

## ORIGINAL ARTICLES

### A comparative study of stroke subtypes between Asians and Caucasians in two hospital-based stroke registries

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#### Abstract

Stroke pattern may differ among different ethnic groups. We carried out a prospective, comparative study between two hospital-based stroke registries - at the University Hospital, Kuala Lumpur and the Austin Hospital, Melbourne - comparing an Asian stroke population with a Caucasian one.

We noted differences in the stroke subtypes. Lacunar infarction and intracerebral haemorrhage were more common in Malaysians and cardioembolic strokes were more common in Australians. There were significant differences in the risk factors for stroke with diabetes mellitus, smoking, hypercholesterolaemia and hypertriglyceridaemia more common in the Asian group while the Caucasian group were older and had more atrial fibrillation.

The older age and greater frequency of atrial fibrillation may contribute to the greater percentage of cardioembolic strokes among the Austin Hospital patients. However, the differences for other stroke subtypes between the two groups could not be explained by analysis of the other known risk factors.

*Key words:* Stroke subtypes, risk factors, Asian, Caucasian, comparative study

#### INTRODUCTION

Stroke is a common neurological disorder that is the third most common cause of death in many countries. There is a wide variation in the mortality rate of stroke in Asia. The mortality rate varies from 16/100,000 population in Malaysia (1981) to 197/100,000 population in Japan (1967-1973).<sup>1</sup> The most likely cause for this disparity is the lack of case ascertainment due to improper data collection in developing countries. Stroke incidence also varies; the incidence of stroke ranges from 182 to 342/100,000 population in Asia.<sup>2</sup> The stroke incidence is relatively lower in Europe (Western more than Eastern) compared to the Chinese (in Beijing) in the WHO MONICA project.<sup>3</sup> There may be intraregional differences as well. The mean age-adjusted stroke incidence in Harbin, China (1986-1990) at 486.4 per 100,000 is 2.5 times higher than Beijing (191.8 per 100,000).<sup>4</sup> The incidence of stroke in Harbin, China is probably among the highest in the world.

Stroke subtypes may differ among different ethnic groups. In the United States, blacks have been found to have a higher incidence of

intracerebral haemorrhage and lacunar infarction compared to whites.<sup>5</sup> The Chinese in Hong Kong are also said to have more small vessel disease viz. lacunar infarcts and haemorrhages.<sup>6</sup> The pattern of cerebrovascular disease is said to be intracranial atherosclerosis rather than extracranial carotid disease.<sup>7</sup> There has, however, been no direct comparative study between an Asian and Caucasian patient population with regards to stroke subtypes.

We carried out the first prospective, comparative study between two hospital-based stroke registries at the University Hospital, Kuala Lumpur, Malaysia, and the Austin Hospital, Melbourne, Australia. The purpose is to compare the major subtypes of stroke and their risk factors between the two ethnic groups, namely an Asian population and a Caucasian population.

#### MATERIALS AND METHODS

In 1994, the University Hospital Stroke Registry (UHSR) was established at the University Hospital, Kuala Lumpur. This is a hospital-based stroke registry. All patients that were admitted in the year from 1.1.1994 till 31.12.1994

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to the hospital with a clinical diagnosis of stroke were seen by a study neurologist (W.K.N.) on admission. History was obtained and physical examination performed on admission. A brain computed-tomography (CT) scan was carried out in all cases. If the CT scan was normal or did not show an area of infarction/haemorrhage that was consistent with the clinical diagnosis, a CT scan was repeated one week later.

Electrocardiogram, chest X-ray, routine haematological and biochemistry tests were done in all cases. Fasting lipid profiles were measured within 48 hours of stroke or delayed for three months to avoid inaccurate measurement.<sup>8</sup> Doppler-ultrasound of the extracranial carotid and vertebral vessels were done in most patients who suffered a cerebral infarct. Magnetic resonance imaging (MRI), cardiac echocardiography and investigations for rare causes of thrombophilia were performed in clinically warranted cases. Risk factors for atherosclerosis were assessed. These include a past medical history of diabetes mellitus, hypertension, smoking, hyperlipidaemia, atrial fibrillation and previous transient ischaemic attack or stroke.

