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RESEARCH ARTICLE

# Stroke etiology is associated with outcome in posterior circulation stroke

Chih-Ping Chung[1,2], Chin-Sern Yong[1], Feng-Chi Chang[2,3,a], Wen-Yung Sheng[1], Hui-Chi Huang[1,4], Jui-Yao Tsai[1,4], Hung-Yi Hsu[5,a] & Han-Hwa Hu[1,2]

[1]Department of Neurology, Taipei Veterans General Hospital, Taipei, Taiwan
[2]National Yang Ming University, Taipei, Taiwan
[3]Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan
[4]National Taipei University of Nursing and Health Sciences, Taipei, Taiwan
[5]Department of Neurology, Tungs' Taichung Metro Harbor Hospital, School of Medicine, Chung Shan Medical University, Taichung, Taiwan

**Correspondence**
Feng-Chi Chang, Department of Radiology, Taipei Veterans General Hospital, No. 201 Sec.2, Shihpai Road, Peitou, Taipei, Taiwan 11217. Tel: 886-2-2875-7046; Fax: 886-2-28757579; E-mail: fcchang@vghtpe.gov.tw

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[a]These authors have same contributions.

## Abstract

**Objective**: Stroke research and clinical trials have focused mainly on anterior circulation stroke (ACS). Since clinical characteristics, mechanisms, and outcomes of posterior circulation stroke (PCS) have been reported different from ACS, more PCS studies are required, particularly researching the etiologies, to help establish an optimal management strategy. **Methods**: The present study analyzed patients of PCS who were consecutively admitted and registered in Taipei Veterans General Hospital Stroke Registry between 1 January 2012 to 28 February 2014. We demonstrated the distribution of etiologies, compared the clinical characteristics/outcomes among different etiology groups, and used univariate/multivariate analyses to identify the predictors for poor functional outcome (modified Rankin Scale ≥5) at discharge and 3 month. **Results**: About 286 patients of PCS were included for analyses. Basilar artery atheromatous branch occlusive disease (BABO, 28.0%) and large artery dissection (25.9%) were the two most common etiologies, followed by large artery atherosclerotic stenosis/occlusion (LAA, 20.6%), cardioembolism (CE, 18.5%) and small vessel disease (7.0%). Age, vascular risk factors, infarct locations and patterns, and outcomes were different among these five etiology groups. Multivariate analyses showed that age >70 y/o (discharge/3 month, OR, 95% CI: 3.05, 1.23–7.56/8.39, 2.32–30.33), admission NIH Stroke Scale >9 (19.50, 8.69–43.75/13.45, 5.59–32.39), and etiology (LAA versus BABO: 5.00, 1.58–15.83/4.00, 1.19–13.4; CE versus BABO: 3.36, 1.02–11.09/4.66, 1.40–15.46) were independently associated with poor functional outcome. **Interpretation**: The etiologies of PCS are heterogeneous and shown to be associated with functional outcomes. Our results have shed lights on future pathophysiological research and designs of clinical trials for PCS.

## Introduction

About a fifth of ischemic stroke are in the territory of posterior circulation which are supplied by the vertebrobasilar arteries and their branches.[1,2] Studies have shown that posterior circulation ischemic stroke (PCS) differs from anterior circulation ischemic stroke (ACS) in many ways such as clinical characteristics, risk factors, and stroke mechanisms.[2–4] Despite its importance and uniqueness, research focusing on PCS are much less than that on ACS. We would need more studies solely on PCS elucidating particularly the causes and predictors of outcomes to help establish an appropriate management strategy for PCS.

Large artery diseases, cardioembolism (CE), and small vessel diseases (SVDs) are most-acknowledged etiologies of PCS.[2] Besides arterial atherosclerotic stenosis/occlusion, there are two other kinds of large artery diseases, which are reported more frequently in PCS than in ACS. One is basilar artery (BA) atherosclerotic plaques with paramedi-

an pontine infarction (atheromatous branch occlusive disease),[5–7] and the other is arterial dissection.[8–12] These two causes of PCS might be overlooked and less discussed since they need more extensive evaluation tools.[2,5–7] In the present study, we analyzed data from a prospective sampling of consecutive patients in the Stroke Registry of Taipei Veterans General Hospital, a tertiary medical center, trying to (1) observe the distribution of etiologies including BA atheromatous branch occlusive disease (BABO) and arterial dissection, (2) find predictors of poor clinical outcomes, and (3) analyze the relationship between the etiologies and outcome in patients with PCS.

