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Impact of revascularization therapies on outcome of posterior circulation ischemic stroke: The Indo-US stroke project

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ABSTRACT

Introduction: Posterior circulation strokes (PCS) have been less extensively studied than anterior circulation strokes (ACS), especially regarding revascularization therapies. We analyzed the differences in baseline stroke characteristics, revascularization therapy and 3-month outcomes between PCS and ACS in a large prospective multicentre Indian stroke registry.

Methods: Patients with acute ischemic stroke recruited in the Indo-US collaborative stroke project from January 2012 to August 2014 were classified into PCS and ACS based on imaging-confirmed infarct location. Demographics, stroke severity, risk factors, and mechanisms were compared. We further compared these parameters in the subgroups who received revascularization therapies (RT) and no revascularization therapies (NRT). The primary outcome was 3-month modified Rankin scale (mRS).

Results: Of 1889 patients (1270 males), 1478 (78.2%) had ACS and 411 (21.8%) PCS. The median NIHSS was lower in PCS (7 vs 11, $p < 0.001$). Diabetes mellitus and hypertension were more common in PCS and rheumatic heart disease in ACS. Small artery occlusion was higher in PCS (23.8% vs 12.9%, $p < 0.001$). Only 28 (6.8%) PCS received RT compared to 213 (14.4%) ACS. At 90 days, a good functional outcome (mRS 0–2) was more common in PCS (56.4% vs 45.9%, $p < 0.001$) in NRT group, while no significant difference was noted in RT group. Stroke territory was not an independent predictor of 3-month outcome in regression analysis. In-hospital mortality was not different between the groups.

Conclusions: The 3-month functional outcome and in-hospital mortality were not different between ACS and PCS. Compared to ACS, PCS received revascularization therapies less often.

1. Introduction

Posterior circulation strokes (PCS) produce ischemia in the regions supplied by the vertebrobasilar arterial system and constitute about one-fifths of all ischemic strokes [1]. The anatomy, function, and physiology of the vertebrobasilar circulation brain territories differ distinctly from those of carotid circulation. In spite of this, more similarities than differences have been reported between ACS and PCS [2–4].

Prospective registries have investigated the clinical presentation, risk factors, stroke mechanisms, and outcome of PCS. Vascular risk factors reported to be more frequent in PCS include male sex and diabetes mellitus, whereas ACS patients are older with more frequent atrial fibrillation [5,6]. Stroke etiology in PCS was commonly noted to be embolic and branch artery disease based on older classification in the seminal PCS registries [3,7,8]. Stroke mechanisms attributed with newer classification systems have shown a higher proportion of small vessel disease in PCS [4,5,9].

Registry-based data have shown that functional outcome of PCS is comparable to ACS [2,3]. In those who had received intravenous thrombolysis (IVT), functional independence in PCS was similar or even

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better than ACS with a very low risk of symptomatic intracranial hemorrhage (sICH) [10–13]. Interestingly, two studies comparing functional outcome in PCS who received IVT against those who did not found the characteristics and outcome predictors to be markedly different between the groups [4,9]. Stroke severity was an independent predictor of outcome in PCS who did not receive IVT whereas it was not predictive in thrombolysed patients [4].

The Indo-US Collaborative Stroke Project (IUCSP) is a large multicentric registry including five large-volume academic stroke centres in India. In this analysis of the IUCSP data, we aimed to study the clinico-demographic features, risk factors, stroke mechanism and 3-month outcomes of ischemic strokes in posterior circulation, with specific focus on the differences between patients who did and did not receive revascularization therapies.

2. Methods

The IUCSP, jointly funded by the United States National Institutes of Health, and the Department of Biotechnology, Government of India, was a prospective study on acute ischemic stroke from five Indian academic hospitals with a coordinating centre in Boston, USA. The detailed methodology and inclusion-exclusion criteria of this study were published previously [14,15]. The study enrolled successive patients aged 18 years and above with ischemic stroke admitted within 2 weeks. Clearance was obtained from Institutional Ethics Committee of each hospital and written informed consent was obtained from all the subjects. Data was collected by trained personnel from January 2012 to August 2014 and entered in a secure web-based electronic database.