Data were recorded on pre-coded interview forms and entered into a computer database. The patients were subdivided into several stroke subtypes based on clinical assessment and investigations. The subtypes are defined as follows:

- (1) *Large vessel atherosclerotic infarct*: Stroke with a cortical infarction on initial/late CT scan or with evidence of cortical signs and symptoms. The cause is presumably due to large vessel atherosclerosis.
- (2) *Lacunar infarct (Small vessel disease)*: Stroke presenting as a lacunar syndrome defined as a pure motor hemiparesis, pure sensory stroke, sensorimotor stroke or ataxic hemiparesis and confirmed lacunar infarct on CT. There should be no cortical signs.
- (3) *Cardioembolic infarct*: Stroke with the presence of a potential cardiac source of embolism.
- (4) *Intracerebral haemorrhage*: Stroke with evidence of intracerebral haemorrhage on immediate CT scan.
- (5) *Stroke of determined cause*: Stroke in the young with evidence of a definite cause of

thrombophilia or hypercoagulable state.

- (6) *Stroke of undertermined cause*: Stroke in the young with no cause demonstrable after extensive investigations.
- (7) *Transient ischaemic attacks*: Transient focal neurological deficits lasting less than 24 hours with complete resolution of symptoms and signs. The symptoms may be an amaurosis fugax or related to a hemisphere.

In 1995, the author spent eight weeks at the Austin and Repatriation Medical Centre, Heidelberg, Melbourne, Australia subtyping the Austin Hospital Stroke Registry (AHSR) of the year 1994 into similar subtypes. The data from Austin Hospital was also prospectively collected in the same year. The data was subsequently combined for comparative analysis.

The differences between the two study groups were determined using the  $\chi^2$  test for categorical data and *t*-test for continuous data. Logistic regression analysis was used to determine the odds ratio of risk factors for each stroke subtype. A value of  $p < 0.05$  was adopted for statistical significance.

## RESULTS

There were 413 patients in the UHSR in 1994. The racial breakdown consist of 201 (48.7%) Chinese, 118 (28.6%) Malays, 86 (20.8%) Indians and 8 (1.9%) other races. The proportion of the racial breakdown is about the same as the ethnic breakdown of the admission to the University Hospital in that year. 245 (40.7%) were males and 168 (59.3%) were females. The mean age of patients in the UHSR is 61.8 years (SD 12.9, Range 14 - 90 years).

In the Austin Hospital Stroke Registry (AHSR) for 1994, there were 375 patients, 195 (52%) male and 180 (48%) female. All were Caucasian. The mean age was 70.39 years (SD 12.0, Range 21 - 94 years). Patients in Australia were older than patients in Malaysia ( $p < 0.001$ , *t*-test). The age range of the patients are shown in Figure 1.

The subtypes of stroke in the Asian (UHSR) and Caucasian (AHSR) are summarised in Table 1 and Figure 2. We find that there are more patients with lacunar infarction ( $\chi^2 = 10.2$ ,  $df = 1$ ,  $p = 0.001$ ) and intracerebral haemorrhage ( $\chi^2 = 4.7$ ,  $df = 1$ ,  $p = 0.03$ ) in UHSR patients compared to AHSR patients. Conversely, there are more patients with cardioembolic strokes in

