

Posterior circulation ischaemic stroke - A retrospective analysis from a General Hospital

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ABSTRACT:

Even though ischemic stroke represents a majority of strokes in general, only a smaller portion originate from posterior circulation. Because of different origin and particular territory involvement, this represents a difficult clinical task. We compared relevant clinical data from literature with results of our patients affected by the posterior circulation stroke (PCS). We analyzed stroke patients admitted from 2018. to 2022. in General Hospital Pula, a touristic oriented county hospital in Croatia on the Adriatic Coast. In that five-year period we admitted 1795 patients with ischemic stroke. 246 or 13,6% of those originated from the posterior circulation, which is significantly less than data from similar reports. Majority of those patients were male, 64%. Comparing the outcome, we found that the PCS had significantly better outcome. Mortality rate was similar in both, 14% for PCS versus 16% in the anterior circulation strokes (ACS). We analyzed the outcome by infarct region or etiology, as well as clinical particularities related to the territory of PCS involvement. We also selected patients having PCS as a result of dissection. According to our results the patients with PCS had better outcome in comparison to ACS. The most frequent site of stroke was cerebellar, followed by pontine stroke. The highest mortality was observed in patients with multiple posterior circulation strokes. Initial NIHSS score was lower in posterior circulation strokes than in anterior circulation strokes, with an important impact on reperfusion therapy rates. Therefore, it is crucial to perform comprehensive clinical evaluation of patients with posterior circulation ischemic strokes.

Key words: Posterior circulation stroke, Anterior circulation stroke, National Institutes of Health Stroke Scale (NIHSS), Risk factors, Modified Rankin Score (mRS)

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SAŽETAK:

ISHEMIJSKI MOŽDANI UDAR STRAŽNJE CIRKULACIJE - RETROSPEKTIVNA ANALIZA IZ OPĆE BOLNICE
Iako ishemijski moždani udar predstavlja većinu moždanih udara općenito, samo manji dio potječe iz stražnje cirkulacije. Zbog različitog podrijetla i zahvaćenosti određenog teritorija, ovo predstavlja težak klinički zadatak. Usporedili smo relevantne kliničke podatke iz literature s rezultatima naših pacijenata pogođenih moždanim udarom stražnje cirkulacije (PCS). Analizirali smo pacijente s moždanim udarom primljene od 2018. do 2022. godine u Općoj bolnici Pula, turističko orijentiranoj županijskoj bolnici u Hrvatskoj na jadranskoj obali. U tom petogodišnjem razdoblju primljeno je 1795 bolesnika

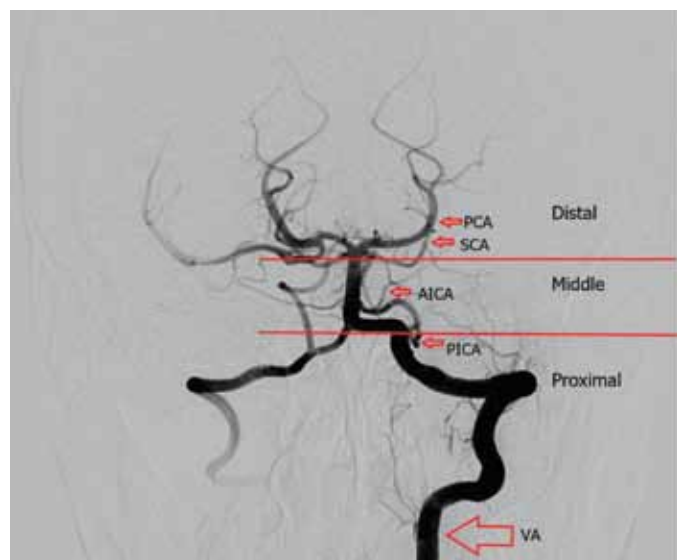
s ishemijskim moždanim udarom. 246 ili 13,6% potječe iz stražnje cirkulacije, što je znatno manje od podataka iz sličnih izvješća. Većina tih pacijenata bili su muškarci, 64%. Uspoređujući ishod, otkrili smo da je PCS imao značajno bolji ishod. Stopa smrtnosti bila je slična u oba, 14% za PCS naspram 16% za udare prednje cirkulacije (ACS). Analizirali smo ishod prema regiji infarkta ili etiologiji, kao i kliničkim posebnostima vezanima uz područje zahvaćenosti PCS-a. Također smo odabrali pacijente koji imaju PCS kao posljedicu disekcije. Prema našim rezultatima bolesnici s PCS-om imali su bolji ishod u usporedbi s ACS-om. Najčešće mjesto moždanog udara bio je cerebelarni, a zatim moždani udar mosta. Najveća smrtnost zabilježena je u bolesnika s višestrukim moždanim udarima stražnje cirkulacije. Početni NIHSS rezultat bio je niži u udarima stražnje cirkulacije nego u udarima prednje cirkulacije, s važnim utjecajem na stope reperfuzijske terapije. Stoga je ključno provesti sveobuhvatnu kliničku procjenu bolesnika s ishemijskim moždanim udarom stražnje cirkulacije.