The current analysis aimed to determine the characteristics and outcome of PCS in this cohort, particularly with respect to revascularization therapies. For this analysis, we included a subset of patients with CT or MRI confirmed acute infarcts in the anterior or posterior circulation territory. Vascular distribution was designated as 'anterior' if acute infarct in CT and/or MRI brain was in the internal carotid, middle cerebral or anterior cerebral artery territories and 'posterior' if located in the vertebrobasilar or posterior cerebral artery territories. Participants with infarcts in both territories and those without acute infarcts in CT or MR brain imaging were excluded. The demographics, clinical manifestations (including stoke severity at presentation measured by National Institutes of Health Stroke Scale [NIHSS]), risk factors, pre-hospital care, stroke mechanism (using 'Causative Classification of Stroke' [CCS] tool), brain imaging and laboratory tests and outcomes until 3 months were compared between the two groups separately for patients who received and did not receive revascularization therapies. The primary outcome of interest was 3-month modified Rankin Scale (mRS).

Statistical analysis was performed using SPSS, version 26.0 Armonk, NY: IBM Corp. Continuous variables were expressed as means (standard deviation) or median (interquartile range). Categorical variables were presented as numbers and percentages. Chi-square/Fischer's and *t*-tests were used for comparisons of proportions and means, respectively. A p value <0.05 was considered significant. Missing data for variables were considered as being absent for analysis. Multivariate logistic regression analysis was performed with the stroke territory (anterior versus posterior), age, sex, vascular risk factors, and initial stroke severity to determine independent predictors of 3-month outcome.

3. Results

3.1. Study population

We included 1889 participants in this analysis after excluding 128 patients with multiple territory infarcts and 49 with negative imaging; 411 (21.8%) had PCS and 1478 (78.2%) had ACS.

The baseline demographic and clinical variables and outcomes of PCS and ACS are summarized in Table 1. The PCS group had diabetes

Table 1
Clinical profile of posterior versus anterior circulation strokes.

Variable	Posterior circulation N = 411	Anterior circulation N = 1478	p value
Demography			
Age in years; mean (SD)	58.5 (13.3)	58.1 (15.1)	0.668
Males; N (%)	286 (69.6)	984 (66.6)	0.250
Time to arrival at index hospital in hours; median (IQR)[a]	61.7 (20.6–148.1)	35.2 (9.2–117.5)	**<0.001**
Clinical features; N(%)			
Altered consciousness	113 (27.5)	453 (30.6)	0.214
Focal neurological deficit	362 (88.1)	1338 (90.5)	0.133
Weakness	291 (70.8)	1341 (90.7)	**<0.001**
Ataxia/diplopia	222 (54.0)	350 (23.7)	**<0.001**
Aphasia/ dysarthria	248 (60.3)	1116 (75.5)	**<0.001**
Other neurological signs	160 (38.9)	344 (23.3)	**<0.001**
NIHSS at admission; median (IQR)[b]	7 (4–12)	11 (6–16)	**<0.001**
Vascular risk factors; N(%)			
Hypertension	272 (66.2)	875 (59.2)	**0.009**
Diabetes mellitus	168 (40.9)	510 (34.5)	**0.017**
Hypercholesterolemia	64 (15.6)	217 (14.7)	0.667
Atrial fibrillation/flutter	18 (4.4)	58 (3.9)	0.698
Rheumatic heart disease	13 (3.2)	91 (6.2)	**0.019**
Coronary artery disease	59 (14.4)	254 (17.2)	0.183
Prior ischemic/ hemorrhagic stroke	84 (20.4)	282 (19.1)	0.541
Prior transient ischemic attack	30 (7.3)	108 (7.3)	0.998
Current cigarette smoking	63 (15.3)	262 (17.7)	0.252
Current alcohol use	142 (34.5)	500 (33.8)	0.785
Family history of stroke	69 (16.8)	228 (15.4)	0.742
Family history of coronary artery disease	69 (16.8)	187 (12.7)	0.093
Imaging diagnostics; N(%)			
CT head	291 (70.8)	1165 (78.8)	**0.001**
MRI brain	348 (84.7)	929 (62.9)	**<0.001**
Vessel imaging done (CTA/ MRA/DSA)	340 (82.7)	1106 (74.8)	**<0.001**
Vascular abnormalities in culprit artery[c]			
Internal carotid artery	–	259 (17.5)	
Middle cerebral artery	–	372 (25.2)	
Anterior cerebral artery	–	39 (2.6)	
Posterior cerebral artery	65 (15.8)	–	
Basilar artery	47 (11.4)	–	
Vertebral artery	68 (16.5)	–	
Mass effect	26 (6.3)	252 (17.1)	**<0.001**
Stroke classification; N(%)			
CCS subtype			
Large artery atherosclerosis	87 (21.2)	469 (31.7)	**<0.001**
Cardio-aortic embolism	83 (20.2)	383 (25.9)	**0.017**
Small artery occlusion	98 (23.8)	190 (12.9)	**<0.001**
Other uncommon	22 (5.4)	41 (2.8)	**0.010**
Undetermined	121 (29.4)	393 (26.6)	0.257
Stroke complications; N(%)			
Failed dysphagia screening (N = 1428)	114 (39.0)	537 (47.3)	**0.012**
Pneumonia	60 (14.6)	186 (12.6)	0.282
Urinary tract infection	42 (10.2)	138 (9.3)	0.596
Deep vein thrombosis or pulmonary embolism	7 (1.7)	23 (1.6)	0.833
In-hospital mortality	25 (6.1)	119 (8.1)	0.183
3-month outcome; N(%)			
Modified Rankin scale (N = 1836)			**<0.001**
Good (mRS score 0–2)	232 (58.1)	678 (47.2)	
Poor (mRS score 3–6)	167 (41.9)	759 (52.8)	
Stroke recurrence (N = 1570)	11 (3.1)	48 (3.9)	0.465
Mortality (N = 1836)	66 (16.5)	273 (19.0)	0.263

