Hemiplegics after a First Stroke: Late Survival and Risk Factors

PABLO SOLZI, M.D., HAIM RING, M.D., THEODORE NAJENSON, M.D., AND YAIR LUZ, I.E.

SUMMARY Scanning 3000 cases admitted for rehabilitation after cerebrovascular accident over a 20-year period produced a sample of 1369 subjects, without age restrictions, admitted within six months of a first stroke of thrombotic etiology.

In this sample, survival rates showed no significant difference between men and women. Age at onset, however, clearly influenced survival chances; the expected mean survival was 6 years at 40 and 2 at age 80; average loss of life was 14 years for the whole sample, meaning a vital prognosis two to three times worse than that of the general population.

At least 86% of the sample presented one or more of five etiological antecedents to stroke: hypertensive heart disease, peripheral vascular disease, diabetes mellitus, myocardial infarction and atrial fibrillation. In 87% of those, HHD and/or PVD were present. Presence of hypertension significantly lowered life expectancy and so did PVD; their influence is felt from the earliest stages. In contrast, diabetes mellitus, the next most common factor, has a late influence, starting about the fifth year after stroke. MI and AF were present in relatively fewer patients, but they contributed towards a considerable decrease in life expectancy, evident from the first stages, the more drastic reduction being observed in the AF group.

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STROKE is recognized as both a killer disease and a major cause of disability. Consequently, in recent years, more research has been directed towards the study of its etiology, incidence, effect on mortality rates and, finally, of means which might help to prevent its occurrence. At the same time, great progress has been recorded in the rehabilitation of stroke-disabled patients and in the improvement of their chances of both surviving and living a satisfactory life afterwards.

This work studies in retrospect data on patients after cerebrovascular accidents causing hemiplegia who were hospitalized at the Loewenstein Rehabilitation Center (Ra'anana, Israel) over a period of twenty years. Its purpose is twofold: to assess the survival rates of these patients after their admittance for rehabilitation, and to identify risk factors which, besides provoking C.V.A. onset, might in the long run affect these patients' mortality and survival rates.

Materials and Methods

About 3,000 records built up in the years 1958–1977 were screened according to the following criteria: stroke was of a clearly vascular origin, the patient had had a single stroke prior to admittance, and the patient had been admitted for rehabilitation within six months from onset of C.V.A.

This selection left 1700 well-documented cases answering the criteria and constituting the sample for this investigation. Each file was attentively studied. The first item to be checked was the patient's status, using the State of Israel population registry; death dates of those deceased were noted down. The following item was etiology. Cases whose etiology could not becontestably established were left out and the remaining cases were classified into five groups, in whom stroke had been caused by:

TABLE 1 Break Down by Etiology and Sex (Average Age Given)

<table>
<thead>
<tr>
<th>Cause of accident</th>
<th>Total no of patients (ABS)</th>
<th>%</th>
<th>Men N</th>
<th>Age (years)</th>
<th>%</th>
<th>Mean</th>
<th>SD</th>
<th>Women N</th>
<th>Age (years)</th>
<th>%</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malformation of brain arteries</td>
<td>24 100</td>
<td></td>
<td>11 46</td>
<td>37 17</td>
<td></td>
<td>13</td>
<td>54</td>
<td>45 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>109 100</td>
<td></td>
<td>28 26</td>
<td>50 11</td>
<td></td>
<td>81</td>
<td>74</td>
<td>53 14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>72 100</td>
<td></td>
<td>41 57</td>
<td>55 12</td>
<td></td>
<td>31</td>
<td>43</td>
<td>58 12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embolism</td>
<td>126 100</td>
<td></td>
<td>77 61</td>
<td>61 12</td>
<td></td>
<td>49</td>
<td>39</td>
<td>58 14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td>1369 100</td>
<td></td>
<td>828 61</td>
<td>64 10</td>
<td></td>
<td>541</td>
<td>39</td>
<td>66 10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1700 100</td>
<td></td>
<td>985 58</td>
<td>63 11</td>
<td></td>
<td>715</td>
<td>42</td>
<td>63 11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Valvular heart disease (generally causing embolism, though not altogether precluding thrombosis) (109 cases).
3. Clear-cut cases of brain hemorrhage (72 cases).
4. Clear-cut cases of embolism not included in Group 2 (126 cases).
5. Cerebral arterial thrombosis (1369 cases). After the previous groups had been defined, the remaining patients may be assumed to constitute a homogeneous group in the sense that the stroke mechanism is uncontestably of the thrombotic type. Diagnosis is limited, of course, to the methods and techniques available during the 20-year period of data-gathering, and cannot now be refined in the light of modern advances.