## Subjects and Methods

### Stroke registry

Taipei Veterans General Hospital Stroke Registry (TVGHSR) has prospectively collected data of all patients of acute stroke consecutively admitted to emergency room or/and wards of Neurology Department since February 2009. We have two specialized nurses supervised by stroke specialized physicians working on patients' data registry and further outcome follow-up. Recorded data include demographic and risk factors, stroke severity at admission, investigation results including brain, vascular or cardiac checkup during hospitalization, and outcomes at discharge and 3 month (by phone call) follow-up. Data analyzed for the current study were retrospectively retrieved from the stroke registry. Institutional Review Board of Taipei Veterans General Hospital has approved the study.

### Analyzed subjects

We retrieved from TVGHSR data of patients who were admitted and registered consecutively between 1 January 2012 to 28 February 2014. Analyzed subjects were selected with inclusion criteria: (1) acute cerebral infarcts in the territory of posterior circulation and (2) having adequate investigations including high-resolution or standard brain magnetic resonance imaging (MRI) and MRA (the lowest scan level was at V2 level) with or without contrast, neck arteries Duplex ultrasound, color-coded transcranial Doppler, 24-h Holter monitor, and echocardiogram. Patients with (1) malignancy, (2) autoimmune diseases, (3) hematological diseases, or (4) simultaneous acute cerebral infarcts over the territory of anterior circulation were excluded.

### Stroke etiologies

Patients' data were reviewed and reached consensus for their stroke etiologies by three neurologists (Dr. Chung, Hsu and Hu) and one radiologist (Dr. Chang) who are all stroke specialists. Infarct locations were categorized as involving proximal (medulla or/and posterior inferior cerebellar artery [PICA]-supplied territory), middle (pons or/and anterior inferior cerebellar artery-supplied territory), or/and distal (midbrain, posterior cerebral artery [PCA], or/and superior cerebellar artery-supplied territory) posterior circulation regions.[8,9] Brain lesions involved more than one category were defined as inclusive lesions; otherwise, it was defined as single lesion.[8,9] We used standardized criteria to classify stroke etiology. The criteria for etiology determination are described below.[5–9]

1 BABO: Vascular and cardiac studies showed absence of relevant vascular occlusion/severe stenosis and cardioembolic risks. BA showed wall thickening by high-resolution or standard MRI T1 (isointense) or/and T2/FLAIR (hypointense) sequence at the level of cerebral infarct. Clinical and brain imaging study were compatible with paramedian pontine/midbrain/upper medulla infarct (usually were basal-brainstem involved and wedge-shaped) due to several penetrating vessels occlusion.
2 Large artery atherosclerotic stenosis/occlusion (LAA): Vascular studies showed occlusion or severe stenosis (>50%) of the vertebral arteries (VAs), BA or the PCAs. There should be multiple or diffusely atherosclerotic changes in the other large arteries. Abrupt cutoff of vessels was considered more likely due to embolism and was not considered for this category. Cerebral infarcts were in the territory of the large artery stenosis/occlusion larger than that of a single branch artery territory, or in distal fields.
3 Large artery dissection (LAD): Vascular studies showed (1) occlusion or severe stenosis (>50%) of the VA, BA, PCA or PICA; (2) gradually tapered or/and long-segmental narrowing of the stenotic/occlusive vessel; and (3) intramural hematoma, intimal flap, or double lumen by high-resolution or standard MRI T1 sequence with or without contrast. There was usually vascular dilatation with or without aneurysm at the level of dissection. Associated atherosclerotic changes in the other large arteries were acceptable. Cerebral infarcts were in the territory of the dissected vessel larger than that of a single branch artery territory, or in distal fields (in most cases).
4 CE: Vascular studies showed an abrupt cutoff of branch or main artery (usually the distal part), or patency of arteries known to supply the infarct. Cerebral infarcts were larger than a single branch artery territory. Cardiac studies showed high or medium risk cardiac sources known to cause embolism. High-risk cardiac sources include: valvular surgery; atrial fibrillation (AF; the commonest encountered), atrial flutter, or sick-sinus

 

syndrome with or without valvular heart disease; ventricular aneurysm; cardiac mural thrombus; cardiomyopathy; global left ventricular hypokinesis; akinetic ventricular regions; endocarditis; intracardiac tumors. Medium risk sources are: myocardial infarction within 6 months; valvular heart disease without AF; atrial flutter, or sick-sinus syndrome; mitral valve prolapse; mitral annulus calcification; atrial septal defect or patent foramen ovale (paradoxical embolism); hypokinetic ventricular segment.