KLJUČNE RIJEČI: moždani udar stražnje cirkulacije, moždani udar prednje cirkulacije, ocjenska ljestvica moždanog udara Nacionalnog instituta za zdravlje (NIHSS), faktori rizika, modificirani Rankinov score (mRS)

INTRODUCTION

The majority of ischemic strokes occurs in the territory of the anterior circulation. 20% to 25% of ischemic strokes are from the posterior circulation (1). Mortality rates of those strokes vary from 3,6% to 18,6% (2).

Posterior circulation ischemia (PCI) involves respectively the proximal division, irrigated by the vertebral artery (VA) and the posterior inferior cerebellar artery (PICA), the middle division with the basilar artery (BA) and the anterior inferior cerebellar artery (AICA) and finally the most frequent, the distal division, irrigated by the posterior cerebellar artery (PCA) and the superior cerebellar artery (SCA) with the penetrating branches of BA and PCA (2,3,4). (Figure 1.)



According to the study by Searls et al. the most common areas of PCS by proportion are distal (41%), multiple territories (25%), proximal (18%) and middle (16%) (3). Posterior circulation irrigation involves the brainstem, including the medulla oblongata, pons and midbrain, the cerebellum, thalamus, the occipital cortex, the medial temporal cortex, and part of the parietal lobe. According to the previously mentioned study, analyzing symptoms and signs of PCI of 407 patients recruited in the New England Medical Center Posterior Circulation Registry, the most frequent symptoms were dizziness (41%), unilateral limb weakness (41%), dysarthria (31%), headache (28%), nausea and vomiting (27%) (3). The most frequent sign was unilateral limb weakness (38%), followed by gait ataxia (31%), unilateral limb ataxia (30%) dysarthria (28%) and nystagmus (24%). The same study found a positive correlation of dysphagia, nausea, vomiting, dizziness and Horner syndrome with the proximal posterior vascular territory, unilateral limb weakness and cranial nerve VII deficit with the middle territory and finally limb sensory deficit lethargy and visual loss positively correlate with the distal territory (3). You may notice that those frequent signs from a proximal territory belong to the lateral medullary syndrome or Wallenberg syndrome.

Generally, posterior circulation stroke events result in a better outcome than anterior circulation stroke. According to the New England Medical Center Posterior Circulation Registry, poor outcome was observed in 3,6% of patients, comparable to study by Bogousslavsky et al., showing 30-day mortality rate of

Figure 1. Anteroposterior projection DSA image of the left vertebral artery. Courtesy of I. Jovanović MD PhD, Department of Radiology, University Hospital Centre Zagreb

5,9% in a population of 1000 patients from the Lausanne Stroke Registry (5,6). A similar low mortality rate of 3% was reported recently by Han Y. et al. after a one-year follow up. The same study has established poor outcome (mRs 3 or larger) in 15.2% of 165 patients (7). Poor outcome in studies by Caplan et al. and Glass was more frequently related to distal territory lesions, up to 77% (2,4). The relative risk (RR) of poor outcome was higher in distal territory ischemia (3,12), compared to 1,88 for middle territory and 0,81 for proximal territory (4).

These results are in coherence with study by Hacke et al. showing a 70% mortality rate in comatose or tetraplegic patients with proven intracranial vertebral artery (ICVA) or basilar artery (BA) occlusion (8). Age, alcohol abuse and previous stroke were associated with a worse outcome. The RR of worse outcome was significantly lower for large artery disease (0,59), compared to cardioembolic stroke (1,89). Finally, multiple infarcts were also more frequently associated with a worse outcome, with reports of 60,5% patients with poor outcome having three brain lesions (4).