Tables 1 and 2 present general characteristics of the complete population of 1700 cases. In table 1, etiological groups are broken down by sex, in table 2, by the incidence of major pathological findings preceding the first cerebrovascular accident. Note that for thrombosis the prevalence of diabetes is double that for other groups. Myocardial infarct is most frequent in embolism-induced strokes and hypertensive heart disease is the major finding prevalent in cases of hemorrhage. Virtually all cases of arterial malformation were characterized by retinopathy, also highly prevalent in all other etiological types.

Statistical analyses of survival rates were performed by means of programs available at the Computer Center of Tel-Aviv University: BMDP1L and SPSS "SURVIVAL." The results of these methods are quite similar; both programs are limited to one-way analysis, i.e. can handle one factor at a time, for any number of patient groups. In the course of preparing this paper multivariate survival analysis (BMDP2L) became available and was used to complete the findings from the one-way techniques.

In defining risk factors on the strength of the patients' medical histories up to the first stroke, we applied the following criteria:
1. Hypertensive heart disease (HHD) was diagnosed if a past history of elevated blood pressure was recorded (at least three findings of diastolic B.P. of over 100 mm Hg); or in the presence of either ECG evidence of left ventricle hypertrophy or hypertensive retinopathy. The final classification was based on the consensus of two independent medical researchers.
2. Diabetes mellitus (DM), blood hyperglycemia and glucosuria were diagnosed on the evidence of at least three samples showing sugar level.
3. Peripheral vascular disease (PVD) was diagnosed on the strength of clinical data and, where performed, of oscillometric findings.
4. Myocardial infarction (MI) was diagnosed only where ECG showed characteristic changes.
5. Atrial fibrillation (AF) was also diagnosed on the base of ECG changes; in most patients it appeared in chronic form.

Results

In figure 1 we present the life expectancy rates obtained for the five etiological categories described above, with a total of 1,700 patients. The difference in survival between those groups is highly significant. This, together with those shown in tables 1 and 2, adds up to a considerable list of group-distinguishing characteristics setting the thrombotic group apart from all the other etiological categories: distribution of sex and mean age, distribution of CVA-concomitant diseases,
distribution of life expectancy rates, and proportion in the total number of patients accepted for rehabilitation (the thrombotics constitute 80% of the total).

We feel therefore justified in concentrating now on this category, which is large and homogeneous in composition. Sixty-one percent are male and 39% female; both constitute the oldest strata in all the etiological types (about 65 ± 10 years of age). The incidence of diabetes prior to the advent of stroke is by far the highest (31%), and that of arterial hypertension, while less than that found among the embolism patients, is still very high (58%). Myocardial infarction occurred in 22% of all thrombotics.

In both one-way and multivariate analysis, we found that patient sex does not affect survival. On the other hand, age at time of stroke is a significant factor, as seen from figure 2. Its relationship with other factors will be examined further on.

The risk factor most frequently encountered was hypertensive heart disease (HHD). Figure 3 compares the survival times of those who had and those who had not HHD. The hypertensive patients' survival expectancy is significantly lower than that of the non-hypertensives.

Peripheral vascular disease (PVD) also significantly influences survival (fig. 4). Diabetes, the next most common factor, is doubly interesting: it is very frequent among thrombotic CVA patients, and its influence on survival is felt at a later stage, roughly after the fifth year. It may be appreciated from figure 5 that during the earlier stage there is very little difference between diabetics and other "thrombotics"; at later stages the differences becomes highly significant.

Both myocardial infarction and atrial fibrillation (fig. 6 and 7 respectively) are represented by relatively small groups; while this certainly points to their relatively low frequency as factors preceding stroke, their presence nevertheless considerably affects fatality after stroke.

We can appreciate the influence of each risk factor in table 3: patients with atrial fibrillation had the most drastic reduction in life expectancy; those with diabetics had the longest average survival period.