5 SVD (perforating artery occlusion): Vascular and cardiac studies showed absence of relevant vascular occlusion/severe stenosis and cardioembolic risks. Cerebral infarct was limited to the territory of one single penetrating branch. Clinically, neurological deficit must be compatible with a single branch territory infarct.

### Statistical analyses

Analyses were performed with SAS software, version 9.1 (SAS Institute, Cary, NC). All values were expressed as mean (SD) for continuous variables and number (percentages) for discrete variables. Group comparisons were done using the nonparametric Kruskal–Wallis test. The $\chi^2$ test or Fisher's exact test was performed for categorical variables as appropriate. To detect factors associated with poor functional outcomes (modified Rankin scale [mRS] $\geq$5) at discharge and 3 month, we used univariate and multivariate regression analyses. Age, gender, admission NIH stroke scale (NIHSS), stroke etiologies, infarct location (proximal, middle or distal), and lesion pattern (inclusive or single lesions), i.v. tissue plasminogen activator (tPA), oral antiplatelets, and anticoagulants prescriptions, the performance of stent insertion, and the presence of hypertension (HTN), diabetes mellitus (DM), hyperlipidemia, AF, and cigarette smoking were the independent variables. Odds ratios were calculated for variables to identify risk factors in univariate and multivariate analyses for poor functional outcomes. Multiple logistic regressions with backward elimination were conducted to evaluate the associated variables. All statistically significant levels were defined as $P < 0.05$.

## Results

From 1 January 2012 to 28 February 2014, TVGHSR prospectively registered 1343 patients with acute ischemic stroke. Among them, there were 318 patients (23.68%) with cerebral infarcts in the territory of posterior circulation. According to our criteria, 17, 3, and 12 patients were excluded due to accompanied infarcts in the territory of anterior circulation, malignancy, and inadequate investigations/undetermined etiology, respectively. Notably, 66% of patients with acute ischemic stroke registered in TVGHSR were men, which is a little bit higher than the results from Taiwan Stroke Registry (60%) which engaged 39 academic and community hospitals and covered the entire country between 2006 and 2008.[13]

There were 286 patients included for analyses: 197 men (68.9%) and 89 women (31.1%) with an average age of 71.5 (13.4) years. The frequency of vascular risk factors were as followed: HTN 223 (78%), DM 129 (45.1%), hyperlipidemia 93 (32.5%), AF 38 (13.3%), and cigarette smoking 56 (25.9%). The location of cerebral infarcts were involved the distal, middle, and proximal territory in 95 (33.2%), 178 (62.2%), and 63 (22%) patients respectively. There were 46 (16.1%) patients having more than one territory of infarct (inclusive lesions). The leading three common regions being involved were pons (167 patients; 58.4%), cerebellum (96; 33.6%) and midbrain/thalamus (62; 21.7).

The average admission NIHSS was 5.8 (6.5). All patients received oral antiplatelets during admission. Among them, two patients (0.7%) received i.v. tPA treatment within 3 h, six patients (2.0%) were performed stent insertion in VA or BA, and 47 patients (16.4%) were prescribed oral anticoagulants (warfarin). The overall outcome were 10 mortality (3.5%) and mean mRS = 3.1 (1.5) at discharge.

The distribution of stroke etiologies in our PCS patients were BABO 80 (28.0%), LAA 59 (20.6%), LAD 74 (25.9%), CE 53 (18.5%), and SVD 20 (7.0%). The clinical characteristics and outcomes of each etiology and their comparisons are listed in Table 1. There were differences in clinical characteristics among five groups. Patients of LAD were younger compared with patients of BABO, LAA, and CE respectively after post hoc analyses. Patients of CE had the highest frequency of AF, distal posterior circulation territory involvement, and inclusive lesions. Patients of LAA and LAD had similar cerebral infarct patterns: mostly involving middle posterior circulation territory and similar frequency of inclusive lesions compared with patients of CE. Middle posterior circulation territory was involved almost in all patients of BABO. Most cerebral infarct lesions in patients of SVD were in distal posterior circulation territory (thalamus). Anticoagulants were prescribed mainly in patients of LAD and CE. Regarding outcomes, mortality within hospitalization occurred mainly in patients of LAA and LAD, and higher mRS was noted in patients of LAA and CE at discharge and 3 month respectively.