Abbreviations: CCS Causative Classification of Stroke, CT computed tomography scan, CTA computed tomography angiogram, DSA digital subtraction angiogram, IQR interquartile range, MRA magnetic resonance angiogram, MRI

magnetic resonance imaging, mRS modified Rankin Scale, N number, NIHSS National Institutes of Health Stroke Scale, SD standard deviation.

[a] 7 in-hospital strokes were excluded from analysis.

[b] NIHSS was not documented for 37 patients who were excluded in this analysis.

[c] Occlusion or stenosis >50% of the artery.

mellitus and hypertension more commonly while rheumatic heart disease was significantly more frequent in ACS. Median NIHSS at admission was lower for PCS compared to ACS (7 vs 11, $p < 0.001$). Small artery occlusion was significantly more common in PCS compared to large artery atherosclerosis and cardio-aortic embolism, which were the predominant stroke subtypes in ACS. Fewer PCS patients presented within 24 h of symptom onset compared to ACS (46.7% vs 55.7%, p < 0.001).

3.2. Revascularization therapies

Among the 1889 participants, 241 (12.8%) received revascularization therapy (RT); 189 had IVT alone, 24 intra-arterial (pharmacological and/or endovascular) alone and 28 bridging therapy (Table 2). 383 patients in PCS group and 1265 in ACS group had no revascularization therapy (NRT). All RT were more common in ACS group than PCS (213 vs 28, $p < 0.001$). Intravenous thrombolysis could be initiated in 13.1% ACS as compared to 5.8% PCS. The median onset-to-door time was significantly longer for PCS in the NRT group (67.7 vs 48.8 h, $p < 0.001$), but not in the RT group. There was no difference in post-thrombolysis sICH between PCS and ACS.

A significantly lower NIHSS was noted for PCS only in the NRT group (median 7 vs 10, p < 0.001), while there was no difference in the group who received thrombolysis (median 11 vs 13, $p = 0.430$). The stroke mechanisms between ACS and PCS in RT group were not statistically different unlike in the NRT. The NRT group showed significant differences between ACS and PCS in post-ischemic hemorrhagic transformation and mass effect, while there was no group difference in these variables in the RT group (Table 3).

Table 2
Revascularization therapy and post-ischemic hemorrhage in posterior versus anterior circulation strokes.

