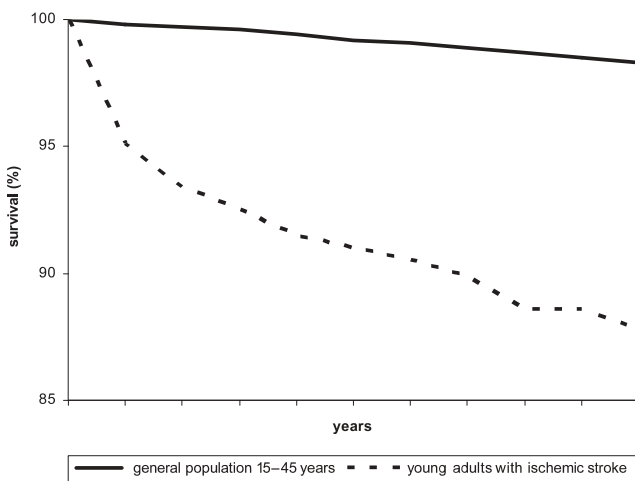
Our study has two methodological limitations. First, the design was retrospective and cases were collected over 27 years during which technological facilities for diagnosis changed. However, these limitations were not

important for evaluating the long-term consequences of stroke in our patients, since we investigated recurrence, death and disability, which can be evaluated easily with the methods we used. Furthermore, the review of the clinical records (including periodic outpatient reviews) and the telephone interviews also have been the main tools for obtaining information about the patients' functional status after the stroke in the main prior studies about consequences of stroke in the young [7–9, 15, 16], including prospective series [8, 9]. Second, our series is based in a speciality department of one hospital and does not include patients who were admitted to an Intensive Care Unit (ICU) or patients who died shortly after admission in the Emergency department. However, this percentage of patients is very low (less than 10%) and only affects results on early mortality, since most of the patients surviving after ICU admission are then admitted to the neurology department in our center. Moreover, this second limitation is present in all studies of this kind [7–9, 15, 16].

The prognosis of ischemic stroke in the young has been described as favorable [19–23]. Our study confirmed this aspect but with important qualifications. The prognosis is better than in the elderly, with lower mortality and recurrence and better functional recovery. But the long-term prognosis is notably worse than in the general population of the same age, with a higher death rate, a higher risk of cardiovascular events and significant limitations in quality of life. In our series, the cumulative risk of death at 10 years was 12.1%. Furthermore, only 57% of the patients followed for more than 3 years who were still alive, were not disabled, had not suffered from recurrent stroke or other vascular events, or had not undergone major vascular surgery. This figure, similar to that described by Kappelle et al. [7], falls to 44% if we only consider patients who had returned to work.

In our series, the mortality rates in the first year (4.9%) and in the following years (1% annual) were similar to those in other studies [8, 9, 23]. Since no studies have follow-ups longer than 8 years, our series (with almost 12 years of mean follow-up) provides very interesting information about long-term survival. Thus, the annual mortality between the second and twentieth year after stroke was 0.9%. We found a lower average annual risk of vascular mortality (0.8%) compared with the study of Kapelle et al. [7] (1.7%), probably as the result of the longer follow-up period in our series. The risk of vascular mortality is higher in the first year after stroke and then falls to lower risk in subsequent years, so the annual vascular mortality rate is lower the longer is the follow-up after the initial stroke. The cumulative risk of mortality at 10 years in young adults with ischemic stroke is almost 10 times higher than in the general population of the same age, as shown in Fig. 3, which compares the survival of our patients against the survival of





**Fig. 3** Graph showing a comparative approximation of the different probabilities of survival at 10 years in young adult patients (15–45 years) with stroke and the general population aged 15–45 years

persons between 15–45 years in the Madrid community [32, 33]. While mean annual mortality for young adults with ischemic stroke at 10 years after the event was 1.2%, the annual mortality for people between 15–45 years was only 0.17%. This indicates that ischemic stroke in the young has a negative effect on survival. However, the mortality of young adults with ischemic stroke is much lower than in older patients, since survival at five years is more than 90% in the young and only 40% in the elderly [34].