Tables 2 and 3 reveal the variables associated with poor functional outcomes (mRS $\geq$ 5) at discharge and 3 month, respectively. Multivariate analyses after adjusting the covariates showed that age, admission NIHSS and stroke etiology were independent factors associated with

 

**Table 1.** Demographic, clinical characteristics, and outcomes comparisons among five patient groups with different etiologies of posterior circulation ischemic strokes (total population = 286).

| | BABO (*n* = 80) | LAA (*n* = 59) | LAD (*n* = 74) | CE (*n* = 53) | SVD (*n* = 20) | *P* |
|---|---|---|---|---|---|---|
| Age, years | 73.3 (11.0) | 74.7 (10.1) | 65.8 (15.6)[1] | 73.4 (13.8) | 70.1 (15.2) | 0.007 |
| Gender, men | 54 (67.5%) | 40 (67.8%) | 56 (75.7%) | 30 (56.6%) | 17 (85%) | 0.097 |
| Risk factors | | | | | | |
| Hypertension | 63 (78.8%) | 52 (88.1%) | 57 (77.0%) | 37 (69.8%) | 14 (70.0%) | 0.171 |
| Diabetes | 42 (52.5%) | 29 (49.2%) | 34 (45.9%) | 17 (32.1%) | 7 (35.0%) | 0.156 |
| Hyperlipidemia | 24 (30.0%) | 20 (33.9%) | 26 (35.1%) | 19 (35.8%) | 4 (20.0%) | 0.700 |
| Atrial fibrillation | 4 (5.0%) | 2 (3.3%) | 5 (6.8%) | 26 (49.1%) | 1 (5.0%) | <0.0001 |
| Smoking | 11 (13.8%) | 10 (16.9%) | 22 (29.7%) | 9 (17.0%) | 4 (20.0%) | 0.350 |
| Cerebral infarct | | | | | | |
| Location | | | | | | |
| Distal | 4 (5.0%) | 17 (28.8%) | 19 (25.7%) | 43 (81.1%) | 12 (60%) | <0.0001 |
| Middle | 72 (90%) | 37 (62.7%) | 47 (63.5%) | 14 (26.4%) | 7 (35.0%) | <0.0001 |
| Proximal | 8 (10%) | 16 (27.1%) | 27 (36.5%) | 10 (18.9%) | 1 (5.0%) | 0.0004 |
| Lesion | | | | | | |
| Inclusive | 4 (5%) | 13 (22%) | 16 (21.6%) | 13 (24.5%) | 0 | 0.0015 |
| Admission NIHSS | 4.6 (3.2) | 5.9 (6.0) | 6.9 (8.3) | 6.6 (8.3) | 3.6 (3.7) | 0.320 |
| Treatments | | | | | | |
| i.v. tPA | 1 (1.3%) | 0 | 0 | 1 (1.9%) | 0 | 0.644 |
| Antiplatelets[2] | 80 (100%) | 59 (100%) | 74 (100%) | 53 (100%) | 20 (100%) | - |
| Anticoagulants[2] | 3 (3.8%) | 10 (16.9%) | 22 (29.7%) | 12 (22.6%) | 0 | <0.0001 |
| Stenting | 0 | 3 (5.1%) | 3 (4.1%) | 0 | 0 | 0.125 |
| Outcomes | | | | | | |
| Discharge | | | | | | |
| Mortality | 1 (1.3%) | 4 (6.8%) | 5 (6.8%) | 0 | 0 | 0.090 |
| mRS | 3.1 (1.1) | 3.4 (1.5) | 3.0 (1.7) | 3.1 (1.5) | 2.3 (1.3) | 0.044 |
| 3 month | | | | | | |
| mRS[3] | 2.2 (1.6) | 2.4 (1.9) | 2.1 (1.8) | 2.6 (2.1) | 1.3 (1.6) | 0.065 |

Presented as means (SD) or number (percentage). BABO, basilar artery atheromatous branch occlusive disease; LAA, large artery atherosclerotic stenosis/occlusion; LAD, large artery dissection; CE, cardioembolism; SVD, small vessel disease; NIHSS, National Institute of Health stroke scale; tPA, tissue plasminogen activator; mRS, modified Rankin Scale.