Stroke etiology study performed on 407 patients from the New England Medical Center Posterior Circulation Registry (NEMC-PCR) by Caplan et al. showed that the most common posterior circulation stroke mechanism was embolic in 40% of cases, of which 24% were of cardiac source and 14% of arterial. Large artery occlusive disease accounted for 32%, perforating and circumferential branch occlusion was the reason for 14% of PCS, migraine 3% and 10% by other reason (2).

Besides the previously mentioned classification in three divisions, posterior circulation was further divided into six groups by Bogousslavsky et al. in 1988: brainstem, cerebellum, superficial, deep (thalamus), PCA territory and multiple location. Forty-eight percent of the vertebrobasilar infarcts were in the brainstem (mainly pons in 27%, mainly medulla in 14%, mainly midbrain in 7%), 7% in the cerebellum, 36% in the PCA territory (entire territory in 7%, deep in 11%, superficial in 18%), and 9% in multiple locations (5). The presumed causes of infarction in this study were defined as atherosclerosis with or without stenosis, embolic heart disease, hypertensive arteriopathy, mixed etiologies, other etiologies like dissections and finally undetermined etiology. Embolic lesions were most frequently present in the cerebellum and in infarcts of multiple locations. Dissections most frequently resulted in brainstem ischemia, they were more prevalent in younger patients and usually posttraumatic by origin (5).

Probably 20% of blood flow belongs to the vertebrobasilar vascular territory (9). That would mean that one in five embolic strokes originate from the posterior circulation. However it has to be considered the geometry of vertebral arteries, their origin and the diameter as opposed to the carotid arteries which may increase the risk of focal atherosclerosis (10). There is a higher frequency of anatomical variants in the vertebrobasilar circulation- mostly fetal variant of artery communication in the PCA and VA hypoplasia. (11 12). For example the VA hypoplasia was observed more frequently in strokes affecting the PICA. There

were not an increased risk of strokes in the fetal PCA. (12.)

The National Institutes of Health Stroke Scale (NIHSS) is the most commonly used scale to validate stroke severity, intended mostly for rt-PA and endovascular intervention, but also indispensable in stroke research. NIHSS correlates with infarct size, clinical severity, and long-term outcome (13). NIHSS scale cut-off for favorable outcome is lower in posterior circulation strokes. An analysis showed important differences between median NIHSS values, median value for AC stroke was seven, compared to two in PC strokes. This study also showed that the majority of PC strokes had a NIHSS score of 4 or less and 15% of those strokes had a poor outcome (14). This suggests that NIHSS underestimates clinical severity in posterior circulation stroke and patients presenting with low NIHSS may wrongly be considered ineligible for reperfusion therapy.

It is known that the questionnaire is more oriented toward the anterior circulation lesions, examines mostly motor and cortical functions, especially language, and contains fewer questions about dysphagia, nystagmus, truncal ataxia or cranial nerve lesions with exemption of facial nerve. Even though a modified version of NIHSS scale showed higher prognostic accuracy and usefulness to identify posterior circulation stroke patients with low NIHSS score and higher risk of poor outcome, it hasn't been widely accepted in any form (15).

SUBJECTS AND METHODS

In this retrospective study we analyzed all ischemic stroke patients admitted to General Hospital Pula in the period between 2018 and 2022. Patients were divided into two main groups, anterior circulation and posterior circulation strokes. In both groups we recorded the following epidemiological data for each patient: sex, age, initial NIHSS at admission, presence or history of atrial fibrillation (AF), administered revascularization therapy and the modified Rankin scale (mRs) after discharge. Poor outcome was defined as mRS 3 to 6 at 3 months from discharge. We particularly studied our posterior circulation stroke patients, examining data about symptoms and signs, defined risk factors such as hypertension, diabetes, hyperlipidemia, AF; and presumed etiology. We identified the involved artery and territory in the posterior circulation stroke. The territories involved were the occipital lobe and other less common cortical lobes, the thalamus, midbrain, pons, medulla oblongata and the cerebellum. The territory of the cerebellum as the widest and in our study the most frequent stroke location was further stratified in subgroups such as VA territory stroke, PICA stroke, AICA or SCA stroke. In addition to these single territories, we also recorded cases with multiple territory involvement.

