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Lacunar Infarction, Mortality Over Time And Mortality Relative to Other Ischemic Strokes

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Objectives.—Determine the overall mortality after lacunar infarction and compare it to the overall mortality after atherothrombotic and cardioembolic strokes. Determine the pattern of increased mortality over time after lacunar infarction.

Methods.—The clinical literature was searched for articles providing mortality data on lacunar infarction having at least 5 years of post stroke follow up. Three such articles were identified, two of which also had post stroke mortality data on the other two types of ischemic stroke, atherothrombotic and cardioembolic stroke. Degree of overall increased mortality was determined for all three stroke types and increased mortality over time was determined for laccunar infarction as well. Standard mortality methodology was used and expectant mortality was determined using appropriate population life tables. Average overall mortality ratios (MR) and average overall excess deaths per thousand per year (EDR) were determined by weighting for the number of entrants in each study.

Results.—The average overall MR for lacunar infarction = 159%, for atherothrombotic stroke = 213% and for cardioembolic stroke = 322%. The mortality ratios for lacunar infarction for the following post-stroke intervals were: 1–5 years = 166%; 6–10 years = 153%; and 11–14 years = 106%.

Conclusions.—Lacunar infarction from onset is associated with moderately increased overall mortality relative to the general population. Post-stroke mortality risks from atherothrombotic and cardioembolic strokes are significantly higher.

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Ischemic strokes, responsible for more than 80% of all strokes, are due to 3 main mechanisms, lacunar infarction, atherothrombosis involving both the extra- and intracranial arteries and cardioembolic events. Demographic trends in aging along with increased survival of those having coronary atherosclerotic heart disease imply that there will likely be increased numbers experiencing ischemic stroke in the coming years. Lacunar infarcts are responsible for up to one quarter of all ischemic strokes.[1] They are relatively small in size (<15 mm) and result from occlusions of subcortical penetrating arteries arising from major arteries of the intracerebral circulation. Central brain structures, including the thalamus, basal ganglia, internal capsule, corona radiata and brainstem are usually affected. Clinically, lacunar infarcts are characterized by well-described syndromes including pure motor hemiparesis, pure sensory stroke and sensorimotor stroke. There should be an

absence of cortical findings such as aphasia, apraxia or hemi-neglect and, typically, there is no associated depression of consciousness or seizure activity. In the past, lacunar infarcts were considered rather benign with a relatively good long term outcome. Initial recovery was rapid relative to other strokes, presumably due to the small primary lesion. However, in recent years it has been recognized that, although initially demonstrating a favourable course, lacunar infarcts, after the passage of four or five years, are associated with increased risk for mortality and recurrent stroke not unlike that found in strokes of other etiology.[1,2]

The purpose of this article is to review the mortality associated with lacunar infarction, especially early mortality, and compare that to mortality due to other causes of ischemic stroke as presented in the studies evaluated.

MATERIAL AND METHODS

The clinical literature was reviewed for relatively recent studies having at least 5 years of follow-up concerning mortality due to lacunar infarction. Three were identified for mortality assessment, two from Sweden and one from Rochester, Minnesota. The longest study included 14 years of follow-up on patients admitted to a stroke unit in Linkoeping, Sweden in 1986, including 47 suffering from lacunar infarction.[3] The second study, also from Sweden, evaluated a group of 178 patients suffering from pure motor stroke due to lacunar infarction who were followed for 10 years.[4] The Rochester, MN study assessed outcomes, including survival, of individuals found to have ischemic stroke in the late 1980s, including 72 with lacunar infarction.[5] Study population characteristics of the latter article are found in a companion paper, also authored by Petty.[6] Data permitting determination of mortality due to atherothrombotic and cardioembolic stroke are found in both the Linkoeping, Sweden and Rochester, MN studies as well.

Mortality rates from these 3 studies were determined using established mortality methodology.[7] Expectant population mortality was derived from the Human Mortality Database (located at: www.mortality.org) for the two Swedish studies. Through the progression of study years, the interval mortalities for each gender were derived from the corresponding year's mortality for that specific age. For example, if a male was 75 in 1986 the corresponding annual qx from the male 1986 Swedish population life table was used. The next year the corresponding annual qx for age 76 from the 1987 Swedish population life table was used, and so forth, for both genders, through the duration of the respective studies. The 1989–1991 United States Minnesota Decennial population life table was used for the Petty study from Rochester, MN. The mortality rates for both observed and expected populations were determined using geometric average annual mortality from which the mortality ratios (MR) and the excess death rates (EDR) were determined. Expected populations were interpolated appropriately for gender and appropriate expected population equivalent-age determinations were made according to methods discussed by Dr. Richard Singer[8] and presented by Dr. David Winsemius.[9] All MR represent observed study mortality relative to unselected general population mortality.