[1]*P* value of post hoc test <0.005 versus BABO, LAA, and CE respectively.

[2]Oral medicines.

[3]Excluding mortality at discharge.

functional outcomes. Age >70 y/o, admission NIHSS >9, stroke etiology LAA and CE were independent predictors for poor functional outcomes both at discharge and 3 month.

## Discussion

We have mainly found that in our population of PCS, (1) BABO and LAD were the two commonest etiologies, (2) stroke etiology was associated with functional outcomes, and (3) age (>70 y/o), worse stroke severity at admission (NIHSS > 9), and stroke etiology LAA and CE were independently associated with poor functional outcomes both at discharge and 3 month.

Current available guidelines for management of patients with PCS are similar to those of ACS though they have several differences in clinical characteristics, diagnosis, disease mechanism, and outcomes.[2–4,14–16] Questions remain regarding the effective acute treatment and secondary prevention for PCS.[2,3,16] Studies have shown that the prognosis of PCS might not be as benign as expected, for example, the risk of recurrent stroke after PCS was reported at least as high as for ACS, and vertebrobasilar stenosis increases the risk threefold.[17–19] Optimal treatment and prevention for diseases need knowledge about diseases' etiologies or mechanisms to be targeted at, unfortunately, stroke studies focused much more in ACS than PCS.[2,3] The results of the present study elucidating the etiologies of PCS, each etiology's characteristics and their relationships between functional outcomes are improving the understanding in this area.

The distributions of stroke etiology in other large stroke registries are listed in Table 4.[1,8,20,21] The present study has revealed a higher frequency of LAD (25.9%) as the etiology of PCS. (1) The advance of vascular images which has facilitated the diagnosis of LAD, and (2) a

 

**Table 2.** Predictors of poor functional outcome with modified Rankin Scale ≥5 at discharge.

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| Characteristics[1] | OR (95% CI) | *P* | OR (95% CI) | *P* |
| Age, > vs. ≤70 years | 3.57 (1.66–7.65) | 0.0006 | 3.05 (1.23–7.56) | 0.016 |
| NIHSS, > vs. ≤9 | 19.65 (9.43–40.94) | <0.0001 | 19.50 (8.69–43.75) | <0.0001 |
| Atrial fibrillation | 2.40 (1.12–5.15) | 0.022 | | |
| Hyperlipidemia | 0.43 (0.21–0.91) | 0.024 | | |
| Infarct location, upper | 2.36 (1.28–4.36) | 0.005 | | |
| Inclusive vs. single lesion | 3.84 (1.92–7.69) | <0.0001 | | |
| Etiology, vs. BABO | | | | |
| LAA | 3.88 (1.48–10.18) | 0.006 | 5.00 (1.58–15.83) | 0.006 |
| LAD | 2.43 (0.92–6.42) | 0.072 | 1.97 (0.61–6.39) | 0.259 |
| CE | 3.74 (1.40–10.05) | 0.009 | 3.36 (1.02–11.09) | 0.046 |
| SVD | 0.55 (0.06–4.74) | 0.585 | 0.87 (0.08–9.73) | 0.907 |

OR, odds ratio; CI, confidence interval; NIHSS, National Institute of Health stroke scale; BABO, basilar artery atheromatous branch occlusive disease; LAA, large artery atherosclerotic stenosis/occlusion; LAD, large artery dissection; CE, cardioembolism; SVD, small vessel disease.
[1]Only listing variables with statistically significance at univariate analysis.