Quantitative data are expressed as mean \pm standard deviation (SD). Qualitative data are expressed as frequency and percentage. Statistical analysis was performed by univariate regression analysis, followed by multivariate logistic regression analysis. A value of $P < 0.05$ was considered statistically significant.

RESULTS

During the five-year period we treated 1549 anterior circulation stroke patients and 246 posterior circulation patients. Over that period we noticed a kind of convergence: the numbers of ACS through those years slowly dropped but PCS seemed to rise in number of cases, though it was not statistically significant (Figure 2.).

Among 1549 ACS patients 818 or 52,81% were women, difference is significant (chi-square test χ^2 4,89; p 0,027). Among 246 PCS patients there were significantly less women than men – we observed 88 or 35,77% of women, according to chi-quadrat test χ^2 value was 19,9; p less than 0,001 (Table 1.).



Figure 2. Ischemic strokes in general Hospital Pula between 2018 and 2022.

Table 1. Differences of age onset between female and male.

ACS				PCS			
N.1549	mean	Range	SD	N.246	mean	Range	SD
All	78	22-100	11,79		69	46-89	11,5
Female	82	22-100	11,52		75	46-89	9,45
Male	73	30-98	11		67,5	30-97	12

In both ACS and PCS groups male patients were younger, $p < 0,001$. The percentage of PCS in the pool of ischemic stroke patients was lower than usual: 13.6%.

Age stratification showed differences between the two types of stroke: PCS patients were younger, with largest proportion in the middle aged group. Greater number of ACS cases occurred in the elderly age (Figure 3.).

In ACS and PCS groups of patients atrial fibrillation was more often present in the female patients (Table 2.).

As shown in (Table 3.), at admission PCS patients had, according to NIHSS value, a less pronounced deficit and also a better outcome later. Results showed lower death rate in the PCS group.

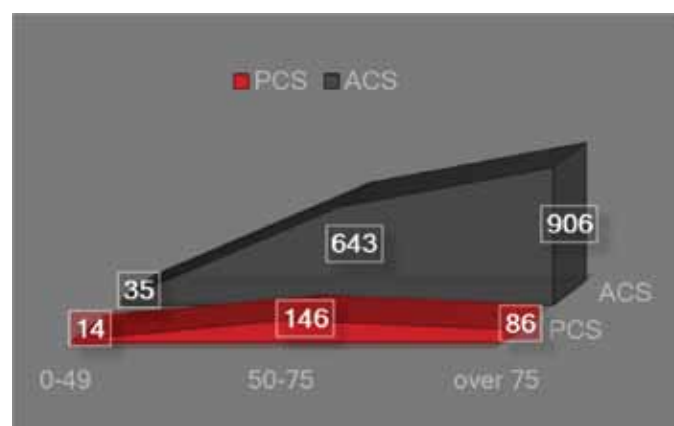


Figure 3. Age stratification for PCS and ACS.

Table 2. Incidence of atrial fibrillation between sexes.

	Sex		Chi-quadrat	p		Sex		Chi-quadrat	p
ACS	Male	197 (27%)	22,38	p<0,001	P	Male	33 (20,89%)	11,23	0,0008
	Female	313 (38,3%)				Female	36 (40,91%)		

Table 3. Epidemiology of posterior circulation stroke, PCS and anterior circulation stroke, ACS.

	PCS n. 246	ACS n. 1549	Ischemic stroke
Mean age (range)	70 (38-97)	76 (22-100)	73
Gender F/M n. (%)	88/158 36/64%	818/1549 53/47%	906/1794 51 (49%)
Mortality n. (%)	34/ (14%)	248 (16%)	282 (16%)
mRS 0-2 n. (%)	117 (48%)	499 (32%)	616 (32%)
AFib n. (%)	69 (28%)	510 (33%)	577 (32%)
NIHSS n. (%)	Mean: 7	Mean: 10	312 (17%)
NIHSS > 15	29 (12%)	283 (25%)	

We performed a multivariate regression analysis, more precisely logistic regression. In this model, we obtained a good predictive power of 83.41% for ACS group, when comparing the outcome with NIHSS, sex, age and AF. We found that Odds ratio for a bad outcome was 20,45. In the PCS patient group there was also a good predictive power of 76,02% but with a lower odds ratio

for a bad outcome, 10,45. There was a twice bigger odd for a bad outcome in the group of ACS patients then in PCS patients. Logistic regression showed that NIHSS ($p < 0.001$, $r = 0.36$) and age ($p = 0.003$, $r = 0.04$) significantly affect the outcome, while gender and FA are not significant predictors in case of PCS patients. (Table 4.).