Using linear approximations, we derived regression curves enabling us to compute mean survival chances (fig. 8) and to predict the average loss of life expectancy relative to the expectancy of the general population (fig. 9) as functions of age at time of stroke. In figure 8 we see that the mean survival to be expected at age 40 is just under 6 years after stroke, the curve gradually dropping to just 1 year after 90. The average loss in life expectancy is...
A general exposition of the relative and joint prevalence of the five risk factors discussed is in order. Out of 1,369 subjects, in 1,179 cases (86% of the sample), the presence of at least one factor was ascertained. For the remainder, the absence of the five risk factors may be safely assumed. Out of the 1,179, 496 presented one factor only, while 683 disclosed various combinations of two to four factors. None had all the five, and in only 8 cases (out of 59) did AF appear alone (table 4).

If we take the ratio of appearance of a factor alone vs. all the cases where it was present, we find 35% for HHD, round 19% for PVD and diabetes, and round 13 for MI and AF.

Further food for thought can be found in the composition of the multi-factor combinations (table 5):

1. Out of 26 cases with four-factor combinations, atrial fibrillation was absent in 21 and PVD in only 2. All contained HHD.
2. In 188 cases three-factor combinations were present; only 20 did not include HHD and 33 lacked PVD.
3. Among the 469 patients showing two-factor combinations, about a third had no HHD and almost a half lacked PVD.
4. Out of 496 appearance of single factors, 56% were of HHD and 20% of PVD.

We tested whether age differentials might not underlie the significance found for the various risk factors.

For each factor, the age distribution of subjects with and without that factor was checked (table 6). At the bottom of the table, we may see that the subjects dead and censored also had similar distributions. Not surprisingly, those free of the various diseases were, on the average, slightly younger. Though a synergistic interaction between age and the other risk factors (as between those factors themselves) is not to be discounted, it appears from the evidence that age differentials cannot, by themselves, explain the significant effects detected for the risk factors. Again, this is confirmed by the results of age stratification tests shown in figure 2.

Multivariate analysis allows us to formulate a joint model and to test the contribution of each factor or combination of factors to the complete model. We find that all the risk factors examined are of importance, and their relative weight is assessed by the program, as shown in table 7. The most important is age, with HHD, PVD and diabetes occupying a slightly lower position. MI and atrial fibrillation come last, because of their lower frequency and therefore reduced overall impact.

However, it is also important to keep in mind the influence of each factor in those cases where it is present: those factors that appear the less important for the whole sample involve the strongest risk for the limited sub-groups presenting them. This should not be overlooked or overshadowed by the results of multivariate analysis, since it greatly affects the prognosis of such patients.

Discussion

This investigation tested the presence of six main risk factors at the onset of cerebro-vascular accidents (CVA) and their influence on the survival of the population of patients accepted for rehabilitation at the Loewenstein Rehabilitation Center over a period of twenty years. From over 3,000 admittances, 1,700 were selected for our database and carefully documented. A further refinement was the elimination of cases of non-thrombotic etiology, leaving 1,369 clinically defined thrombotics. This sample size should ensure a fair representation of the possible modalities of thrombosis; this is regarded as a clinically homogeneous category in need of rehabilitation.
TABLE 3 50-percent Survival Periods for Patients Presenting Given Risk Factors (in Months from Stroke)

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Survival period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>51</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>38</td>
</tr>
<tr>
<td>Peripheral vascular dis.</td>
<td>56</td>
</tr>
<tr>
<td>Hypertensive heart dis.</td>
<td>50</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>62</td>
</tr>
</tbody>
</table>

The study's main significance lies in the provision of guidelines — from both the medical and care provision standpoints — to the life expectancy of patients admitted for rehabilitation. Evidently, it applies to subjects who survived the acute phase, with impairments that cannot be attended to in ambulatory clinics, yet show a reasonable capability for benefiting from the rehabilitation process. The concept of rehabilitation through the efforts of a multidisciplinary team, as practised at the Loewenstein Hospital, is becoming universally accepted; the results obtained with such a large sample should prove of interest to other rehabilitation hospitals or wards.

The overall population from which our patients were drawn covers about 75% of the Israeli population and is not limited to any particular age group, social stratum, region, trade, ethnic group or hospital area of service. We trust that this and the other characteristics described will make it an important forerunner for further investigations into both general and specific populations of rehabilitation patients.

A further benefit derived from the uniform system of registration throughout the Histadrut Sick Fund with which our Hospital is affiliated is the completeness of data on previous heart conditions. This probably explains our finding that only 14% of the patients had no previous history of cardiovascular risk factors, while Aho found 26% among aged patients and 36% among younger ones.