**Table 3.** Predictors of poor functional outcome with modified Rankin Scale ≥5 at 3 month.

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| Characteristics[1] | OR (95% CI) | *P* | OR (95% CI) | *P* |
| Age, > vs. ≤70 years | 10.05 (3.02–33.43) | <0.0001 | 8.39 (2.32–30.33) | 0.001 |
| NIHSS, > vs. ≤9 | 13.52 (6.34–28.86) | <0.0001 | 13.45 (5.59–32.39) | <0.0001 |
| Atrial fibrillation | 2.84 (1.28–6.32) | 0.008 | | |
| Infarct location, upper | 2.10 (1.08–4.10) | 0.027 | | |
| Inclusive vs. single lesion | 3.48 (1.64–7.38) | 0.0007 | | |
| Etiology, vs. BABO | | | | |
| LAA | 3.40 (1.19–9.70) | 0.023 | 4.00 (1.19–13.41) | 0.025 |
| LAD | 1.37 (0.44–4.30) | 0.586 | 1.14 (0.30–4.27) | 0.851 |
| CE | 4.80 (1.72–13.38) | 0.003 | 4.66 (1.40–15.46) | 0.012 |
| SVD | 1.35 (0.25–7.26) | 0.725 | 2.49 (0.37–16.85) | 0.349 |

Excluding mortality at discharge when analyzing. OR, odds ratio; CI, confidence interval; BABO, basilar artery atheromatous branch occlusive disease; LAA, large artery atherosclerotic stenosis/occlusion; LAD, large artery dissection; CE, cardioembolism; SVD, small vessel disease; NIHSS, National Institute of Health stroke scale.
[1]Only listing variables with statistically significance at univariate analysis.

100% performance rate of MRI/MRA (some even with high-resolution or contrast enhancement) and (3) thorough investigations in our patients with a lower rate of undetermined etiology may contribute to the result. Besides, we retrospectively evaluated every patient's vessel walls of vertebrobasilar arteries and their branches on MRI/MRA images to determine their stroke etiology, which would avoid overlooking the diagnosis of LAD. In addition, like Hallym Stroke Registry (HSR) in Korea, we had a higher percentage of patients with infarctions contributed by penetrating artery occlusion. This may due to the racial difference in the study population, for example, Asian people are susceptible to penetrating artery infarction. Notably, BABO was not differentiated from SVD among these patients in most stroke registries of PCS.

Though as expected, patients with LAD were younger than the other etiology groups (BABO, LAA, and CE), the age range of these patients was from 21 to 91 (mean 65.82) years old. The current data told us that we should not overlook LAD as the etiology of PCS in the elderly patients. Besides, there was a similar mortality rate by discharge between LAD and LAA groups (both were 6.8%), prognosis of LAD-induced PCS might not as benign as previous thought. Few PCS study has included vascular dissection for interetiologies characteristics and outcomes comparison. Previous studies mostly classified stroke mechanisms either as hemodynamic impairment versus embolism, or large artery diseases versus the others, some even excluded vascular dissection in their study design,[1,4,8,9,20–23] therefore LAD was seldom able to be

 

**Table 4.** Stroke etiologies in other stroke registries.

| | TVGHSR ($n$ = 298)[1] | HSR ($n$ = 591) | NEMC ($n$ = 407) | LSR ($n$ = 233) | ASR ($n$ = 259) |
|---|---|---|---|---|---|
| Years | 2012–2014 | 1996–2002 | 1988–1996 | 1982–1987 | 1992–1997 |
| LAA | 20% | 50% | 31% | 16% | 16% |
| Arterial dissection | 25% | <2%[2] | 1% | 9% | <2%[2] |
| Cardioembolism | 18% | 5% | 24% | 16% | 23% |
| Penetrating artery[3] | | 34% | 14% | 16% | 23% |
| SVD | 7% | | | | |
| BABO | 27% | | | | |
| Undetermined | 4% | 9% | 3% | 14% | 26% |

TVGHSR, Taipei Veterans General Hospital Stroke Registry; HSR, Hallym Stroke Registry in Korea; NEMC, New England Medical Center; LSR, Lausanne Stroke Registry; ASR, Athens Stroke Registry; BABO, basilar artery atheromatous branch occlusive disease; LAA, large artery atherosclerotic stenosis/occlusion; SVD, small vessel disease.

[1]Patients with undetermined etiology was included for comparisons with the other registries.

[2]Arterial dissection was included in the category of "other stroke etiology". Explicit number of patients with arterial dissection was not mentioned.