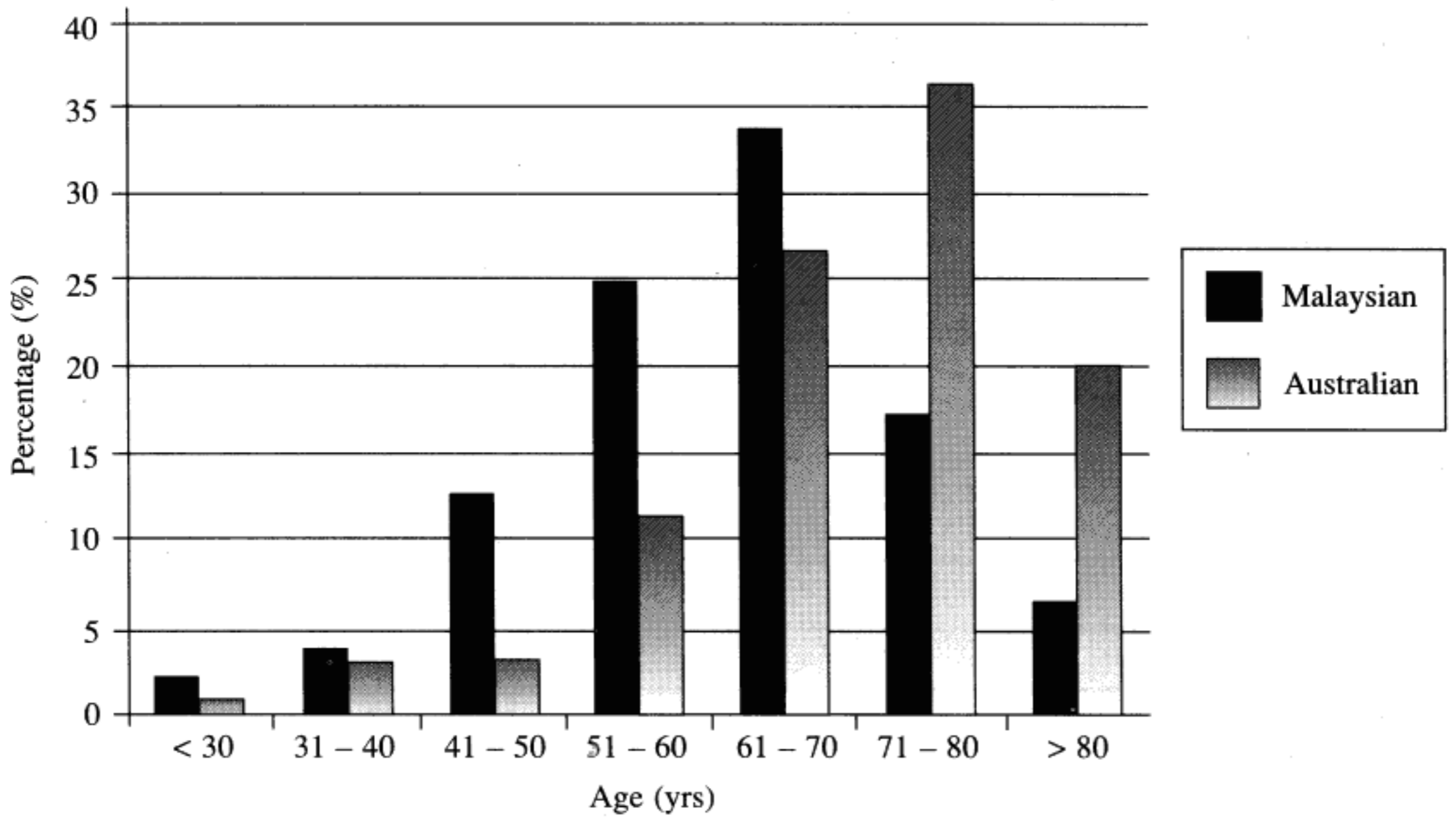


FIG. 1: Age range of patients in the UHSR and AHSR

the Austin Registry ( $\chi^2 = 14.6$ ,  $df = 1$ ,  $p = 0.001$ ). There were no significant differences between the two groups for other stroke subtypes.

We compared the stroke risk factors between the two study populations and found that diabetes mellitus ( $p < 0.00001$ ), smoking ( $p < 0.0005$ ), hypercholesterolaemia ( $p < 0.00001$ ) and hypertriglyceridaemia ( $p < 0.00001$ ) were more common among UHSR patients. However there were more atrial fibrillation among the AHSR

patients ( $p < 0.0005$ ). The comparison of risk factors between the two groups for all stroke subtypes is shown in Table 2.

In an attempt to determine whether differences in risk factors between the two stroke populations can explain the differences in the stroke subtypes, we analysed risk factors for lacunar infarction, intracerebral haemorrhage and cardioembolic strokes - stroke subtypes which were different between the two study groups - compared to