The presence of cardiovascular risk factors (in particular, arterial hypertension [8]), completed stroke [8] and heart and/or vascular disease [8] have been associated with mortality in young adults with ischemic stroke. Our series also demonstrated that age above 35, male gender and unfavourable initial course are associated with higher risk of mortality. All these factors are associated with an atherosclerotic risk profile, which is present in older and male patients in whom premature atherosclerosis is much more prevalent [35] and prognosis is worse. Stroke due to dissection of extracranial arteries, stroke associated with migraine, poststroke anticoagulation therapy and hypercholesterolemia were associated with lower long-term mortality in our study. Our results show a good prognosis for patients with stroke associated with classical migraine. The role of therapy with oral anticoagulation in the reduction of long-term vascular mortality in young adults after ischemic stroke (relative risk of 0.3;  $p=0.05$ ) has yet to be explained, since this reduction only occurred in patients with cardioembolic stroke and those with undetermined multiple possible etiologies, who usually receive permanent oral anticoagulation, and not in patients with atherothrombotic or non-atherosclerotic vasculopathy strokes. The protective role of hypercholes-

terolemia therapy (relative risk of mortality of 0.3 in our study;  $p=0.03$ ) has recently been described, in the young [8] as well as in the elderly [36]. This is due to the neuroprotective effect of drugs such as statins or fibrates, which are prescribed in young adults with stroke and hypercholesterolemia.

Ischemic stroke caused by atherothrombosis and cardioembolism has been associated with a poor prognosis [7, 8, 37]. In our series, as in others [9], no specific etiology of ischemic stroke was identified as a statistically significant risk or protective factor for mortality. However, in bivariate analysis several causations showed a lower percentage of mortality: lacunar infarct (relative risk of 0.4;  $p=0.4$ ), non-atherosclerotic vasculopathy (RR: 0.4;  $p=0.1$ ), hypercoagulable state (RR: no event;  $p=0.3$ ) and unknown etiology (RR: 0.3,  $p=0.4$ ). This suggests that these four causes have a better prognosis.

With respect to functional recovery, the prognosis for young adults with stroke is good, especially when compared with the elderly. In our series, 90% of patients with a long-term follow-up were independent for all activities of daily living and 95% walked without any assistance in spite of previous stroke. These figures, similar to those in other series [7–9], reflect the low percentage of young adults with residual dependency after ischemic stroke (10% if we consider dependent a BI score less than 90 and 15% if we consider a mRS score higher than 2). This is different from the elderly, in whom 35–40% of patients with stroke are dependent on other persons after the stroke [38, 39]. However, ischemic stroke in the young leads to limitations in the

**Table 3** Studies about follow-up in young adults with stroke

	N	T	Follow-up (years)	t. s.
Hindfelt and Nilsson [15]	74	I	16	P
Marini et al. [8]	330	I	8	P
Kappelle et al. [7]	296	I	6	R
Lanzino et al. [22]	155	I	5.8	P
Camerlingo et al. [23]	135	I	5.7	P
Bogousslavsky [20]	38	I	3.8	C
Ferro and Crespo [16]	215	I	3.5	P
Leys et al. [9]	287	I	3	P
Chancellor [31]	59	I	3	R
Matías-Guiu et al. [24]	386	I	2.8	P
Hearer and Smith [26]	207	I + H	1.5–5	R
Grindal et al. [28]	34	I	2.7	R
Wells and Timberger [27]	77	I	0–2.5	R
Snyder and Ramirez [29]	52	I	2.4	R
Srinivasan [30]	46	I	2	R
Leno et al. [17]	81	I + H	1	P
Varona et al.	272	I	11.7	R

N number of patients; T stroke subtype; t. s. type of study; I ischemic; H hemorrhagic; R retrospective; P prospective; C consecutive cases

quality of life and occupational status [7, 22, 23, 40]. In our series, after a long-term follow-up, only 53% of young adults with stroke returned to work, and 23% of them had to make changes in their jobs due to their inability to perform the same activity after stroke. Other studies have reported similar figures [7, 8]. Transient ischemia (71%), undetermined stroke (69%) and non-atherosclerotic vasculopathy (64%) were associated with a higher probability of returning to work.

Furthermore, 22% had significant depression that required psychiatric assistance, 16% had frequent episodes of headache and 10% had poststroke seizures (a higher percentage than in other series [9]). In our series, the predictive factors for better long-term functional recovery and/or a return to work were age below 35, transient ischemic stroke, favorable initial course without severe handicaps at discharge and stroke associated with migraine and/or oral contraceptives. Other studies have described good functional recovery in stroke associated with migraine and oral contraceptives [9]. No etiology was significantly associated with a better or poorer functional recovery, but lacunar infarct and unknown etiology had a slightly better prognosis.

