



Classification analysis of young stroke in zhuhai city, China

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Abstract

Background: The morbidity and mortality rates in young Chinese stroke patients have increased, and the appropriate classification of stroke is very important to identifying the cause, pathogenesis, severity, outcome, and preventive and therapeutic strategies. This study sought to analyse the young stroke subtype in a coastal city Zhuhai of southern China.

Methods: Hospitalised young stroke patients in the two largest local hospitals were retrospectively analysed from July 2002 to July 2009. The percentage of every stroke subtype was calculated.

Results: A total of 416 young stroke patients (age 18–45 years) were included. There were 225 (54.1%) cases of ischemic stroke (IS), 145 (34.9%) cases of intracerebral haemorrhage (ICH), 38 (9.1%) cases of subarachnoid haemorrhage (SAH), and 8 (1.9%) cases of mixed stroke (MS). Cases of IS were divided into four groups using the OCSP criteria: 15 (6.7%) total anterior circulation infarcts (TACI), 117 (52.0%) partial anterior circulation infarcts (PACI), 61 (27.1%) lacunar infarcts (LACI), and 32 (14.2%) posterior circulation infarcts (POCI). Cases of IS were divided into five groups using the TOAST criteria: 14 (6.2%) cases of large-artery atherosclerosis (LAA), 15 (6.7%) cases of cardioembolism (CE), 108 (48%) cases of small-artery occlusion (SAO), 16 (7.1%) cases of stroke of other determined aetiologies (SOE), and 72 (32%) cases of stroke of undetermined aetiology (SUE).

Conclusions: The results suggested that within the locality, the majority of cases of young stroke were IS and ICH, and the minority were SAH and MS; additionally, the most common IS subtypes were PACI, LACI or SAO and SUE, which could contribute to the local prevention and control of stroke.

Keywords: Young stroke, subtype, OCSP, TOAST, China

Introduction

In recent years, studies have shown that morbidity and mortality rates in young Chinese stroke patients have increased [1,2] and the hospitalisation rates of young American stroke patients have also tended to rise [3]. Young adults with stroke have longer expected survival rates relative to older people with stroke, and young adults are more likely to be gainfully employed after stroke occurs than the very elderly. Therefore, more attention should be paid to the prevention and control of young stroke [4]. The aetiology of stroke is heterogeneous, and the aetiology, risk factors, and prognosis of young stroke are different from those of older stroke [5]. Additionally, variations in the aetiology and risk factors in different areas lead to variant stroke incidences and subtypes [6,7]. Therefore, the proper classification of stroke is critical to indicate the cause, pathogenesis, severity, outcome and preventive and therapeutic strategies [8,9]. The city of Zhuhai is an emerging economic power with a subtropical marine climate on the coast of southern China. Its population has increased yearly, and inland immigrants and migrant workers account for more than 80% of the population, most of whom are young and postadolescent adults. Currently, the subtypes of young stroke within this region remain unclear. This study aimed to analyse these subtypes in order to facilitate the local prevention and

control of stroke.

Methods

Patients

Young patients (aged between 18 and 45 years) with first-ever acute stroke who were hospitalised at our hospital and at Zhuhai People's Hospital (the two largest local hospitals) from July 2002 to July 2009 were included in the study. The diagnosis of stroke met the World Health Organization criteria [10] and was verified by brain CT/MRI or lumbar puncture. Traumatic strokes, intracranial tumours or infections, demyelinating lesions of the brain, concurrent severe insufficiencies of internal organs, and mutilations or malformations of limbs originated by other causes were excluded. The patients' medical records were retrospectively analysed by an attending neurologist specialising in stroke. The data extracted from the case history, medical and neurological examinations, laboratory reports (routine blood examinations, blood glucose, blood lipids, liver and renal function tests, blood electrolytes, blood C-reactive proteins, erythrocyte sedimentation rates, hemorheology and cerebrospinal fluid), electrocardiograms and imaging tests (chest x-ray, Cranial CT/CTA, Cranial MRI/MRA, Cranial DSA, colour Doppler ultrasonography of the carotid/vertebral artery and heart, transcranial Doppler) were entered into a database. The

Table 1. Baseline characteristics (n = 416).