Variable	Posterior circulation N = 411	Anterior circulation N = 1478	p value
Revascularization therapy			
Any revascularization therapy	28 (6.8)	213 (14.4)	**<0.001**
Intravenous thrombolysis	24 (5.8)	193 (13.1)	**<0.001**
Intra-arterial thrombolysis	8 (1.9)	44 (3.0)	0.259
Intra-arterial pharmacological	4 (1.0)	11 (0.7)	
Intra-arterial mechanical	5 (1.2)	33 (2.2)	
Bridging therapy	4 (1.0)	24 (1.6)	0.488
Follow-up imaging	163 (39.7)	578 (39.1)	0.839
Symptomatic intracranial hemorrhage	2 (0.5)	13 (0.9)	0.546
Serious hemorrhage[a]	0	5 (0.3)	0.592
Post-ischemic hemorrhage			
Hemorrhagic transformation	29 (7.1)	176 (11.9)	**0.013**
Petechial hemorrhage, type 1	14 (3.4)	73 (4.9)	
Petechial hemorrhage, type 2	7 (1.7)	54 (3.7)	
Parenchymal hematoma, type 1	4 (0.97)	20 (1.4)	
Parenchymal hematoma, type 2	4 (0.97)	29 (2.0)	

[a] Serious hemorrhage was defined as life-threatening, serious systemic hemorrhage <36 h of thrombolysis.

3.3. Outcomes

At 3 months, mRS was available for 1836 (97.2%) patients; 2.8% were lost for follow up in the ACS group and 2.9% in the PCS group. A good outcome at 3 months (mRS 0–2) was noted for 910 (49.6%) patients. The 3-month outcome was similar for PCS and ACS in the RT group. In the NRT group, PCS had good outcome (mRS 0–2) at 3 months more frequently compared to ACS in univariate analysis (58.7% vs 46.4%, $p < 0.001$). Stroke territory did not show an independent association with the 3-month outcome in multivariable logistic regression model after correcting for initial stroke severity (NIHSS), vascular risk factors and stroke etiology (Table 4). In-hospital mortality, 3-month mortality and stroke recurrence were not different between PCS and ACS.

4. Discussion

In this study, we compared risk factors, stroke mechanisms, and functional outcome in PCS to that of ACS in a prospective registry-based multicentric study from India, with particular reference to the subset who received revascularization therapies. Patients with PCS received revascularization therapies less frequently than ACS. The NIHSS at admission and 3-month stroke outcome were more favourable in PCS in univariate analysis, but stroke territory was not an independent outcome predictor in regression analysis. Similar to previous studies [4,9], we noted that stroke severity at onset, stroke mechanism and outcomes were not different between PCS and ACS in the subgroup who received revascularization therapies while significant differences in these parameters were noted in the subgroup who did not receive revascularization therapies.

Observational studies suggest that 3-month functional outcome and mortality are comparable between ACS and PCS [2,4,16]. A study including both thrombolysed and non-thrombolysed patients with PCS and ACS did not show any difference in the outcomes between the two groups, however, stroke severity at onset was a predictor of 3-month outcome in PCS only in the non-thrombolysed group [4]. A recent study by Sommer et al. in a large cohort of matched ACS and PCS patients noted that the 3-month functional outcome was worse in PCS in non-thrombolysed patients, especially when the onset to door time exceeded 4.5 h or was unknown [9]. No difference in outcome was demonstrated based on vascular territories in patients who received thrombolysis [9]. In our cohort, the onset-to-door time and 3-month outcomes were not different in the patients who received revascularization therapies. However, in contrast to the study by Sommer et al. [9], PCS had better functional outcome in the no-revascularization group in univariate analysis. This difference was no longer significant after adjusting for other variables.

Real-world registries of patients who received IVT have shown better or similar functional outcomes in PCS compared to ACS [10–13,17,18]. One of the reasons for the observed good outcome of PCS could be the exclusion or low number of large vessel occlusions in the cohorts [11,12,18]. Posterior circulation emergent large vessel occlusion is associated with an extremely poor outcome, especially in basilar artery occlusion where the mortality exceeds 50% [19]. As these patients are candidates for endovascular therapy [20], they are under-represented in most of the registries reporting IVT. Our study included patients who had undergone all revascularization procedures and basilar artery disease was noted in 35.7% among PCS patients who received revascularization therapies.

An important predictor of outcome after thrombolysis is symptomatic intracerebral hemorrhage (sICH), the incidence of which is shown to be uniformly lower in PCS than ACS [11,13,18]. Lower infarct volumes in PCS [21], better collaterals in posterior circulation [22] and higher tolerance to blood brain barrier disruption [23] are the reasons cited for

Table 3
Comparison of posterior and anterior circulation strokes based on revascularization therapies.

