Research in Progress

Italian Multicenter Study on Reversible Cerebral Ischemic Attacks: Population Characteristics and Methodology


CEREBRAL VASCULAR DISEASES in Italy have a mortality rate of 136/100,000/year, representing 15% of all deaths; these data, registered in 1975, do not differ from those of other countries. Preventive treatment of patients at risk is a guideline to reduce incidence and mortality of such severe diseases.

Patients with focal reversible cerebral ischemia (RIA) are considered those typically at risk of stroke and cerebrovascular death. Since many strokes are not preceded by RIAs, these latter unfortunately do not identify all "risk patients" however, the fact that these events are easily recognizable has served to direct much attention and research effort toward the prevention of ischemic phenomena in this special group of patients.

The natural history and aggravating factors of this disease arefar from being clarified and very few data are available in Italy; this is preliminary to any study of therapeutic efficacy and to correctly planning protocols of health care delivery. Therefore, in 1975 the Italian National Research Council (I.N.R.C.) included the present study in the Special Project Preventive Medicine: Atherosclerosis, to be carried on in a six year period, 1977–1982.

The goals of this research are: 1) to study the clinical, neuroradiological, neuropsychological and laboratory features of a consecutive population of patients with recent RIAs; 2) to record the modification of these data under close observation and treatment and to correlate the former to the incidence of new cardio- and cerebro-vascular events (new RIAs, strokes, myocardial infarction, death) for a subsequent period of four years. Clinical characteristics of the 462 patients form the object of this report.

Participating Units

This study (Organ Disease 2 (OD2) of the Special Project Preventive Medicine-Atherosclerosis of the I.N.R.C.) has been carried on in 12 Units (see Appendix):
1) Central biostatistical and epidemiological unit (Pisa);
2–3) Two neuroradiological consulting units (Padua and Rome);
4) One neuropsychological consulting unit (Modena);
5–12) Eight neurological or neurosurgical University Departments (Milan, Pavia I, Pavia II, Padua in Northern Italy; Siena, Florence, Rome in Central Italy; Naples in Southern Italy).

Eligibility

All consecutive patients were considered eligible if they had had:
1) one or more RIAs within the past 12 months (71% were within 1 month);
2) age less than 70 years.

Patients were hospitalized to complete the protocol at entry.

Exclusions

1) Patients with general (hepatic, renal) or cardiological contraindications to cerebral angiography (atrial fibrillation, recent myocardial infarction, embolic heart disease);
2) patients with an incomplete or unsuccessful angiographic study;
3) patients who refused to participate;
4) patients with neurological diseases other than cerebrovascular and/or with severe diseases placing the patient at risk of death within the following four years.

Participating units were asked to submit information on all patients excluded from the study.

Protocol

The clinical assessment at entry included:
1) medical history collected following the questionnaires of Rose and Blackbourne and original questionnaires;
2) neurological history for an extensive documentation of RIAs collected following the questionnaires of the American Heart Association;
3) neuropsychological evaluation of speech (Token test, Visual naming, Babcock's Sentence), of visuo-spatial abilities (Copying Drawings and Corsi's test), of memory (Digits Forward) was performed by single specialist for each unit, after a specific training provided by the Neuropsychological consulting unit. Details of this part of the study are reported elsewhere;
4) detailed medical and neurovascular examinations. Laboratory exams at entry included:
a) standardized blood chemistry tests submitted to quality controls;
b) electrocardiogram including an exercise stress activation;\textsuperscript{16}
d) chest and abdominal x-ray studies to identify arterial calcifications;
e) cerebral angiography with visualization of extra and intracranial arteries of the symptomatic territory performed in all patients under study. In many cases (30\%) the angiographic study was extended to four vessels.

Computerized tomography (CT) was performed in only 29\% of patients because in 1976 many units were not yet equipped. All radiological films were evaluated by the local neuroradiologist and subsequently by one or both of the consulting neuroradiologists.

All patients were re-evaluated every six months for 4 years. At each follow-up visit, the interim neurological and medical history was obtained and detailed neurological and medical examinations were repeated. Blood tests were also repeated at each follow-up visit, resting and stress testing ECG were repeated yearly for 4 years, neuropsychological tests were repeated at the first follow-up visit and at the end of the study.