Recurrent stroke is frequent in the young (25% of our patients), but lower than in older patients, so cumulative recurrence rate at 5 years is almost half in the young (15.4%) than in older (29.5%) [41] patients. Recurrence is more frequent in patients with atherothrombotic (5.3% annual) than in those with non-atherosclerotic

vasculopathy (2.2%). Recurrent stroke may result in an important limitation in vital and functional prognosis; thus 16% of patients died as the result of the recurrence, 33% had severe handicaps with residual dependent status (while only 7% of patients without recurrence were dependent) and 51% received permanent disability pension as a result of the recurrent stroke. This finding underlines the importance of a proper secondary prevention therapy to avoid recurrence. The predictive factors for recurrence in our study were age over 35 years, the presence of cardiovascular risk factors (especially, diabetes mellitus) and atherothrombotic stroke in the carotid territory. Stroke associated with migraine and stroke due to extracranial arteries dissection had a lower risk of recurrence. As in other studies [1, 15, 22], patients with unknown etiology had a lower annual recurrent stroke rate than patients with other etiological subtypes.

In summary, our long-term study shows that less than 50% of young adults recover fully after the initial ischemic stroke, since an important percentage have significant declines in the quality of life. Being aged over 35 years and severe handicaps at discharge are associated with disability, and the atherosclerotic risk profile has the highest risk of recurrent stroke and mortality. Furthermore, an age below 35 years, an initial favorable course and the stroke associated with dissection, migraine and/or contraceptives are predictive factors for a good long-term outcome.

## References

- Bogousslavsky J, Pierre P (1992) Ischemic stroke in patients under age 45. *Neurol Clin* 10:113–124
- Shriver ME, Prockop LD (1993) The economic approach to the stroke work-up. *Curr Opin Neurol Neurosurg* 6:74–77
- Hart RG, Miller VT (1983) Cerebral infarction in young adults: a practical approach. *Stroke* 14:110–114
- Lidegaard O, Sol M, Andersen MVN (1986) Cerebral thromboembolism among young women and men in Denmark 1977–1982. *Stroke* 17: 670–675
- Nencini P, Inzitari D, Baruffi MC, et al. (1988) Incidence of stroke in young adults in Florence, Italy. *Stroke* 19: 977–981
- Marini C, Totaro R, De Santis F, Ciancarelli I, Baldassarre M, Carolei A (2001) Stroke in young adults in the Community-Based L'Aquila registry. Incidence and prognosis. *Stroke* 32: 52–56
- Kappelle LJ, Adams HP Jr, Heffner NL, Torner JC, Gomez F, Biller J (1994) Prognosis of young adults with ischemic stroke. A long term follow-up study assessing recurrent vascular events and functional outcome in the Iowa registry of stroke in young adults. *Stroke* 25:1360–1365
- Marini C, Totaro R, Carolei A (1999) Long-term prognosis of cerebral ischemia in young adults. *Stroke* 30: 2320–2325
- Leys D, Bandu L, Henon H, et al. (2002) Clinical outcome in 287 consecutive young adults (15 to 45 years) with ischemic stroke. *Neurology* 59:26–33
- National Institute of Neurological Disorders and Stroke (1990) Classification of cerebrovascular disease III. *Stroke* 21:637–741
- Adams HP Jr, Bendixen BH, Kappelle LJ, et al. (1993) Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical Trial. *Stroke* 23:35–41
- Goldstein LB, Jones MR, Matchar DB, et al. (2001) Improving the reliability of Stroke group Classification Using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) Criteria. *Stroke* 32:1091–1097
- Rankin J (1957) Cerebrovascular accidents in patients over the age of 60. II: Prognosis. *Scott Med J* 2:200
- Mahoney FI, Barthel DW (1965). Functional evaluation: The Barthel Index. *Md State Med J* 14:61–65
- Hindfelt B, Nilsson O (1977) The prognosis of ischaemic stroke in young adults. *Acta Neurol Scand* 55:123–130
- Ferro JM, Crespo M (1994) Prognosis after transient ischemic attack and ischemic stroke in young adults. *Stroke* 25:1611–1616
- Leno C, Berciano J, Combarros O, et al. (1993) A prospective study of Stroke in young adults in Cantabria, Spain. *Stroke* 24:792–795
- Rozenhul-Sorokin N, Ronen R, Tamir A, Geva H, Eldar R (1996). Stroke in the young in Israel. *Stroke* 27:838–841