Variable	Revascularization group			Non-revascularization group		
	PCS	ACS	p	PCS	ACS	p value
	N (%)	N (%)	value	N (%)	N (%)	
	N = 28	*N* = 213		*N* = 383	*N* = 1265	
Baseline and hospitalization						
Age (years); mean (SD)	63.5 (12.7)	57.7 (15.7)	**0.032**	58.1 (13.3)	58.2 (14.9)	0.912
Male sex; N(%)	18 (64.3)	139 (65.3)	0.919	268 (70.0)	845 (66.8)	0.245
Time to arrival at index hospital in hours; median (IQR)[a]	5.4 (3.3–10.2)	4.6 (2.6–7.3)	0.191	67.7 (25–156.8)	48.8 (16.1–127.5)	**<0.001**
Time to arrival at index hospital (categorized); N(%)[a]			0.075			0.085
0–3 h	19 (67.9)	154 (72.3)		28 (7.4)	123 (9.8)	
3–4.5 h	3 (10.7)	41 (19.2)		15 (3.9)	77 (6.1)	
>4.5 h	6 (21.4)	18(8.5)		337 (88.7)	1061 (84.1)	
NIHSS at admission; median (IQR)[b]	11 (6–19)	13 (9–17)	0.430	7 (4–12)	10 (5–16)	**<0.001**
Mass effect; N(%)	2 (7.1)	30 (14.1)	0.391	24 (6.3)	222 (17.5)	**<0.001**
Hemorrhagic transformation; N(%)	3 (10.7)	42 (19.7)	0.311	26 (6.8)	134 (10.6)	**0.030**
CCS subtype; N(%)						
Large artery atherosclerosis	11 (39.3)	65 (30.5)	0.389	76 (19.8)	404 (32.0)	**<0.001**
Cardio-aortic embolism	8 (28.6)	79 (37.1)	0.378	75 (19.6)	304 (24.1)	0.068
Small artery occlusion	2 (7.1)	20 (9.4)	0.698	96 (25.1)	170 (13.5)	**<0.001**
Other uncommon	1 (3.6)	2 (0.9)	0.238	21 (5.5)	39 (3.1)	**0.028**
Undetermined	6 (21.4)	47 (22.1)	0.939	115 (30.0)	346 (27.4)	0.315
In-hospital mortality; N(%)	2 (7.1)	18 (8.5)	0.814	23 (6.0)	101 (8.0)	0.198
3-month outcome; N(%)						
mRS score 0–2 (N = 1836)	13 (50.0)	109 (51.7)	0.873	219 (58.7)	569 (46.4)	**<0.001**
Stroke recurrence (N = 1570)	3 (13.0)	11 (6.3)	0.235	8 (2.4)	37 (3.6)	0.315
Mortality (N = 1836)	4 (15.4)	43 (20.4)	0.547	62 (16.6)	230 (18.8)	0.349

Abbreviations: ACS Acute circulation stroke, CCS Causative Classification of Stroke, IQR interquartile range, mRS modified Rankin Scale, N number, NIHSS National Institutes of Health Stroke Scale, PCS Posterior circulation stroke, SD standard deviation.

[a] 7 in-hospital strokes were excluded from analysis.

[b] NIHSS was not documented for 37 patients who were excluded from this analysis.

Table 4
Multivariable logistic regression analysis for good outcome (mRS 0–2) at 3 months.

Variable	Odds Ratio	95% CI	p value
Posterior circulation stroke	1.086	0.832–1.416	0.545
Age > 60 years	0.540	0.432–0.675	**< 0.001**
Female sex	0.979	0.771–1.243	0.860
CCS subtype[a]	3.305	1.701–6.425	**<0.001**
NIHSS >5	0.085	0.060–0.121	**<0.001**
Diabetes mellitus	0.800	0.634–1.009	0.059
Hypertension	1.094	0.866–1.382	0.450
Coronary heart disease	1.050	0.783–1.409	0.745
Rheumatic heart disease	1.246	0.763–2.034	0.380
Current smoking	0.969	0.724–1.295	0.830
Thrombolytic treatment	1.743	1.293–2.375	**<0.001**

Abbreviations: CCS Causative Classification of Stroke, CI confidence interval, mRS modified Rankin Scale, NIHSS National Institutes of Health Stroke Scale.