Hospitalization was offered to repeat the entry protocol (including angiography) whenever new events had occurred.

During the study no compulsory treatment was adopted but general criteria were reinforced in scheduled discussions. No patients had been submitted to vascular surgery prior to entry.

Results of all follow-up data and of special studies on risk factors (including angiographical findings) are not the object of the present report and they will be subsequently reported. Preliminary reports on baseline studies\textsuperscript{15} and follow-up data at two years have been published.\textsuperscript{17, 18}

Definitions and Diagnostic Groups

According to the reported duration of the attack and results of the neurological examination, patients were considered as:

a) Transient Ischemic Attacks (TIAs) (subjective duration less than 24 hours, neurological examination absolutely normal);
b) Prolonged Transient Ischemic Attacks (P-TIAs)\textsuperscript{19} (subjective duration more than 24 hours, neurological examination absolutely normal within 4 weeks);
c) Transient Ischemic Attacks with Incomplete Recovery (TIA-IR)\textsuperscript{20} (subjective duration more or less than 24 hours with minimal residual symptoms after 4 weeks). Asymmetry of deep reflexes suffices to include patients as TIA-IR.

These three categories are grouped together as RIA (Reversible Focal Cerebral Ischemic Attacks).

According to established criteria\textsuperscript{21} vascular territories were defined as carotid (right or left) vertebrobasilar (V-B) mixed (V-B and carotid or bilateral carotid attacks in patients with multiple events) and undefined (patients presenting isolated hemianopia or pure motor paresis not extending to face, arm and leg).

Patients with isolated symptoms such as vertigo or diplopia were excluded from this study because they were considered as uncertain RIA patients.\textsuperscript{15}

Quality Control Study

The experimental protocol was identical to the first similar study performed in 1979 and each examiner was the same, for each center, as for the first study.\textsuperscript{22}

In this second study the effects of training on the quality of a multi-center study of RIAs have been evaluated.

Central Registry

The central biostatistical and epidemiological unit located at the University of Pisa was responsible for collection, analysis and storage of all data submitted by the participants.

Every six months a responsible investigator for each unit participated at “ad hoc” meetings to review all data and to discuss all instances of doubtful diagnosis.

Results

Six hundred twenty-two eligible patients (one or more RIAs within the past 12 months) were observed from 1977 to 1978. Four hundred sixty-two patients (74.3\%) actually entered the study.

Among the 160 excluded, 40\% of patients were older than 70 years, 26.2\% had severe diseases other than cerebrovascular, and 33.8\% refused participation in the study because of distant residence or for fear of angiography or because the latter was unsuccessful.

Among the 462 selected patients 75 (16.2\%) were TIAs, 25 (5.4\%) P-TIAs and 362 (78.4\%) TIA-IR. The main features of these three clinical groups are reported in table 1.

Followup ended in 1982 (results will be reported), and it was completed in more than 97\% of patients.

Sex, Age, Arterial Territory

The ratio male/female was 2.6 for all cases, 2.4 for TIAs, 2.1 for P-TIAs and 2.9 for TIA-IR patients. A test of marginal association between sex and these three diagnostic groups did not show significant differences ($X^2 = 3.74$ $P = 0.1538$).

The two decades 45–64 years included 73.3\% of males and 61.3\% of females. Patients below 45 years were 19.7\% of all cases including 26.7\% of TIAs, 4\% of P-TIAs and 19.3\% of TIA-IR patients.

A test of marginal association between age and diagnostic groups did not reach statistical significance ($X^2 = 6.91$ $P = 0.1538$).

Carotid attacks included 67.5\% of cases (52.9\% left, 41.0\% right and 61.1\% bilateral). 21.2\% of patients had vertebrobasilar attacks and in 8.9\% both carotid and V-B territory were involved (mixed-type patients). A diagnosis of arterial territory was not reached in 2.4\% of patients.

Ratio between carotid and V-B attacks was 3.2 in all cases, 1.7 in TIA, 1.7 in P-TIA and 3.9 in TIA-IR patients. This relatively higher frequency of TIAs in the V-B territory in contrast to the higher frequency of TIA-IR
in the carotid territory reached a statistical significance \( (X^2 = 20.92 \ P = 0.0019) \).