RESULTS

The results are presented in two tables. Table 1 records the respective research articles along with their study locations, years, patient demographics and entrant survivals over time. Table 2 presents the geometric average annual observed and expected mortality rates, the mortality ratios and excess death rates. Each table presents the above information grouped by type of ischemic stroke (survival data for atherothrombotic and cardioembolic strokes are found only in the Petty[5] and Eriksson[3] articles). Overall

Table 1. Lacunar Infarction

Study Author	Study Site (Study years)	Entrants (No.)	Mean Age (Yrs.)	% Male	Overall Survival (%)		
					5 Years	10 Years	14 Years
Lacunar Infarction							
Staaf et al[4]	Sweden (1983–1999)	178	72.5	59.6	68	34.5	
Petty et al[5]	Rochester, MN (1985–1992)	72	73 (±10)	43	65		
Eriksson[3]	Sweden (1986–2000)	47	70.6	55.3	62	37.5	28
Atherothrombotic Stroke							
Petty et al[5]	Rochester, MN (1985–1992)	74	72 (±11)	67.6	67.5		
Eriksson[3]	Sweden (1986–2000)	191	71.1	45	50.5	26	16
Cardioembolic Stroke							
Petty et al[5]	Rochester, MN (1985–1992)	132	80 (±12)	33.3	20		
Eriksson[3]	Sweden (1986–2000)	71	78.3	36.6	31.5	12.5	5.5

average MR and EDR (weighted per number of respective study entrants) are presented for each type of stroke. Interval MR and EDR (similarly weighted) are presented for lacunar infarction as well.

Lacunar Infarction Experience

The overall mortality is found to be moderately elevated (MR = 159%) with interval mortality rates progressively falling from the first 5-year interval MR of 166%. Mortality after 10 years (only available in the Eriksson study) was demonstrated to be minimal (MR = 106%).

Atherothrombotic and Cardioembolic Stroke Mortality

The overall mortality was significantly higher than that of lacunar infarction with MR = 213% for atherothrombotic stroke and 322% for cardioembolic stroke.

The EDR for cardioembolic stroke was extremely high at 157.4.

DISCUSSION

Mortality in the initial years after lacunar infarction has previously been described as minimal, increasing mortality becoming apparent after 4 to 5 years. The article authored by Staaf[4] has similar conclusions with increased mortality relative to age and sex-matched controls becoming apparent after 4 years (see Figure 1.) In the Staaf article the expected population mortality was determined thusly: ''Survival rates for the whole normal Swedish population, matched for age and sex for the actual time period, were calculated and compared with corresponding data for the patient group by means of a computer program (SURV 2, version 2.01) developed for the Finnish Cancer Registry.''[4] We don't know what criteria were used for classifying an individual as ''normal.'' It is apparent that Staaf's expected population has mortality that varies from that of the Swedish population life tables used in this paper. Staaf's study population had an average age of 72.5 years with an extremely broad range from ages 28 to 97, making determination of the optimal expected population equivalent-age difficult (age 75 was chosen) and possibly inaccurate. This fact along with some potential expected population selection bias in the Staaf article may account for some (but not all) of the observed discrepancy. In contrast to Staaf's findings, when mortality methodology, using expected general population mortalities, is applied to these three survival analyses an opposite and consistent pattern is discernible. Increased mortality appears in