[a] Comparison of small artery disease to large artery atherosclerosis is noted in the table, comparison of the other CCS subtypes was not significant.

this observation. In the current study, no difference in sICH was noted between ACS and PCS, which is attributable to the relatively small size of the cohort who received RT and less severe strokes.

In our cohort, a good functional outcome was noted in univariate analysis for PCS only in patients in the NRT group. This group had a lower stroke severity by NIHSS, and significantly lower incidence of mass effect and post-ischemic hemorrhage, which are predictors of poor outcome. We did not find an increased risk of early recurrent stroke in PCS as was reported previously [24,25].

Though PCS represents 20 to 25% of patients [1,7] with acute ischemic stroke, it has been under-represented in the pivotal randomised control trials of IVT [12]. The proportion of PCS in observational studies of IVT range from 10 to 15% [10–12,17,18]. In this study, while PCS comprised 21.8% of the entire cohort, it constituted only 11.6% of the patients who received any revascularization therapy. The under-representation of PCS in RT group is attributable to the higher proportion of atypical and non-specific clinical presentations and lower NIHSS in them. Our PCS patients reached index hospital significantly later than ACS.

The onset-to-door time and door-to-needle time have been noted to be delayed in PCS compared to ACS [4,26,27]. The delayed onset-to-door time is more pertinent in developed countries like India where access to and utilization of emergency medical services are poor [15]. The widely adopted face-arm-speech test (FAST) for stroke identification is poorly sensitive for diagnosis of PCS [28]. In our study, PCS had significantly less weakness and speech and language deficits compared to ACS. Non-focal symptoms like dizziness, confusion, and a sense of discomfort are far more common with posterior circulation disease [29] which translate into a delay in diagnosing a stroke. Even after arrival to the emergency department, diagnosis of a basilar artery stroke was delayed by about 5.5 times as compared to left middle cerebral artery disease [30]. Intra-hospital delay is also accentuated by the poor sensitivity of CT scan for PCS [31] and need for MRI for diagnostic confirmation.

NIHSS is a relatively weak tool for assessing clinical features of PCS [32] and tends to underestimate its severity [33]. An NIHSS $\leq$4 can lead to a decision against thrombolysis and PCS is more likely to be affected in this manner than ACS. This flaw in the scale also results in an apparent poor correlation of initial stroke severity with functional outcome and mortality in PCS [9,33]. In the current study, median NIHSS was significantly lower in PCS compared to ACS. In patients who presented within 4.5 h and were not thrombolysed, mild stroke was attributed in 37.2% of PCS compared to 26.5% of ACS.

We used a well-validated and novel tool for documenting stroke mechanisms. Small vessel disease was the dominant stroke mechanism in PCS, whereas ACS more commonly had large artery atherosclerosis and cardioaortic embolism. Rheumatic heart disease, but not atrial fibrillation, was more common in ACS group. A recent study using CCS for classification similarly noted that small vessel occlusion was more

common in PCS compared to ACS [5]. They noted that isolated brainstem lesions were more commonly due to small vessel occlusion although vessel imaging is necessary to rule out co-existing proximal vessel stenosis and branch vessel disease. Cerebellar and PCA territory lesions more commonly resulted from large artery atherosclerosis or cardioembolic source [5]. More regions in the posterior circulation are supplied by penetrating end arteries than anterior circulation increasing the likelihood of lacunar strokes in the posterior circulation. Higher prevalence of diabetes mellitus and hypertension in the PCS group in our study could predispose to small vessel occlusion.

The strength of the study was the robust methodology of data collection and analysis in the largest multicentre stroke study from India, as described previously [14,15]. The classification of ACS and PCS was based on the acute infarct location in imaging as opposed to the less reliable technique centered on clinical characteristics. While the inclusion criteria allowed stroke <2 weeks to be enrolled, the majority (55.7%) were enrolled within 24 h. Our study has limitations. The sample of patients who underwent various thrombolytic therapies was relatively low, making subgroup analysis less reliable. The low number of mechanical thrombectomy group in the cohort prevented a detailed analysis of the impact of endovascular therapy between the groups. All the five centres were tertiary level stroke units and may represent a specific and probably a more severe spectrum of strokes in the community. The data was collected from 2012 to 2014 and hence the results may not represent the current treatment guidelines in stroke.