Table 4. Comparison of predictors for outcome in ACS and PCS patients.

ACS	Logistic regression Predictive variables	Regression coefficient	$c^2=787$ $p < 0,001$
1	NIHSS	0,42	$p < < 0,001$
2	Sex	0,33	P 0,03
3	Age	0,04	P < < 0,001
4	Atrial fibrillation	0,01	0,928

PCS	Logistic regression Predictive variables	Regression coefficient	$c^2=100,65$ $p < 0,001$
1	NIHSS	0,36	<<0,001
2	Sex	0,11	0,74
3	Age	0,04	0,003
4	Atrial fibrillation	0,21	0,569

The most frequent symptom in PCS patients were dizziness (68%) and dysarthria in 59% of patients. The most frequent sign was dysarthria followed by limb ataxia. Cranial nerve involvement was also frequent, in 46% of patients (Table 5.). It's notable that there were no statistically significant differences in occurrence of dysarthria depending on the location of affected

vascular territory. According to the territory involved and corresponding leading sign we may say that the cerebellum where more related with ataxia, medulla with nystagmus, dysarthria and cranial nerve involvement meanwhile distal territories where more related with limb paresis. (Table 6.)

Table 5. symptoms and signs in PCS

Symptoms	n. (%)	Signs	n. (%)
Dizziness	169 (68%)	Unilateral limb weakness	108 (44%)
Unilateral limb weakness	132 (48%)	Gait ataxia	98 (40%)
Dysarthria	144 (59%)	Unilateral limb ataxia	132 (54%)
Headache	79 (32%)	Dysarthria	150 (61%)
Nausea and vomiting	117 (48%)	Nystagmus	61 (25%)
		Skin sensation impairment	57 (23%)
		Cranial nerve involvement	114 (46%)

Table 6. Most frequent signs in PCS.

Vascular territory	Most prominent sign	%
1. Midbrain	Cranial nerve palsy	63,6 %
2. Pons	Dysarthria	74 %
3. Medulla	Nystagmus, Cranial nerve palsy and dysarthria	63 %
4. Occipital lobe	Limb paresis	54 %
5. Thalamus	Limb paresis	69,6 %
6. Cerebellum	Limb and gait ataxia	68,9 %
7. Multiple territories	Limb paresis and dysarthria	62,5 %

Table 7. Territories involved as division involved in PCI.

Cerebellum	medulla	pons	midbrain	thalamus	Occipital lobe	Multiple location
74 (30%)	27 (11%)	50 (20%)	11 (4,5%)	23 (9,5%)	37 (15%)	24 (10%)
Proximal division	Middle division	Distal division	Multiple division			
81 (33%)	70 (28%)	71 (29%)	24 (10%)			

Most frequently affected territory was the cerebellum in 30% of PCS cases, followed by the pons in 20% of cases. Therefore, PCS was more frequent in the proximal territory. Distal territories were proportionally less involved in PCS (Table 7.).

When observing cerebellar infarcts particularly, the most frequent was the PICA irrigated territory followed by the mas-

sive hemispheric infarction. Distal arteries were less frequently affected. Ischemic lesions in the territory of VA or PICA were more often related to atrial fibrillation. PICA territory infarct had the greatest incidence of AF, 41%. A good outcome for the cerebellar infarcts was present in 39% of patients, less than the average for PCS reported in literature (Fig 4).