Parameter	Value
Age	-
Range (years)	18 - 45
Mean (years \pm S.D.)	37.17 \pm 0.70
Men [n(%)]	227 (66.60)
Risk factors or causes of stroke [n(%)]	-
Hypertension	145(34.86)
Diabetes mellitus	31(7.45)
Smoking	107(25.72)
Drinking	51(12.26)
Dyslipidaemia	188(45.19)
Cardioembolism	-
Coronary heart disease	5(1.20)
Rheumatic heart disease	9(2.16)
Atrial myxoma	1(0.24)
Blood hyperviscosity	17(4.09)
Arteriovenous malformation of brain	13(3.13)
Vasculitis	5(1.20)
Brain aneurysm	5(1.20)
Puerperium	2(0.48)
Leukaemia	1(0.24)
Family history	-
Hypertension	41(9.86)
Stroke	16(3.85)
Cardiac disease	2(0.48)

study was approved by the local research ethics committee.

Definitions

Historically, atherosclerosis was considered to be the cause of stroke when a patient presented evidence on a blood vessel image or exhibited two and more atherosclerosis risk factors for atherosclerosis without another determined aetiology [11]: hypertension, diabetes mellitus, smoking/drinking, dyslipidaemia, coronary heart disease, transient ischemic attack, and family history. Other causes of stroke were determined according to the specific history, CT/MRI detection, cerebrovascular image, colour Doppler ultrasonography of the heart, and blood tests and so on. Hypertension was defined as having a history of hypertension or at least two different records of systolic blood pressure \geq 140 mm Hg/diastolic blood pressure \geq 90 mm Hg after the acute phase of stroke. Diabetes mellitus was defined as having a history of diabetes mellitus or a morning fasting glucose $>$ 7.0 mmol/L and a random glucose/two-hour postprandial glucose $>$ 11.1 mmol/L after the acute phase. Smoking was defined as a history of cigarette use $>$ 5 years, the current use of $>$ 10 cigarettes/day, or the cessation of smoking within the past year. Drinking was defined as a history of drinking $>$ 5 years or a current habit of drinking $>$ 500 g/week. Dyslipidaemia was defined as a total fasting cholesterol $>$ 5.7 mmol/L, fasting triglyceride $>$ 1.7 mmol/L, high-density lipoprotein cholesterol $<$ 1.0 mmol/L, low-density lipoprotein cholesterol $>$ 3.2 mmol/L, lipoprotein(a) $>$ 300mg/L, or apoprotein A1 $<$ 1.0 g/L, and apoprotein B100 $>$ 1.0 g/L.

Classification of stroke

Stroke was classified as either ischemic stroke (IS), intracerebral haemorrhage (ICH), subarachnoid haemorrhage (SAH), or mixed stroke (MS). Then, IS was divided into subtypes by

two independent consultant neurologists according to the Oxfordshire Community Stroke Project (OCSP) classification and the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification [12,13], respectively. The OCSP classification includes the total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), posterior circulation infarcts (POCI) and lacunar infarcts (LACI). The TOAST classification includes large-artery atherosclerosis (LAA), cardioembolism (CE), small-artery occlusion (SAO), stroke of other determined aetiology (SOE), and stroke of undetermined aetiology (SUE).

Statistical analysis

SPSS 13.0 (SPSS Inc., Chicago, IL, USA) was employed in our study. Measurement data were expressed as mean \pm S.D, and numeration data were expressed as the number of cases or as percentages (%). The chi-square test (χ^2) was also used when appropriate, and statistical significance was set as $P <$ 0.05.

Results

Baseline characteristics

A total of 416 Han Chinese patients with stroke were enrolled in this study. Their ages ranged between 18 and 45 years (mean age 37.17 \pm 0.70 years), and 227 of them were men (66.6%). All of the patients underwent blood tests, electrocardiograms, chest x-rays and cranial CT/MRI scans; 62 patients underwent CTA or DSA; 37 patients underwent a transcranial Doppler; 100 patients underwent colour Doppler ultrasonography of the heart; 117 patients underwent colour Doppler ultrasonography of the carotid/vertebral artery; and 23 patients underwent lumbar puncture. The risk factors and causes of stroke are shown in (Table 1).

Subtypes of stroke

A total of 225 cases of IS (54.1%), 145 cases of ICH (34.9%), 38 cases of SAH (9.1%) and 8 cases of MS (1.9%) were identified among the patients. All of the patients were divided into one of three age groups: 18 to 28 years, 29 to 39 years, and 40 to 45 years. The number of the patients in each group was 64 (15.4%), 146 (35.1%), and 206 (49.5%), respectively, and the ratio of the sexes was 2.1:1, 1.8:1 and 2:1, respectively. Differences were observed in the occurrence of IS ($P = 0.000$), ICH ($P = 0.014$) and MS ($P = 0.020$) between the age groups. The occurrences of IS and ICH tended to increase with age and were most common in patients between 40 and 45 years old, and IS increased more obviously. MS was the most common in 18- to 28-year-olds. However, the distributional difference of SAH was not statistically significant ($P = 0.138$) between the age groups (Table 2).