Our study is the largest and first multicentric study from India documenting the baseline characteristics in PCS strokes who received and did not receive revascularization therapies. The 3-month functional outcome and mortality were comparable between ACS and PCS in multivariate analysis in both the groups. Significant differences in NIHSS, risk factors and stroke mechanism were confined to patients who did not receive revascularization therapies. The study underscores the disparity in care and diagnosis of PCS with longer onset-to-door time and the lower numbers eligible for thrombolysis. More studies on endovascular therapy and intravenous thrombolysis in PCS can inform management decisions in the future.

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Declaration of Competing Interest

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References

[1] H.S. Markus, H.B. van der Worp, P.M. Rothwell, Posterior circulation ischaemic stroke and transient ischaemic attack: diagnosis, investigation, and secondary prevention, Lancet Neurol. 12 (2013) 989–998.
[2] R.B. Libman, T.G. Kwiatkowski, M.D. Hansen, et al., Differences between anterior and posterior circulation stroke in TOAST, Cerebrovasc. Dis. 11 (2001) 311–316.
[3] L.R. Caplan, R.J. Wityk, T.A. Glass, et al., New England Medical Center posterior circulation registry, Ann. Neurol. 56 (2004) 389–398.
[4] G.M. De Marchis, A. Kohler, N. Renz, et al., Posterior versus anterior circulation strokes: comparison of clinical, radiological and outcome characteristics, J. Neurol. Neurosurg. Psychiatry 82 (2011) 33–37.
[5] P. Frid, M. Drake, A.K. Giese, et al., Stroke genetics network (SiGN), the international stroke genetics consortium (ISGC), and the MRI-genetics Interface exploration (MRI-GENIE) Study. Detailed phenotyping of posterior vs. anterior circulation ischemic stroke: a multi-center MRI study, J. Neurol. 267 (2020) 649–658.
[6] A. Di Carlo, M. Lamassa, M. Baldereschi, et al., European BIOMED Study of stroke care group. Risk factors and outcome of subtypes of ischemic stroke. Data from a multicenter multinational hospital-based registry. The European Community stroke project, J. Neurol. Sci. 244 (2006) 143–150.
[7] J. Bogousslavsky, G. Van Melle, F. Regli, The Lausanne stroke registry: analysis of 1,000 consecutive patients with first stroke, Stroke 19 (1988) 1083–1092.
[8] K. Vemmos, C. Takis, K. Georgilis, et al., The Athens stroke registry: results of a five-year hospital-based study, Cerebrovasc. Dis. 10 (2000) 133–141.
[9] P. Sommer, A. Psekany, W. Serles, et al., Is functional outcome different in posterior and anterior circulation stroke? Stroke. 49 (2018) 2728–2732.
[10] A. Förster, A. Gass, R. Kern, et al., Thrombolysis in posterior circulation stroke: stroke subtypes and patterns, complications and outcome, Cerebrovasc. Dis. 32 (2011) 349–353.
[11] H. Sarikaya, M. Arnold, S.T. Engelter, et al., Outcomes of intravenous thrombolysis in posterior versus anterior circulation stroke, Stroke. 42 (2011) 2498–2502.
[12] X. Tong, X. Liao, Y. Pan, et al., Intravenous thrombolysis is more safe and effective for posterior circulation stroke: data from the thrombolysis implementation and monitor of acute ischemic stroke in China (TIMS-China), Medicine (Baltimore) 95 (2016), e3848.
[13] X. Zhu, N. Wang, H. Lin, P. Zhang, L. Chen, M. Zhang, B. Deng, T. Wu, Safety and efficacy of intravenous thrombolytic therapy in patients with acute posterior circulation stroke: a single-center study, J. Stroke Cerebrovasc. Dis. 29 (2020) 104537.
[14] D. Khurana, J. Pandian, P.N. Sylaja, et al., The indo-US collaborative stroke registry and infrastructure development project, Neurol. India 66 (2018) 276–278.