Among the remaining associations of 2nd and 3rd order between sex, age, arterial territory and clinical groups we found a significant association between sex and territory, with more carotid attacks in males in opposition to more V-B attacks in females \( (X^2 = 13.20 \ P = 0.0042) \).

### Symptoms

Table 2 lists symptoms of the carotid and V-B attacks. Aphasia and dysarthria are grouped together under the heading "speech," since they are not always differentiated by clinical history.

Carotid attacks included a number of nonspecific symptoms, besides specific ones such as unilateral motor, sensory and visual field defects and speech distur-

<table>
<thead>
<tr>
<th>Table 1 Clinical Groups</th>
<th>TIA</th>
<th>P-TIAs</th>
<th>TIA-IR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>75</td>
<td>25</td>
<td>362</td>
<td>462</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>53</td>
<td>17</td>
<td>270</td>
<td>340</td>
</tr>
<tr>
<td>Females</td>
<td>22</td>
<td>8</td>
<td>92</td>
<td>122</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 44</td>
<td>20</td>
<td>1</td>
<td>70</td>
<td>91</td>
</tr>
<tr>
<td>45-54</td>
<td>20</td>
<td>13</td>
<td>128</td>
<td>161</td>
</tr>
<tr>
<td>55-64</td>
<td>26</td>
<td>9</td>
<td>128</td>
<td>163</td>
</tr>
<tr>
<td>65-70</td>
<td>9</td>
<td>2</td>
<td>36</td>
<td>47</td>
</tr>
<tr>
<td>Arterial territory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.A.</td>
<td>41</td>
<td>14</td>
<td>257</td>
<td>312</td>
</tr>
<tr>
<td>V.B.</td>
<td>24</td>
<td>8</td>
<td>66</td>
<td>98</td>
</tr>
<tr>
<td>mix.</td>
<td>7</td>
<td>3</td>
<td>31</td>
<td>41</td>
</tr>
<tr>
<td>unknown</td>
<td>3</td>
<td>—</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Lengths of attacks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1 h.</td>
<td>53</td>
<td>—</td>
<td>76</td>
<td>129</td>
</tr>
<tr>
<td>1-24 h.</td>
<td>22</td>
<td>—</td>
<td>71</td>
<td>93</td>
</tr>
<tr>
<td>&gt; 24 h.</td>
<td>16</td>
<td>25</td>
<td>215</td>
<td>240</td>
</tr>
<tr>
<td>Number of attacks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>single</td>
<td>13</td>
<td>9</td>
<td>106</td>
<td>128</td>
</tr>
<tr>
<td>multiple</td>
<td>62</td>
<td>16</td>
<td>256</td>
<td>334</td>
</tr>
<tr>
<td>Months from single RIA to entry (multiple attacks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1 month</td>
<td>8</td>
<td>3</td>
<td>74</td>
<td>85</td>
</tr>
<tr>
<td>≤3 months</td>
<td>3</td>
<td>5</td>
<td>24</td>
<td>32</td>
</tr>
<tr>
<td>≤6 months</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>≤12 months</td>
<td>13</td>
<td>9</td>
<td>106</td>
<td>128</td>
</tr>
<tr>
<td>Months from last RIA to entry (multiple attacks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1 month</td>
<td>43</td>
<td>11</td>
<td>186</td>
<td>240</td>
</tr>
<tr>
<td>≤3 months</td>
<td>13</td>
<td>2</td>
<td>42</td>
<td>57</td>
</tr>
<tr>
<td>≤6 months</td>
<td>2</td>
<td>3</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>≤12 months</td>
<td>62</td>
<td>16</td>
<td>256</td>
<td>334</td>
</tr>
<tr>
<td>Months from first RIA to entry (multiple attacks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1 month</td>
<td>7</td>
<td>3</td>
<td>36</td>
<td>46</td>
</tr>
<tr>
<td>≤3 months</td>
<td>12</td>
<td>2</td>
<td>25</td>
<td>39</td>
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<tr>
<td>≤6 months</td>
<td>8</td>
<td>2</td>
<td>27</td>
<td>37</td>
</tr>
<tr>
<td>≤12 months</td>
<td>10</td>
<td>6</td>
<td>50</td>
<td>66</td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>25</td>
<td>3</td>
<td>118</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>62</td>
<td>16</td>
<td>256</td>
<td>334</td>
</tr>
</tbody>
</table>
We realize that these exclusions may underestimate the incidence of V-B attacks. We have listed vertigo (9.6%), dizziness (9%), abnormalities of vigilance (7.7%).