Subtypes of IS

The patients (155 men, 70 women) with IS were between 18 and 45 years old (mean age of 37.24 \pm 1.17 years). According to the OCSP criteria, there were 15 cases of TACI (6.7%), 117 cases of PACI (52.0%), 61 cases of LACI (27.1%) and 32 cases

Table 2. Distribution of stroke type in different age groups.

Stroke type	N			χ^2	P
	18-28 y	29-39 y	40-45 y		
IS	21	21	130	19.094	0.000
ICH	31	31	60	8.469	0.014
SAH	8	8	13	3.960	0.138
MS	4	4	3	7.778	0.020

Abbreviations:

IS=ischemic stroke
 ICH =intracerebral haemorrhage
 SAH= subarachnoid haemorrhage
 MS= mixed stroke

Table 3. Sex distribution of the ischemic stroke subtypes.

Subtype	Male(n)	Female(n)	χ^2	P
OCSF	-	-	-	-
TACI	11	4	0.148	0.700
PACI	84	33	0.960	0.327
LACI	41	20	0.110	0.741
POCI	19	13	1.576	0.209
TOAST	-	-	-	-
LAA	5	9	5.378	0.020
CE	13	2	3.464	0.063
SAO	62	46	4.489	0.034
SOE	13	3	2.123	0.145
SUE	52	20	2.795	0.095

Abbreviations:

OCSF = Oxfordshire Community Stroke Project
 TACI= total anterior circulation infarcts
 PACI = partial anterior circulation infarcts
 LACI= lacunar infarcts
 POCI = posterior circulation infarcts
 TOAST = Trial of Org 10172 in Acute Stroke Treatment
 LAA = large-artery atherosclerosis
 CE = Cardioembolism
 SAO = small-artery occlusion
 SOE = stroke of other determined aetiology
 SUE = stroke of undetermined aetiology

of POCI (14.2%) among the patients. According to the TOAST criteria, there were 14 cases of LAA (6.2%), 15 cases of CE (6.7%), 108 cases of SAO (48%), 16 cases of SOE (7.1%) and 72 cases of SUE (32%) among the patients. Every OCSF subtype occurred more often in men than in women and increased with age, but not with significant differences (Table 3,4). In addition to LAA, the other TOAST subtypes also occurred more often in men than in women, and the sex differences in LAA ($P = 0.020$) and SAO ($P = 0.034$) were statistically significant (Table 3). Additionally, the number of SOE cases reported less in 29- to 39-year-olds was less than that in 18- to 28-year-olds and in 40- and 45-year-olds. The remainder of the TOAST subtypes generally increased with age, but only the age group distributions of SAO ($P = 0.023$) and SOE ($P = 0.007$) were significantly different (Table 4).

Discussion

Constitutive characteristics of young stroke subtypes

Generally, IS is the main form of stroke, and haemorrhagic

Table 4. Distribution of the ischemic stroke subtypes in different age groups.

Subtype	18-28 y	29-39 y	40-45 y	χ^2	P
OCSF	-	-	-	-	-
TACI	2	6	7	0.866	0.649
PACI	13	39	65	1.048	0.592
LACI	3	19	39	2.374	0.305
POCI	3	10	19	0.047	0.977
TOAST	-	-	-	-	-
LAA	3	3	8	2.532	0.282
CE	1	7	7	1.830	0.400
SAO	6	29	73	7.525	0.023
SOE	5	2	9	10.064	0.007
SUE	7	29	36	4.347	0.114

Abbreviations:

OCSF = Oxfordshire Community Stroke Project
 TACI = total anterior circulation infarcts
 PACI = partial anterior circulation infarcts
 LACI= lacunar infarcts
 POCI = posterior circulation infarcts
 TOAST = Trial of Org 10172 in Acute Stroke Treatment
 LAA = large-artery atherosclerosis
 CE = Cardioembolism
 SAO = small-artery occlusion
 SOE = stroke of other determined aetiology
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stroke is the second most common form; this pattern is also observed in cases of young stroke [14]. However, a disparity exists regarding the stroke types in different regions due to the geographic incidence of stroke [6,7]. Typically, stroke morbidity in China was higher in the North than in the South, but ICH occurred more often in the South than in the North [6,15]. However, the incidence of ICH was lower in the economically emerging areas on the southern coast, such as Shanghai, Guangdong, and Hong Kong. This trend may be due to increases in the risk factors for IS, such as atherosclerosis, diabetes mellitus and overweight, as a result of the relatively developed economy and influence of the western lifestyle in these areas [6]. In addition, this trend may be correlated with climate, living environment, eating habits and genetic factors. It should be noted that site of bleeding in ICH affect the patients' outcome. A previous study confirmed that the in-hospital mortality rates were multiple topographic ICH > Primary intraventricular haemorrhage > brainstem ICH > thalamic ICH > lobar ICH > cerebellar ICH > internal capsule/basal ganglia ICH [16]. In foreign countries, IS, SAH and ICH accounted for 21.0% and 77.9%, 9.6% and 55.4%, and 3.7% and 38.5% of all young strokes, respectively [14]. A Chinese multicentre study of hospital patients (age range of 18 to 45 years) showed that 63.6% of cases exhibited IS and 36.4% exhibited haemorrhagic stroke [17]. There were four stroke types in our study; IS was present in more than half of cases, ICH accounted for more than one-third of cases, SAH was present in less than one-tenth of cases, and MS was the least prevalent. These results indicated that the main form of young stroke in this locality was IS and the second was ICH, which

Table 5. TOAST classification of young stroke in different studies.

Country/region	Time	Study design	Age (yr)	Patients (n)	Stroke subtype (%)				
					LAA	CE	SAO	SOE	SUE
Taiwan	2002	Hospital-based Retrospective	18-45	264	7.2	17.8	20.5	22.3	23.5
Italy, Turin	2004	Hospital-based Prospective	16-49	273	16	24	17	19	24
Switzerland, Bern	2005	Hospital-based Prospective	16-45	203	4	24	9	30	33
Iran	2006	Hospital-based Prospective	15-45	124	6.45	54	2.4	8.1	28.2
Italy, Rome	2006	Hospital-based Prospective	14-47	394	12	34	2.5	13	23.8
China Guangzhou	2008	Hospital-based Retrospective	18-44	41	26.8	7.3	7.3	26.8	31.8
China Beijing	2008	Hospital-based Retrospective	16-45	243	22.2	12.8	16	7.0	42
China Anhui	2009	Hospital-based Prospective	≤ 45	78	22.5	12.5	16	9	40
Finland Helsinki	2009	Hospital-based Prospective	15-49	731	8.2	17.9	13.5	24.6	35.7
Finland Helsinki	2010	Hospital-based Prospective	15-49	807	8.4	18.7	13.9	25.9	33.1
Thailand	2011	Hospital-based Prospective	16-50	99	11.1	13.1	23.2	22.2	25.3
Finland Helsinki	2011	Hospital-based Prospective	15-49	655	5.6	18.0	13.6	29.3	33.4
Germany	2012	Hospital-based Prospective	19-45	104	10.6	21.2	9.6	19.2	39.4
Italy Ferrara	2012	Population-based Prospective	15-44	24	16.6	29.2	20.8	29.2	4.2
UK	2012	Hospital-based Prospective	16-55	106	6	28	11	22	33

was in accordance with the reported stroke occurrence in coastal areas in southern China [6]. In our study, the number of men exceeded that of women in the four stroke types, and the occurrences of IS and ICH increased with age, which fit the general rules of stroke occurrence. However, the age or sex differences of most IS subtypes were non-significant when IS was reclassified for analysis. It was possible that the reduction of patients in each IS subtype attenuated the statistical efficiency. For SAH and MS, the statistical results might also be insufficient in reflecting the age-related characteristics of occurrence due to the lower number of patients studied.

It is worth mentioning that MS was considered to be an independent form of stroke, and it referred to the simultaneous or successive occurrence (within 24 hours) of IS and ICH in different areas of the patient's brain [18]. The international literature has rarely reported on MS. A previous report from China showed that MS accounted for 11.6% of cases (8 MS cases in 115 stroke autopsies) [18]. MS accounted for 1.9% of cases in our study, which suggested that MS was uncommon in the young population studied.