[15] P.N. Sylaja, J.D. Pandian, S. Kaul, et al., Ischemic stroke profile, risk factors, and outcomes in India: the indo-US collaborative stroke project, Stroke. 49 (2018) 219–222.
[16] E. Zürcher, B. Richoz, M. Faouzi, et al., Differences in ischemic anterior and posterior circulation strokes: a clinico-radiological and outcome analysis, J. Stroke Cerebrovasc. Dis. 28 (2019) 710–718.
[17] T. Dorňák, M. Král, M. Hazlinger, et al., Posterior vs. anterior circulation infarction: demography, outcomes, and frequency of hemorrhage after thrombolysis, Int. J. Stroke 10 (2015) 1224–1228.
[18] B. Keselman, Z. Gdovinová, D. Jatuzis, et al., Safety and outcomes of intravenous thrombolysis in posterior versus anterior circulation stroke: results from the safe implementation of treatments in stroke registry and meta-analysis, Stroke. 51 (2020) 876–882.
[19] W.S. Smith, M.H. Lev, J.D. English, et al., Significance of large vessel intracranial occlusion causing acute ischemic stroke and TIA, Stroke. 40 (2009) 3834–3840.
[20] Y. Kayan, P.M. Meyers, C.J. Prestigiacomo, et al., Current endovascular strategies for posterior circulation large vessel occlusion stroke: report of the society of NeuroInterventional surgery standards and guidelines committee, J. Neurointerv. Surg. 11 (2019) 1055–1062.
[21] A. Lindgren, B. Norrving, O. Rudling, et al., Comparison of clinical and neuroradiological findings in first-ever stroke. A population-based study, Stroke. 25 (1994) 1371–1377.
[22] J.L. Ostrem, J.L. Saver, J.R. Alger, et al., Acute basilar artery occlusion: diffusion-perfusion MRI characterization of tissue salvage in patients receiving intra-arterial stroke therapies, Stroke. 35 (2004) e30–e34.
[23] J. Pagola, M. Ribo, J. Alvarez-Sabin, et al., Thrombolysis in anterior versus posterior circulation strokes: timing of recanalization, ischemic tolerance, and other differences, J. Neuroimaging 21 (2011) 108–112.
[24] E. Flossmann, P.M. Rothwell, Prognosis of vertebrobasilar transient ischaemic attack and minor stroke, Brain. 126 (Pt 9) (2003) 1940–1954.
[25] N.L. Paul, M. Simoni, P.M. Rothwell, Oxford Vascular Study, Transient isolated brainstem symptoms preceding posterior circulation stroke: a population-based study, Lancet Neurol. 12 (2013) 65–71.
[26] A. Sarraj, S. Medrek, K. Albright, et al., Posterior circulation stroke is associated with prolonged door-to-needle time, Int. J. Stroke 10 (2015) 672–678.
[27] P. Sommer, L. Seyfang, A. Posekany, et al., Prehospital and intra-hospital time delays in posterior circulation stroke: results from the Austrian stroke unit registry, J. Neurol. 264 (2017) 131–138.
[28] G. Gulli, H.S. Markus, The use of FAST and ABCD2 scores in posterior circulation, comparedwith anterior circulation, stroke and transient ischemic attack, J. Neurol. Neurosurg. Psychiatry 83 (2012) 228–229.
[29] A. Compter, L.J. Kappelle, A. Algra, et al., Nonfocal symptoms are more frequent in patients with vertebral artery than carotid artery stenosis, Cerebrovasc. Dis. 35 (2013) 378–384.
[30] J.D. Burns, R.S. Rindler, C. Carr, et al., Delay in diagnosis of basilar artery stroke, Neurocrit. Care. 24 (2016) 172–179.
[31] D.Y. Hwang, G.S. Silva, K.L. Furie, et al., Comparative sensitivity of computed tomography vs. magnetic resonance imaging for detecting acute posterior fossa infarct, J. Emerg. Med. 42 (2012) 559–565.
[32] W.D. Tao, M. Liu, M. Fisher, et al., Posterior versus anterior circulation infarction: how different are the neurological deficits? Stroke. 43 (2012) 2060–2065.
[33] M.J. Schneck, Current stroke scales may be partly responsible for worse outcomes in posterior circulation stroke, Stroke. 49 (2018) 2565–2566.