More than one-third (35.7%) of certified V-B attacks consisted of the association of two or more of the following: binocular visual symptoms, diplopia, dysarthria, vertigo, dizziness, drop attacks. Any of these, when isolated, were not accepted as symptomatic of focal ischemic attacks. The remaining 64.3% had one or more of the preceding symptoms associated with bilateral or alternate sensory-motor-visual field defects. We realize that these exclusions may underestimate "minor" V-B attacks.

### Length and Number of Attacks

Two hundred and twenty-two patients (48.1%) had attacks lasting less than 24 hours; in 58.1% of them the attacks lasted less than 1 hour.

However only 75 of these 222 patients (33.8%) have been listed as TIAs since 147 (66.2%) showed minimal persistent neurological signs compatible with the site of the "subjectively" reversible attacks.

Patients with pure TIAs had a ratio of "short" (less than 1 hour) to "long" (1-24 hours) of 2.4. By contrast, patients with anamnestic TIAs, but positive signs at neurological examination, had a ratio "short" to "long" episodes of 1.07. This difference is statistically significant ($X^2 = 6.93 P = 0.0085$).

Three hundred and thirty-four patients (72.3%) experienced multiple attacks and the remaining 128 (27.7%) had a single attack.

The attacks tended to recur in the same territory: in 82.0% of cases with multiple attacks, V-B or carotid attacks were repeated in the same territory, while the remaining 18% of cases had multiple attacks in different territories, either V-B plus carotid (41 cases) or bilateral carotid (19 cases).

Multiple attacks were significantly more frequent among TIA (82.6%) than TIA-IR patients (70.7%) ($X^2 = 7.43 P = 0.0244$ for the log linear model with sex and age).

A significant association was also found between length and number of attacks: patients with multiple attacks had a higher frequency of short attacks (less than 1 hour) in contrast to a higher frequency of episodes lasting 1-24 hours in patients with single attacks ($X^2 = 8.49 P = 0.0036$).

### Interval Between Attacks and Entry

More than two-thirds (70.3%) of patients (85 with single and 240 with multiple attacks) had their last (or only) attack within 30 days before entry (see table 1). 19.3% of patients (32 with single and 57 with multiple attacks) had their last (or only) attack within 30-90 days before entry and only 10.4% (11 with single and 37 with multiple attacks) within 3-12 months before entry.

Among the 334 patients with multiple attacks 25.5% had their first attack within 3 months before entry, 30.8% within 3-12 months and 43.7% earlier than 12 months before entry.

### Quality Control

#### a) Neurological Past History (table 3)

The concordance between any two examiners ranged between 85-89% (table 3) for numerical variables such as number of episodes, time of the first episode and duration of attacks. The concordance is lower (73-76%) for more qualitative information such as average frequency of attacks, type and occasion (at rest, in bed, . . .). Discrepancies, in the first subset of questions, mainly depended on the omission of reporting an early episode by one of the two examiners; the more recent the RIA, the more reliable its description.

#### b) Symptoms (table 4)

The recall of individual neurological target symptoms of attacks occurring within the past 12 months is reported with an agreement of 84% for motor symptoms (occurrence and site), of 73% and 61% respectively for verbal and sensory symptoms. Visual symptoms were reported by one or both observers in 17 patients only (30% of those included in the reliability

```
TABLE 2  Symptomatology

<table>
<thead>
<tr>
<th>Carotid Attacks</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory</td>
<td>9</td>
<td>(2.9)</td>
</tr>
<tr>
<td>Motor</td>
<td>36</td>
<td>(11.5)</td>
</tr>
<tr>
<td>Sensory-motor</td>
<td>81</td>
<td>(26.0)</td>
</tr>
<tr>
<td>Visual</td>
<td>3</td>
<td>(1.0)</td>
</tr>
<tr>
<td>Visual and sensory-motor</td>
<td>27</td>
<td>(8.7)</td>
</tr>
<tr>
<td>Speech</td>
<td>7</td>
<td>(2.2)</td>
</tr>
<tr>
<td>Speech and sensory-motor</td>
<td>149</td>
<td>(47.7)</td>
</tr>
<tr>
<td>Total</td>
<td>312</td>
<td>(100)</td>
</tr>
</tbody>
</table>

V-B Attacks

| Two or more symptoms* | 35  | (35.7)|
| One or more symptoms* associated with: | | |
| Motor                  | 16  | (16.3)|
| Sensory                | 22  | (22.4)|
| Sensory-motor          | 25  | (25.6)|
| Total                  | 98  | (100)|

*Binocular visual symptoms, diplopia, dysarthria, vertigo, dizziness, drop attacks.
```