Of the various problems that could be profitably investigated, we have chosen two aspects: co-morbidity (the presence of various risk factors) and survival expectancy. We do compare our findings with some of the results published, without forgetting that, given the different characteristics of the populations investigated, any comparisons must be made with the utmost circumspection. Among works published there were community studies; there were hospital studies; age-distributions were not always comparable or even reported; some samples did not include patients older than 65 years, which naturally enhances the life expectancy. None specifically considered the population surviving the first month (with its high mortality) and referred for rehabilitation.

The Presence of Different Risk Factors

Practically all the authors concur on the paramount importance of hypertension and HHD as risk factors for stroke: Whisnant, Matsumoto, Eisenberg, Kagan, Rabkin, Okada, Sahs and their co-workers. Beevers found significant differences in stroke recurrence after anti-hypertensive therapy (from 55% to 16%). Kannell in one of the Framingham cohort studies found the risk of stroke three-fold in patients with congestive heart failure or ECG signs of LVH; and sixfold in the presence of acute or chronic atrial fibrillation. Diabetes mellitus has also been mentioned as a risk factor. Olivares placed it as the third in importance; the Framingham team found a high risk associated with even a mild impairment of glucose tolerance. In another of their studies, Wolff points out the importance of AF in stroke etiology; we found that its presence dramatically reduces life expectancy.

In our sample HHD appeared as the most frequent

![Figure 8. Average years of survival vs. age at time of stroke.](http://stroke.ahajournals.org/)

![Figure 9. Average life expectancy loss vs. age time of stroke.](http://stroke.ahajournals.org/)

![Table 4 Frequency of Appearance of Five Risk Factors, Singly or Coupled](http://stroke.ahajournals.org/)
factor, both in isolation and coupled with others; in 56% of single-factor cases; in 70% of all two-factor combinations; in 89% of three-factor cases and in all four-factor combinations. HHD appeared alone in one-third of all cases where it was present; PVD and diabetes in 20%; myocardial infarction and atrial fibrillation in only 13% of all instances. This might suggest a complex mechanism whereby the most virulent factors require, as a rule, the concurrence of other impairments to cause stroke and to shorten survival chances.

Survival Expectancy

Evidently, the presence of various risk factors before stroke and their influence on ultimate survival are different problems. The latter aspect has been less highlighted by researchers.

In our sample of thrombotics, the median survival time was 5.2 years for men and 4.9 years for women. This represents an average loss of 14 years relative to the life expectancy of general populations (ranging from a loss of 5 years for those aged 80 to a loss of 30 years for those of age 40). Among risk factors, the highest curtailment of life is due to the presence of atrial fibrillation (31 months compared to other patients); myocardial infarction, hypertensive heart disease and peripheral vascular disease cause a median loss ranging from 21 down to 18 months. The impact of diabetes mellitus is felt mostly after the fifth year from onset; its presence reduces life expectancy by 10 months.

Table 6  Age Distributions of Subjects With or Without Various Risk Factors, Dead and Censored (in percents)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Up to 54</th>
<th>55-64</th>
<th>65-74</th>
<th>75+</th>
<th>Mean age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive heart disease +</td>
<td>13.3</td>
<td>34.5</td>
<td>38.2</td>
<td>14.0</td>
<td>64.8</td>
</tr>
<tr>
<td>-</td>
<td>15.8</td>
<td>29.8</td>
<td>34.4</td>
<td>20.1</td>
<td>64.9</td>
</tr>
<tr>
<td>Peripheral vascular disease +</td>
<td>11.4</td>
<td>28.8</td>
<td>40.7</td>
<td>19.1</td>
<td>66.0</td>
</tr>
<tr>
<td>-</td>
<td>16.1</td>
<td>34.8</td>
<td>34.1</td>
<td>15.0</td>
<td>64.1</td>
</tr>
<tr>
<td>Diabetes mellitus +</td>
<td>10.7</td>
<td>32.4</td>
<td>41.0</td>
<td>15.9</td>
<td>65.7</td>
</tr>
<tr>
<td>-</td>
<td>16.0</td>
<td>32.6</td>
<td>34.6</td>
<td>16.9</td>
<td>64.5</td>
</tr>
<tr>
<td>Myocardial infarction +</td>
<td>10.1</td>
<td>31.2</td>
<td>42.3</td>
<td>16.4</td>
<td>66.0</td>
</tr>
<tr>
<td>-</td>
<td>15.5</td>
<td>32.9</td>
<td>35.0</td>
<td>16.6</td>
<td>64.5</td>
</tr>
<tr>
<td>Atrial fibrillation +</td>
<td>6.8</td>
<td>23.7</td>
<td>42.4</td>
<td>27.1</td>
<td>68.8</td>
</tr>
<tr>
<td>-</td>
<td>14.7</td>
<td>32.9</td>
<td>36.3</td>
<td>16.1</td>
<td>64.7</td>
</tr>
<tr>
<td>Death</td>
<td>10.4</td>
<td>31.9</td>
<td>37.4</td>
<td>20.3</td>
<td>-</td>
</tr>
<tr>
<td>Censored</td>
<td>18.4</td>
<td>33.2</td>
<td>35.7</td>
<td>12.7</td>
<td>-</td>
</tr>
</tbody>
</table>