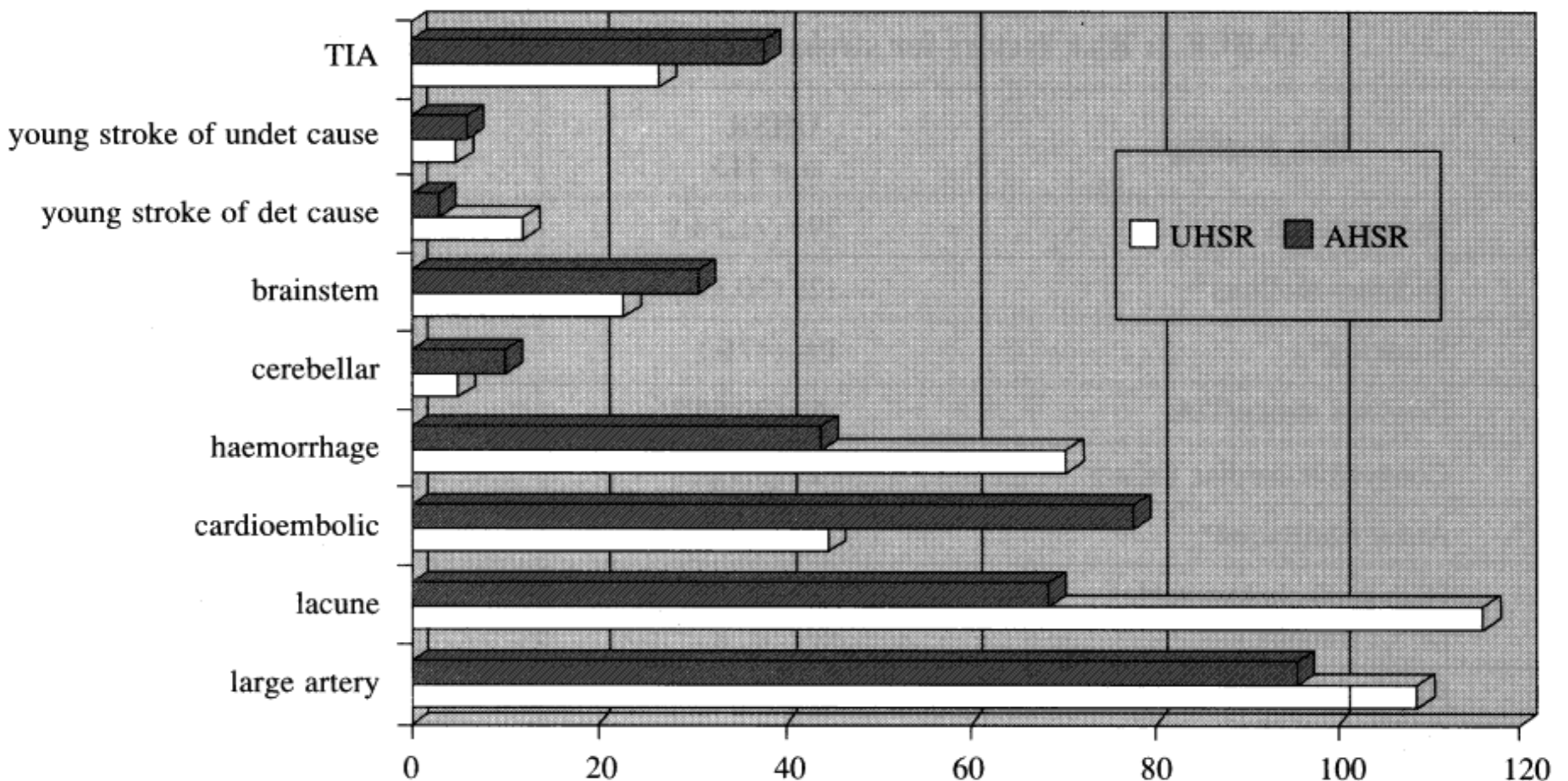


FIG. 2: Comparison of stroke subtypes between UHSR and AHSR for year 1994

**TABLE 1: Stroke subtypes in the UHSR and AHSR (1994)**

Stroke Subtype	University Hospital Stroke Registry (UHSR) n = 413		Austin Hospital Stroke Registry (AHSR) n = 375	
	Number	%	Number	%
Large artery infarct	109	26.4	96	25.6
Lacunar infarct*	116	28.1	69	18.4
Cardioembolic infarct*	45	10.9	78	20.8
Intracerebral haemorrhage*	71	17.2	44	11.7
Cerebellar infarct	5	1.2	10	2.7
Brainstem infarct	23	5.6	31	8.3
Young Stroke of determined cause	12	2.9	3	1.0
Stroke of undetermined cause	5	1.2	6	1.6
Transient Ischaemic Attack	27	6.5	38	10.1

\**P* < 0.05

other stroke subtypes as a whole for all patients in the two registries. Using univariate analysis, we find that high serum cholesterol was significant for lacunar infarction (66.5% for lacunes vs. 48.8% for non-lacunes) and hypertension was significant for intracerebral haemorrhage (83.9% vs. 71.8%). Atrial

fibrillation (63.4% vs. 1.5%) and age (mean 69.8 years vs. 65.2 years) were significant for cardioembolic strokes. However, taken into further logistic regression, no risk factors were found to have a significant odds ratio for the stroke subtypes of interest. Tables 3 and 4 list the risk factors for each of the major stroke