[3]BABO was not differentiated from SVD in other stroke registries.

recognized for further analyses. LAD would mimic LAA especially when there are accompanied atherosclerotic changes in relevant or other large vessels, and limited investigation tools able to detect the vessel walls of stenotic large vessels. Our results hence have emphasized the importance of LAD in PCS, and it deserves further studies on the pathophysiology to obtain an optimal acute treatment, and primary and secondary prevention strategy for vertebrobasilar dissection.

BABO is another large artery disease causing stroke, more commonly found in PCS than ACS.[4–9] Its nature is atherosclerotic plaque in large vessel which occludes the opening of several penetrating branches. Besides BABO, some studies would also classify or name it as "large artery disease without stenosis" or "local branch occlusion". BABO-related stroke almost involves pontine which mimics SVD clinically and on cerebral images.[6,7] Like LAD, it would need more extensive investigations on vessel walls to make this large artery disease differentiated from SVD. Whether Asian population are more susceptible to this etiology, and whether medications able to make plaque regression could prevent stroke primarily and secondarily in these patients deserve further investigations.

Predictors for poor functional outcomes have less studied in patients of PCS compared with ACS. We have found age and stroke severity at admission very strong factors to determine functional outcomes in patients of PCS. Besides, we have revealed stroke etiology another factor associated with functional outcomes. LAA and CE, compared with the other etiologies, had more frequent poor functional outcomes both at discharge and 3 month. Applying our results into clinical practices, patients of PCS with these factors should be monitored and treated more aggressively. In univariate analysis, characteristics of etiology CE or LAA such as AF, distal posterior circulation territory, and inclusive cerebral lesions were also found associated with poor functional outcomes. After adjusting for covariates including stroke etiology in multivariate analyses, these factors showed no statistically significant difference.

Patients of CE are always having associated cardiac diseases such as AF, recent valvular surgery, myocardial infarction, etc., and these comorbidities may contribute to a worse functional outcome in this etiology group of PCS patients. As to LAA, chronic hemodynamic insufficiency in posterior circulation territory by severe vertebrobasilar artery stenosis may lead to more severe dysfunction and poor recovery after stroke. Besides, previous population- and hospital-based studies have showed severe vertebrobasilar stenosis (>50%) a risk factor of early stroke recurrence in patients with PCS,[18,19] may also explain poor outcomes in patients with LAA. Unfortunately, we did not have the data of stroke recurrence in our patients with PCS. A prospective study in the future will help elucidate the mechanism.

There are limitations of our study. Firstly, study population was retrospectively recruited from our hospital's stroke registry (TVGHSR). Since (1) TVGHSR was prospectively recruiting every consecutively admitted stroke patients' data during hospitalization and 3 month follow-up, (2) the standard protocol for stroke management in our hospital includes very extensive investigations, and (3) we had four stroke specialists together reviewing patients' clinical data to determine the stroke characteristics and etiology, the present study should be as explicit as a prospective one. Secondly, we excluded 17 patients of PCS with simultaneous cerebral infarcts in the territory of

 

anterior circulation. Since cerebral infarcts involve more than one vascular territory are usually caused by CE, we may underestimate the frequency of CE and its association with a poor functional outcome. Lastly, we did not look at and analyze the involved large vessels in our PCS patients. The main purpose of the present study was focusing on the relationship between stroke etiologies and functional outcomes. Since not each etiology of PCS such as CE and SVD has relevant large vascular lesions, taking them into account might obscure the role of these etiologies in PCS. We would leave this part for future PCS studies.

In summary, our study showed that patients of PCS had heterogeneous etiologies which possessed distinctive clinical characteristics. Furthermore, stroke etiology was associated with functional outcomes; LAA and CE had worse functional outcome at discharge and 3 month respectively in PCS. These findings are improving our understanding on mechanisms of PCS and helpful not only for establishment of future etiology-centered management strategy but also designs of clinical trials specific for PCS patients. PCS is a heterogeneous disease. Any clinical trials of medicines or devises for PCS should take stroke etiology into consideration when designing the protocol.

## Author Contributions

Study designs, patients' data analyses, and manuscript drafting: Dr. Chih-Ping Chung, Feng-Chi Chang, and Hung-Yi Hsu. Patients' stroke etiology determination and reaching consensus: Dr. Chih-Ping Chung, Feng-Chi Chang, Han-Hwa Hu, and Hung-Yi Hsu. Stroke registry case management and follow-up, and patients' data processing: Mr. Chin-Sern Yong, Ms. Hui-Chi Huang, and Jui-Yao Tsai. Statistical analyses: Ms. Wen-Yung Sheng.