A significant association was also found between length and number of attacks: patients with multiple attacks had a higher frequency of short attacks (less than 1 hour) in contrast to a higher frequency of episodes lasting 1-24 hours in patients with single attacks ($X^2 = 8.49 P = 0.0036$).

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TABLE 3  Quality Control: Index of Agreement on Features of Ischemic Episodes

<table>
<thead>
<tr>
<th></th>
<th>Index of agreement %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical territory</td>
<td>82%</td>
</tr>
<tr>
<td>Number</td>
<td>85%</td>
</tr>
<tr>
<td>Time of the first</td>
<td>87%</td>
</tr>
<tr>
<td>Frequency</td>
<td>73%</td>
</tr>
<tr>
<td>Duration</td>
<td>89%</td>
</tr>
<tr>
<td>Type</td>
<td>76%</td>
</tr>
<tr>
<td>Occasion</td>
<td>74%</td>
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TABLE 4  Index of Agreement on Neurological Signs and Symptoms: Sample Size of Quality Control Study = 55 Patients

<table>
<thead>
<tr>
<th>Neurological features</th>
<th>Total no. of patients with positive signs</th>
<th>Index of agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck bruits</td>
<td></td>
<td>43%</td>
</tr>
<tr>
<td>Visual field defects</td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Minor limb weakness</td>
<td></td>
<td>73%</td>
</tr>
<tr>
<td>Deep tendon reflexes</td>
<td></td>
<td>66%</td>
</tr>
<tr>
<td>Cranial nerves</td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Muscle tone</td>
<td></td>
<td>60%</td>
</tr>
<tr>
<td>Cerebellar</td>
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<td>14%</td>
</tr>
<tr>
<td>Ophthalmoscopic</td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Sensory</td>
<td></td>
<td>18%</td>
</tr>
<tr>
<td>Extensor plantar response</td>
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<td>38%</td>
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<tr>
<td>Motor</td>
<td></td>
<td>84%</td>
</tr>
<tr>
<td>Verbal</td>
<td></td>
<td>73%</td>
</tr>
<tr>
<td>Visual</td>
<td></td>
<td>47%</td>
</tr>
<tr>
<td>Sensory</td>
<td></td>
<td>61%</td>
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Discussion

The present record represents a true reflection of patients with focal reversible cerebral ischemic attacks (RIAs) observed by neurological and neurosurgical departments in Italy.

This population is biased by explicit sampling limitations:

a) our patients are referred or return spontaneously to the neurological institutions: subjects treated in the community, or by Depts. of Internal Medicine, of Vascular Surgery or Cardiology, are not included. This is a fact common to other studies; b) criteria of exclusion have eliminated 25.7% of patients observed in the recruiting period of two years. As a result, age is relatively lower than that observed in other studies and severe cardiopathies are excluded; c) All recruited patients have had at least one RIA within 12 months, independent of the fact that it was the first attack, or the last one of a series. 89.6% had the last (or only) attack within 3 months prior to entry.

The present case material is exactly the population seeking (spontaneously, or after their doctor’s advice) complete neurological workup, hence accepting hospitalization and angiography at this point in time (1977–1978). The amount of change following more diffuse knowledge of this condition and its risks (not to be uncritically overestimated) is hard to know and difficult to discuss at this time. A growing knowledge in the field allows us to state that TIAs “per se” may be less harmful than was previously thought as far as the hard endpoints (myocardial infarction, stroke, death) are concerned. On the other hand patients with TIA or minor stroke have been recently considered at risk of multi-infarct dementia.