Table 2. Lacunar Infarction

		Lacunar Infarction											
		Observed mort ($\hat{q}$)			Expected mort. ($\hat{q}'$)			Mortality Ratio ($\hat{q}$ / $\hat{q}'$ × 100) %			Excess Deaths / 1000 / Year		
	Yrs. post lacunar infarct	0–5	6–10	11–14	0–5	6–10	11–14	0–5	6–10	11–14	0–5	6–10	11–14
Study Author	Staaf et al[4]	.0742	.1269		.0551	.0858		135	148		19.1	41.1	
	Petty et al[5]	.0825			.0443			186			38.3		
	Eriksson[3]	.0912	.0957	.0704	.0362	.0550	.0662	252	174	106	55.0	40.6	4.2
	Interval Averages (Weighted per Number of Study Entrants)							166	153	106	29.4	41	4.2
	Overall Average (Weighted per Number of Study Entrants)								159			32.9	
	Atherothrombotic Stroke												
	Petty et al[5]	.0755			.0510			148			24.6		
	Eriksson[3]	.1277	.1243	.1143	.0365	.0578	.0882	349	215	130	91.1	66.5	26.1
	Overall Average (Weighted per Number of Study Entrants)								213			52.8	
	Cardioembolic Stroke												
	Petty et al[5]	.2752			.0688			400			206.4		
	Eriksson[3]	.2063	.1688	.1856	.0754	.1191	.1796	274	142	103	130.9	49.7	5.9
	Overall Average (Weighted per Number of Study Entrants)								322			157.4	

the first 5-year period and persists through the second 5-year period, becoming much less after 10 years. The overall mortality due to lacunar infarction is moderate (overall MR = 159%) and significantly less than that due to the other types of ischemic strokes. Atherothrombotic strokes (overall MR = 213%) have a better prognosis than cardioembolic strokes (overall MR = 322%). This same hierarchy of ischemic stroke mortality severity has been previously documented.[8] It appears that average age of onset for lacunar infarction and atherothrombotic stroke is about the same (71 to 73 years) whereas that of cardioembolic stroke is older (about 79 years of age). There is a significant increase in expected mortality between ages 72 and 79, which makes the high cardioembolic stroke EDR of 157.4 very helpful in appreciating the true mortality risk represented by the cardioembolic type of stroke.

Stroke etiology is not the only factor to consider in determining post-stroke prognosis. It is known that functional status after ischemic stroke is also associated with long term survival.[10] We have some indication of post stroke functional status in Eriksson's article[3] although no mortality calculations can be made. Of the entrants having lacunar infarction, 57.5% were classified as having a ''minor'' stroke, 31.9% a ''moderate'' and 10.6% a ''major'' stroke. To better characterize these categories it is helpful to consider the modified Rankin Scale (mRS) method of classifying post stroke function.[11] Minor stroke (mRS 2 or less) refers to those who have, at worst, slight disability but are able to look after all of their own affairs without assistance. Moderate stroke (mRS 3) is classified as having a degree of disabilitly requiring some help from others but the individual is able to ambulate without assistance. Major stroke refers those who have moderately severe disability requiring assistance of another with bodily needs and with ambulation (mRS4 or worse). In contrast to lacunar infarction, Eriksson found that those suffering from atherothrombotic and cardioembolic strokes had the following respective classifications: ''minor'' 53.9%, 31.0%, ''moderate'' 15.7%, 14.0% and ''major'' 30.4%, 55.0%. The functional impairment after lacunar infarction is found to be relatively less and this certainly contributes to the better prognosis of this type of stroke.

The numbers of entrants and length of follow up represented by the studies considered in this article ideally would be larger. However, when placed in context of Norrving's review ''Long-term prognosis after lacunar infarction,''[2] it might be concluded that this article reports the best of ''long-term'' mortality information available regarding lacunar infarction. Norrving's review sites 23 articles, of which only 6 had more than 150 entrants and only 3 had duration of follow up greater than 4 years. One of those with longer follow up was a Japanese study, the other two are included in the 3 studies considered in this paper. Perhaps some bias is introduced in the Staaf article[4] because only presumed lacunar infarcts due to pure motor stroke were considered rather than a broader spectrum of lacunar infarction deficits. Finally, there is always concern regarding accuracy of diagnosis and this is especially true for lacunar infarction where up to 50% of CT or MRI scans done acutely show no infarct at all, with the diagnosis being made clinically.

CONCLUSIONS

Early mortality due to lacunar infarction is not as favourable as has been described and actually is slightly higher in the first 5-year period than in years 6 through 10. After 10 years, increased mortality risk from lacunar infarction appears to diminish to relatively minimal levels. Overall mortality risk after lacunar infarction is significantly less and post stroke level of function significantly better relative to cardioembolic stroke with mortality risk and level of function being intermediate for atherothrombotic

stroke. Further studies having larger numbers and longer follow up periods are needed for more accurate determination of mortality risk due to lacunar infarction.

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