**TABLE 2: Risk factors for stroke in the UHSR and the AHSR**

<u>Risk Factors</u>	<u>UHSR</u> n = 413	<u>AHSR</u> n = 375
Hypertension	294 (71.2%)	285 (76%)
Diabetes mellitus*	125 (30.3%)	50 (13.3%)
Smoking*	194 (47%)	126 (33.6%)
Previous stroke/TIA	85 (20.6%)	62 (16.5%)
Congestive cardiac failure	22 (5.3%)	14 (3.7%)
Atrial fibrillation*	29 (7.0%)	59 (15.7%)
High total cholesterol* (> 5.2 mmol/L)	288 (69.7%)	129 (34.4%)
High serum triglyceride* (> 1.9 mmol/L)	135 (32.7%)	62 (16.5%)

\**P* < 0.05

**TABLE 3: Risk factors for large vessel-infarction and lacunar infarction in UHSR and AHSR:**

Risk factors	Large artery infarction				Lacunar infarct			
	Malaysia n = 109		Australia n = 96		Malaysia n = 116		Australia n = 69%	
	No	%	No	%	No	%	No	%
Hypertension	71	65.1	72	75	84	72.4	57	82.6
Diabetes Mellitus	45	41.2	12	12.5	42	36.2	11	15.9
Prior stroke or transient ischaemic attack	33	30.3	12	12.5	25	21.5	15	21.7
Smoking	54	49.5	37	38.5	57	49.1	28	40.6
Alcohol > 30 g/day	17	15.6	45	46.9	20	17.2	40	57.9
Congestive cardiac failure	4	3.6	2	2.0	0	0	1	1.4
High total cholesterol > 5.2 mmol/l	73	66.9	34	35.4	92	79.3	30	43.4
High triglyceride > 1.8 mmol/l	34	31.2	14	14.5	52	44.8	10	14.5

**TABLE 4: Risk factors for cardioembolic strokes and intracerebral haemorrhage in UHSR and AHSR**

Risk factors	Cardioembolic strokes				Intracerebral Haemorrhage n = 71			
	UHSR (n = 45)		AHSR (n = 77)		UHSR (n = 71)		AHSR (n = 44)	
	No	%	No	%	No	%	No	%
Hypertension	28	62.2	57	73.1	60	84.5	36	81.8
Diabetes Mellitus	6	13.3	12	15.4	11	15.5	3	6.8
Smoking	20	44.4	20	25.6	28	39.4	15	34.1
Previous Stroke or TIA	6	13.3	17	21.8	8	11.2	2	4.5
Congestive Cardiac Failure	16	35.5	10	12.8	9	12.6	1	2.3
High total cholesterol (> 5.2 mmol/l)	28	62.2	23	29.5	22	30.9	4	9.1
High Triglyceride (> 1.9 mmol/l)	24	53.3	10	12.8	19	42.2	3	6.8

**TABLE 5: Cause of cardioembolic infarct of both UHSR and AHSR**

Potential cardioembolic cause	University Hospital Stroke Registry n = 45		Austin Hospital Stroke Registry n = 78	
	Number	%	Number	%
Valvular atrial fibrillation	4	8.8	2	2.6
Non-valvular atrial fibrillation	20	44.4	56	71.2
Dilated cardiomyopathy	13	2.9	7	8.9
Prosthetic Heart Valves	1	2.2	3	3.8
Sick Sinus Syndrome	1	2.2	0	0
Infective endocarditis	1	2.2	1	1.2
Patent foramen ovalae	0	0	6	7.7
Recent acute myocardial infarct	5	11.1	2	2.5

subtypes among the two study groups. Table 5 list the causes of cardioembolic strokes among the two groups.

## DISCUSSION

Stroke pattern differs among different ethnic groups. Accurate classification of stroke subtypes is found in the prospective, community-based studies. In the Perth Community Stroke Study, large artery infarction accounted for 47.3% of all first ever strokes while lacunar infarction accounted for only 10% of strokes.<sup>9</sup> In the Harvard Cooperative Stroke Registry an estimated 18% of 756 consecutive stroke cases were lacunar infarction.<sup>10</sup> In the Oxfordshire Community Stroke Project 108/515 (21%) of first ever strokes in a population based study, were lacunar infarction.<sup>11</sup>