## Conflict of Interest

None declared.

### References


1. Bogousslavsky J, Van Melle G, Regli F. The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke. Stroke 1988;19:1083–1092.
2. Markus HS, van der Worp HB, Rothwell PM. Posterior circulation ischaemic stroke and transient ischaemic attack: diagnosis, investigation, and secondary prevention. Lancet Neurol 2013;12:989–998.
3. Merwick Á, Werring D. Posterior circulation ischaemic stroke. BMJ 2014;348:g3175.
4. Kim JS, Nah HW, Park SM, et al. Factors and stroke mechanisms in atherosclerotic stroke: intracranial compared with extracranial and anterior compared with posterior circulation disease. Stroke 2012;43:3313–3318.
5. Fisher CM, Caplan LR. Basilar artery branch occlusion: a cause of pontine infarction. Neurology 1971;21:900–905.
6. Klein IF, Lavallée PC, Schouman-Claeys E, Amarenco P. High-resolution MRI identifies basilar artery plaques in paramedian pontine infarct. Neurology 2005;64:551–552.
7. Klein IF, Lavallée PC, Mazighi M, et al. Basilar artery atherosclerotic plaques in paramedian and lacunar pontine infarctions: a high-resolution MRI study. Stroke 2010;41:1405–1409.
8. Caplan LR, Wityk RJ, Glass TA, et al. New England medical center posterior circulation registry. Ann Neurol 2004;56:389–398.
9. Caplan L, Chung CS, Wityk R, et al. New England medical center posterior circulation stroke registry: I. Methods, data base, distribution of brain lesions, stroke mechanisms, and outcomes. J Clin Neurol 2005;1:14–30.
10. Caplan LR, Baquis GD, Pessin MS, et al. Dissection of the intracranial vertebral artery. Neurology 1988;38:868–877.
11. Mokri B, Houser OW, Sandok BA, Piepgras DG. Spontaneous dissections of the vertebral arteries. Neurology 1988;38:880–885.
12. Schievink WI. Spontaneous dissection of the carotid and vertebral arteries. N Engl J Med 2001;344:898–906.
13. Hsieh FI, Lien LM, Chen ST, et al. Get With the Guidelines-Stroke performance indicators: surveillance of stroke care in the Taiwan Stroke Registry: Get With the Guidelines-Stroke in Taiwan. Circulation 2010;122:1116–1123.
14. Paul NL, Simoni M, Rothwell PM; Oxford Vascular Study. Transient isolated brainstem symptoms preceding posterior circulation stroke: a population-based study. Lancet Neurol 2013;12:65–71.
15. Chalela JA, Kidwell CS, Nentwich LM, et al. Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison. Lancet 2007;369:293–298.
16. Caplan L. Posterior circulation ischemia: then, now, and tomorrow. The Thomas Willis Lecture-2000. Stroke 2000;31:2011–2023.
17. Flossmann E, Rothwell PM. Prognosis of vertebrobasilar transient ischaemic attack and minor stroke. Brain 2003;126:1940–1954.
18. Marquardt L, Kuker W, Chandratheva A, et al. Incidence and prognosis of > or = 50% symptomatic vertebral or basilar artery stenosis: prospective population-based study. Brain 2009;132:982–988.
19. Gulli G, Khan S, Markus HS. Vertebrobasilar stenosis predicts high early recurrent stroke risk in posterior circulation stroke and TIA. Stroke 2009;40:2732–2737.
20. Vemmos KN, Takis CE, Georgilis K, et al. The Athens stroke registry: results of a five-year hospital-based study. Cerebrovasc Dis 2000;10:133–141.


 

21. Lee JH, Han SJ, Yun YH, et al. Posterior circulation ischemic stroke in Korean population. Eur J Neurol 2006;13:742–748.
22. De Marchis GM, Kohler A, Renz N, et al. Posterior versus anterior circulation strokes: comparison of clinical, radiological and outcome characteristics. J Neurol Neurosurg Psychiatry 2011;82:33–37.
23. Akhtar N, Kamran SI, Deleu D, et al. Ischaemic posterior circulation stroke in State of Qatar. Eur J Neurol 2009;16:1004–1009.

 