Subtype constituents of IS

The OCSP classification can predict the severity and prognosis of stroke [19,20], but it has seldom been applied to young stroke research. Nedeltchev *et al.*, [21] prospectively studied 203 cases of young IS (in 16- to 45-year-olds), in which the number of OCSP subtypes was PACI > POCI > LACI > TACI and the severity of nervous impairment was TACI > PACI > POCI > LACI. The LACI exhibited the best three-month outcome, followed by PACI and POCI; TACI exhibited the poorest outcome. The presence of TACI and the National Institutes of Health Stroke Scale (NIHSS) scores were independent predictors of poor outcome. These findings were the same as those in middle-aged and old stroke [19,20]. The 40 cases of young IS studied by Khan *et al.*, included 40% TACI, 12.5% PACI, 42.5% LACI and 5% POCI, in which there were more cases of major

stroke (TACI) [22]. However, our study had more cases of PACI and LACI and fewer numbers of TACI, which suggested a greater prevalence of moderate and minor stroke among the local young people, and thus a better prognosis.

Generally, LACI is the most common form of IS and has a good outcome. LACI accounted for 75% of cases in the cilostazol stroke prevention study from Japan [23], and also reached a majority in China [24]. The ratios of LACI seem to be broadly similar around the world, except for Argentina, Australia and Switzerland according to Shinohara's study [25]. However, our and other's study indicated the dissimilar ratios of LACI in young IS [21,22].

The TOAST classification has been widely used to classify the aetiology of IS. Only just reports from 2002 to 2012 years have shown a great diversity in TOAST subtypes in young IS patients (Table 5) [26–39]. In addition to differences in research design, areas, composition and sources of patients, sample size, and other factors, it was assumed that this diversity also may be due to the fact that the aetiology of young stroke is more complex than that of elderly patients and that the TOAST classification is not suitable for young stroke [40]. A previous study showed that nontraditional causes including dissections and thrombophilias were the most frequent in distribution of aetiologies by TOAST in young IS [40]. Another study on IS of unusual cause enrolled 70 patients and showed hematological disorders in 17 cases, infection in 11, migraine stroke in 10, cerebral infarction secondary to venous thrombosis in 9, primary inflammatory vascular conditions in 6 and miscellaneous causes in 17, and an age of 45 years or less was one of independent predictors of the stroke [41]. Our study displayed the most cases of SAO, followed by SUE, LAA, CE and SOE, which suggested that hypertension and diabetes mellitus are primary risk factors and that more cryptogenic stroke occurs in the local young IS patients. Most of the patients came from inland, and their eating habits and inadequate aetiology testing may have

contributed to these results. The different aetiologies of stroke could affect the long-term mortality and recurrence of stroke, but these aetiologies are not related to long-term functional recovery [42].

Retrospective analysis was the primary shortcoming of our study. Therefore, it was difficult to avoid missing or inaccurate data, coupled with the fact that the TOAST classification may be unsuitable for young stroke, which limited the precision of the study results. We hope that prospective research will compensate for the shortcoming in the future. Nevertheless, our study used the largest sample size among similar studies in China, the study results are valid as a reference for the prevention and treatment of young stroke in the local population because the patients came from the two largest hospitals in the locality.

In conclusion, there were four stroke types in our study sample from the city of Zhuhai, including many cases of IS and ICH and fewer cases of SAH and MS. Most of the IS subtypes included PACI and LACI or SAO and SUE.

List of Abbreviations

CT: Computed Tomography
MRI: Magnetic Resonance Imaging
CTA: Computed tomographic angiography
MRA: Magnetic resonance angiogram
DSA: Digital subtraction angiography
IS: Ischemic stroke
ICH: Intracerebral haemorrhage
SAH: Subarachnoid haemorrhage
MS: Mixed stroke
OCSF: Oxfordshire Community Stroke Project
TOAST: Trial of Org 10172 in Acute Stroke Treatment
TACI: Total anterior circulation infarcts
PACI: Partial anterior circulation infarcts
LACI: Lacunar infarcts
POCI: Posterior circulation infarcts
LAA: Large-artery atherosclerosis
CE: Cardioembolism
SAO: Small-artery occlusion
SOE: Stroke of other determined aetiologies
SUE: Stroke of undetermined aetiology

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Li Z suggested the concept and design this work, and wrote manuscript. Wang J participated in the design of this work and writing the manuscript, and performed the data collection. Luo S participated in the design of this work and performed OCSF classification of stroke. Wei J helped to draft the manuscript and performed TOAST classification of stroke. Hu X performed the statistical analysis.

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