According to researchers, the most virulent factors require, as a rule, the concurrence of other impairments to cause stroke and to shorten survival chances.

Conclusion

Out of the sample of 1369 patients referred for rehabilitation within six months of a first stroke of thrombotic etiology, at least 86% presented one or more of the following antecedents: hypertensive heart disease, peripheral vascular disease, diabetes mellitus, myocardial infarction and atrial fibrillation (the first two were present in 87% of these cases). The average loss of life expectancy postulated on the predicted mean survival time as function of age at time of stroke was 14 years.

Regarding the effect of different traits on survival, four main points emerge: (a) there is no clearcut difference between sexes; (b) all five risk factors significantly influence survival; (c) AF appears with the least frequency (usually with other factors) and when it does, markedly curtails life expectancy; (d) the strongest single influence is that of age, but it was established that the other five factors maintain the same relative effect over different age strata. We should like to see comparable results from other sources.

Acknowledgments

The authors gratefully acknowledge the contributions of Dr. Stella (Dolly) Appelman-Yoffe in data collection, screening and coding, and of Jedisa Brachfield, B.A., who prepared and edited the manuscript. Useful contributions to the statistical side of this study were made by the late Professor M.B. Tartakovsky.

References

Factors Contributing to Stroke in Patients with Atherosclerotic Disease of the Great Vessels: The Role of Diabetes

JESSE WEINBERGER, M.D., VICTORIA BISCARRA, R.N., MICHAEL K. WEISBERG, B.S., AND JULIUS H. JACOBSON, M.D.

SUMMARY The incidence of carotid artery disease and cerebrovascular symptoms were determined in 102 consecutive patients with peripheral arterial disease. Symptoms were correlated with risk factors of age, hypertension, smoking and diabetes and with the extent of disease at the carotid bifurcation. The incidence of stroke with permanent neurological deficit was twice as high in diabetics as in non-diabetics with equivalent atherosclerotic vascular disease (p < .05). In women, the incidence of stroke was three times higher in diabetics (p < .02). The number of transient ischemic attacks was significantly higher in non-diabetics (p < .02). The total number of ischemic episodes in diabetics and non-diabetics was equivalent. This indicates that diabetics are more prone to irreversible destruction of ischemic brain tissue regardless of the nature of the circulatory disturbance.

THE ASSOCIATION OF Atherosclerotic DISEASE at the carotid artery bifurcation with both transient ischemic attack and stroke is firmly established. However, a large proportion of patients with carotid disease remain asymptomatic. In addition, the majority of patients with transient ischemic attacks do not develop irreversible neurologic deficits. Therefore, it is imperative to determine what factors are responsible for permanent damage to neurons when the brain is subjected to disruption of circulatory perfusion.

In order to delineate the role of disease of the great vessels in stroke, we examined 102 consecutive patients with atherosclerotic peripheral arterial disease (PAD) who were referred to the vascular laboratory for non-invasive carotid artery testing. While this group of patients is not randomly selected, they all had a similar propensity to atherosclerotic arterial disease of the great vessels so that valid comparisons of other factors can be made.
Hemiplegics after a first stroke: late survival and risk factors.
P Solzi, H Ring, T Najenson and Y Luz

Stroke. 1983;14:703-709
doi: 10.1161/01.STR.14.5.703

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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