The sample had the following main characteristics:

1) Males prevailed over females: other hospital series of TIA patients have found a similar male prevalence ranging from 60% to 68%.

2) There was a significant interaction between sex and territory: more carotid attacks occurred in males, more V-B attacks in females. This phenomenon was not influenced by age nor by clinical groups (TIA vs. TIA-IR).

3) Episodes with incomplete recovery (TIA-IR) prevailed over entirely reversible attacks, lasting less or more than 24 hours (TIAs and P-TIAs). This latter is a critical point: 48.1% of patients, in fact, stated to the examiner that they had recovered completely in less than 24 hours; yet, only ½ of the latter (16.2%) are classified as TIAs in the present study, since in the remaining ½ a detailed and expert neurological examination disclosed minimal but definite neurological signs. These minimal residual did not depend on the number of attacks, nor on the territory (V-B vs. carotid). Rather, the duration of attacks was important, since TIAs were more frequent in cases declaring recovery in less than 1 hour than in those whose attacks lasted 1–24 hours. Among protracted attacks (more than 24 hours) P-TIAs were a minority compared with TIA-IR. In agreement with Pessin we concluded that most “pure” TIAs last less than 1 hour, while those lasting longer tended to leave more minimal focal signs, even if not reported by the patient.
4) The patients were classified as TIAs, P-TIAs or TIA-IR according to the history plus the examination.
a) the ratio of carotid V/B attacks was 1.7 for TIA patients, quite similar to the ratio (1.9) observed in the Rochester study. Conversely in TIA-IR this ratio was significantly higher (3.9). This could mean either a more complete regression of V-B ischemia or a larger scope for minimal, non invalidating neurological signs in the larger carotid territory.
b) multiple attacks were reported by 72.3 of the patients but they were significantly more frequent in TIA (82.6%) than in TIA-IR patients (70.7%). Patients with multiple attacks had a higher frequency of short attacks in contrast to a higher frequency of episodes lasting 1–24 hours in patients with a single attack.
5) The lack of other clinically relevant differences between these three subgroups of RIAs favours the unifying hypothesis. Moreover the present "reliability study" shows that this differentiation is not based on solid ground. "Minimal" signs are reported by the examiners with such inconsistency, as to make them a non-objective criterion of classification, in a multi-center study at least. In fact, the lack of interobserver reproducibility of the neurological examination has remained essentially the same as in our previous reliability study:22 the average agreement for four items of the examination of the motor system was 60% in the first, and 62% in the present study. In addition, it is important to comment upon the real day to day variability of the neurological status and the poor concordance between pathological (or CT) demonstrations of small infarcts, and neurological signs. All this renders the subdivision between TIA and TIA-IR less realistic. For descriptive purposes we have kept these subgroups separated but, in our opinion, the term RIA should be used in diagnostic and therapeutic studies to indicate all episodes of reversible ischemic neurological deficit independent of duration (less or more than 24 hours) and on persistence of minor permanent signs without subjective complaint. Before advocating this we wish to evaluate results of the diagnostic and follow-up studies.
6) The repeated reliability study, while showing no improvement of inter-observer reproducibility of neurological examination, has indicated a positive effect of training in recording anamnestic data. Average agreement in details of the clinical history improved from 62% to 78% between the first22 and the present study; diagnosis of the arterial territory of RIA improved from 65.4% to 82.0%.
This improvement indicates that even specialized examiners benefit by specific training in the performance of multi-center studies on RIAs.

7) All these discussions might be of less importance if among the RIA patients the risk of a subsequent stroke depended more on the angiographic or other laboratory findings than on clinical characteristics. However, among the latter the arterial territory, the multiplicity and the interval between episodes are commonly accepted criteria. Among the large proportion (72.3%) of patients with multiple attacks the interval between the first attack and entry is quite variable: 25.5% had their first attack within 3 months but 43.7% reported the first episode earlier than 12 months before entry. The relevance of this interval and of other clinical characteristics to prognosis will be subsequently analyzed. These baseline data will be compared with the neuro-radiological, cardiological and laboratory findings and with the follow-up data at four years to identify possible subgroups of patients with different risk of stroke or death.

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References


APPENDIX

Special Project Ischemic Brain Disease OD2

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