In 1991, 52 out of 240 (21.7%) of strokes in a hospital-based stroke registry in Taiwan were lacunar strokes.<sup>12</sup> In Hong Kong, 117/540 (21.7%) patients in a hospital-based study are having lacunar infarction.<sup>13</sup> In the Shatin stroke registry in Hong Kong, 18.5% of strokes were due to lacunar infarction.<sup>14</sup> While these studies have raised the possibility that lacunar infarction may be more common among Asian patients, the shortcoming of these studies were the lack prospective data collection and a uniform method of stroke subtyping. In the earlier stroke registries, often very little neuroimaging (for example computed tomography (CT) scan) were carried out. This may lead to inaccurate

classification of stroke subtypes. However, large prospective community based studies on stroke require large financial support and manpower. In developing countries with limited resources, prospective hospital-based studies will give an estimate of stroke pattern and subtypes.

The UHSR and AHSR are prospectively collected data of two hospital-based stroke registries with standardised subtyping of strokes comparing between an Asian vs. a Caucasian population. We find that lacunar infarction and intracerebral haemorrhage were more common and cardioembolic strokes less common in the UHSR compared to the AHSR in this study. Lacunar infarction is the most common stroke subtype in the Malaysian patients. This study confirms that Asians have more lacunar strokes compared to Caucasians.

The lacunar infarct has long been believed to be due to a microangiopathy of penetrator vessels as a result of longstanding hypertension leading to the pathological entity of lipohyalinosis as described by C. M. Fischer.<sup>15</sup> However, many have challenged the invariable association of hypertension and lacunes.<sup>16</sup> Furthermore, a proportion may be due to small vessel disease impinging on the origin of small penetrators.<sup>17</sup> The prevalence of hypertension in the UHSR is 71.2% vs. 76% in the AHSR. There is no significant difference in the prevalence of hypertension between the two study groups. Diabetes mellitus, hypercholesterolaemia, hypertriglyceridaemia and smoking are more

common risk factors in the UHSR compared to the AHSR. Malaysian patients were also younger compared to the Australian patients. It is tempting to consider whether the higher frequency of these risk factors among Malaysian stroke patients explain the more common occurrence of lacunar strokes in the UHSR. However on multivariate analysis, we were unable to find any of the above risk factors significant.

Cardioembolic infarction on the other hand, is more common among Caucasians 78/375(20.8%) vs. 45/413(10.9%). (Table 4) The most common cause of cardioembolic stroke among patients in both groups is non-valvular atrial fibrillation. The proportion of patients with atrial fibrillation was higher and the mean age of patients in the AHSR is about 10 years older than that of the patients in the UHSR. (Figure 1) As the prevalence of non-valvular atrial fibrillation increases with age,<sup>18</sup> the higher incidence of cardioembolic stroke among Caucasians may be explained in part by the older stroke population. The proportion of atrial fibrillation for the population in Busselton, Western Australia increases from 1.1% in the 60-64 age group to 15% in the age group greater than 75 years.<sup>19</sup>

Intracerebral haemorrhage is more common in UHSR 71/413(17.2%) vs. 44/375 (11.7%). In the UHSR, 85% of patients have hypertension, making primary hypertensive intracerebral bleed the most common cause of cerebral haemorrhage. Primary intracerebral haemorrhage accounted for 66/675 (10%) of patients in the Oxfordshire Community Stroke Project and hypertension preceded the stroke in 58% of cases.<sup>20</sup> In the Lausanne Stroke Registry in Switzerland, 109/1000 (10.9%) of strokes were due to intracerebral haemorrhage.<sup>21</sup> The prevalence of intracerebral bleed in a population based cohort study of 8,562 people followed up for 4 years in Taiwan is 22%.<sup>22</sup> In a review of stroke among the Chinese, the proportion of patients with intracerebral haemorrhage was estimated at between 25 to 30% and was thought to be more common compared to western (Caucasian) series.<sup>23</sup> This impression is further confirmed in our study in which the study population included Chinese but also Malays and Indians.

Comparative studies using hospital-based stroke registries does have its limitations. Not all patients with a stroke in a defined area will present to the hospital. Minor strokes and deaths at home will go undetected. Nonetheless, the diagnosis of all patients presenting to a hospital allows accurate subtyping of stroke.

This study showed that when comparing two prospective hospital-based stroke registries there exist major differences between stroke subtypes among Asians and Caucasians. There are more lacunar infarcts and intracerebral haemorrhage but less cardioembolic strokes in Asians compared to Caucasians. We were however unable to explain this differences on the basis of differences in the known risk factors for stroke.

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