19. Qureshi AI, Safdar K, Patel M, Janssen RS, Frankel MR (1995) Stroke in young black patients. Risk factors, subtypes, and prognosis. *Stroke* 26:1995–1998
20. Bogousslavsky J, Regli F (1987) Ischemic stroke in adults younger than 30 years of age: cause and prognosis. *Arch Neurol* 44:479–482
21. Marshall J (1982) The cause and prognosis of strokes in people under 50 years. *J Neurol Sci* 53:473–488
22. Lanzino G, Andreoli A, Di Pasquale G, et al. (1991) Etiopathogenesis and prognosis of cerebral ischaemia in young adults. A survey of 155 treated patients. *Acta Neurol Scand* 84: 321–325
23. Camerlingo M, Casto L, Censori B, et al. (2000) Recurrence after first cerebral infarction in young adults. *Acta Neurol Scand* 102:87–93
24. Matias-Guiu J, Alvarez-Sabin J, Falip R, Codina J (1991) Prognosis of ischaemic stroke in young adults. Presented at the ECST collaborators meeting; September 12–15; Edinburgh, Scotland
25. Abraham J, Shetty G, Jose CJ (1971) Strokes in the young. *Stroke* 2:258–267
26. Haerer AF, Smith RR (1970) Cerebrovascular disease of young adults in a Mississippi Teaching Hospital. *Stroke* 1:466–476
27. Wells CE, Timberger RJ (1961) Cerebral thrombosis in patients under fifty years of age. *Arch Neurol* 4:268–271
28. Grindal AB, Cohen RJ, Saul RJ, Taylor JR (1978) Cerebral infarction in young adults. *Stroke* 9:39–42
29. Snyder BD, Ramirez-Lassepas M (1980) Cerebral infarction in young adults: long-term prognosis. *Stroke* 11(2):149–153
30. Srinivasen K (1984) Ischemic cerebrovascular disease in the young: two common causes in India. *Stroke* 15: 733–735
31. Chancellor AM, Glasgow GL, Ockelford PA, Johns A, Smith J (1989) Etiology, prognosis and haemostatic function after cerebral infarction in young adults. *Stroke* 20:477–482
32. Instituto de Estadística. Consejería de Economía e Innovación Tecnológica. Comunidad de Madrid. Estadísticas del movimiento natural de la población de la Comunidad de Madrid 1999. III. Defunciones. 3 [3105] p 178
33. Censo de población. INE (MINECO). Padrón Municipal de habitantes. INE (MINECO).www.comadrid.es. May, 2003
34. Hankey GJ, Jamrozik K, Broadhurst RJ, et al. (2000) Five-years survival after first-ever stroke and related prognostic factors in the Perth Community Stroke Study. *Stroke* 31:2080–2086
35. Carolei A, Candelise L, Fiorelli M, Francucci BM, Motolese M, Fieschi C (1992) Long-term prognosis of transient ischemic attacks and reversible ischemic neurological deficits: a hospital-based study. *Cerebrovasc Dis* 2:266–272
36. Vauthey C, de Freitas GR, van Melle G, Devuyst G, Bogousslavsky J (2000) Better outcome after stroke with higher serum cholesterol levels. *Neurology* 54:1944–1949
37. Biller J, Adams Jr HP, Bruno A (1991) Mortality in acute cerebral infarction in young adults: a ten-year experience. *Angiology* 42:224–230
38. Dewey HM, Sturm J, Donnan GA, Macdonell RAL, McNeil JJ, Thrift AG (2003) Incidence and outcome of subtypes of ischaemic stroke: initial results from the North East Melbourne Stroke Incidence Study (NEMESIS). *Cerebrovasc Dis* 15:133–139
39. Bath PMW, Lees K (2000) Acute stroke. *BMJ* 320:920–923
40. Adunsky A, Hershkowitz M, Rabbi R (1992). Functional recovery in young stroke patients. *Arch Phys Med Rehabil* 73:859–862
41. Burn J, Dennis M, Bramford J, Sandercock P, Wade D, Warlow C (1994) Long-term risk of recurrent stroke after a first-ever stroke: the Oxfordshire community stroke project. *Stroke* 25: 333–337