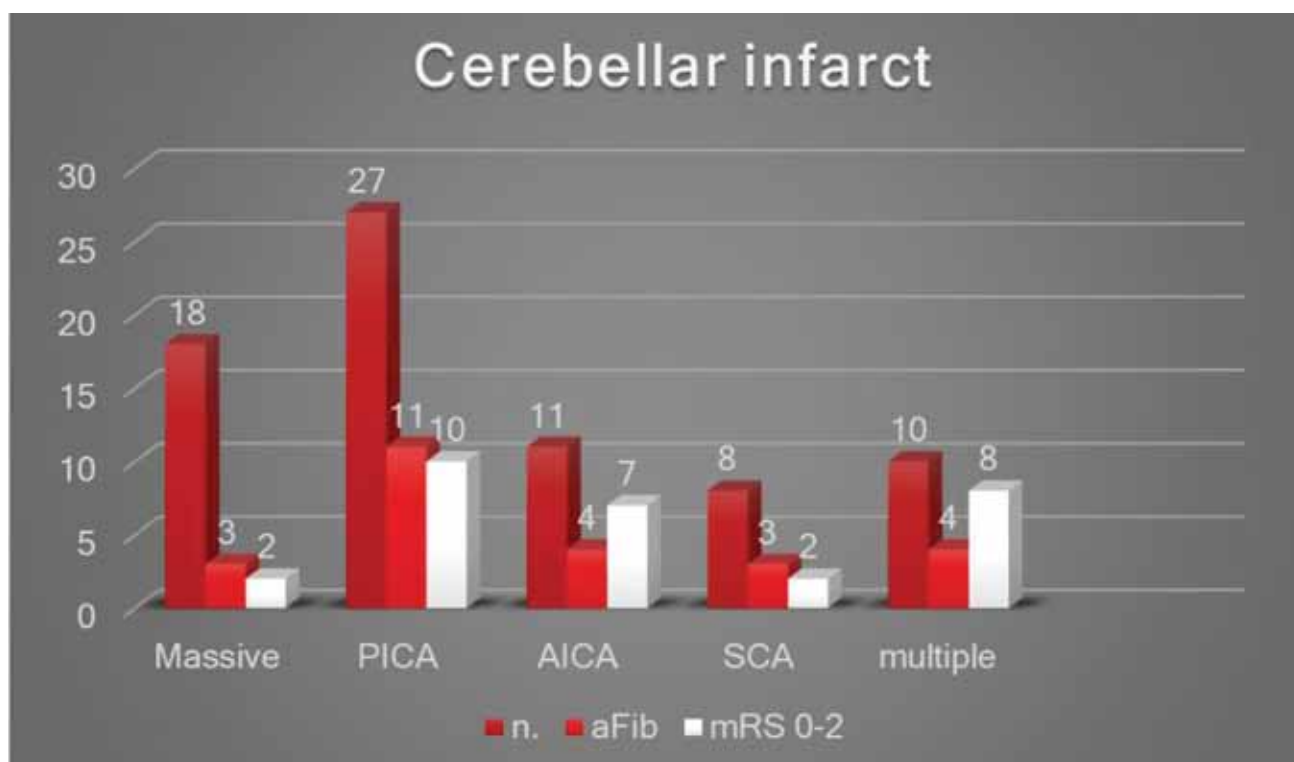


Figure 4. Distribution of patients with different cerebellar territory infarct, presence of aFib as a risk factor and good outcome in our PCS group (absolute numbers).

The most frequent risk factor was hypertension. There were fewer PCS patients with atrial fibrillation than ACS patients - 28% versus 32% of patients (Table 8).

Distribution of PCS by etiology in our cohort was respectively: embolic stroke, large artery disease, penetrating artery disease and dissections. Most frequently stroke was caused by emboli, 32%, 28% from a cardiac origin. Large artery disease was similarly frequent, in 28% of cases, followed by penetrating artery

disease in 23% of cases. We had 10 patients with different dissections (4,2%), obviously involving proximal arteries like VA and PICA (Table 9).

In this analysis we didn't find a statistically positive relation between small vessel disease or perforator artery occlusion with common risk factors like hypertension, diabetes and hyperlipidemia (Table 10.).

Table 8. Risk factors in PCS.

Risk factor	n.	%
Hypertension	221	90
Diabetes mellitus	88	36
Hyperlipidemia	161	65
Atrial fibrillation	69	28

Table 9. Presumed etiology of PCS.

Etiology	GH Pula n. (%)
Large artery disease	68 (28%)
Embolism	78 (32%)
Cardiac source	69 (28%)
Penetrating artery disease	56 (23%)
Dissection	10 (4,2%) 7 VA, 2 PICA and 1 SCA

Table 10. Relation between common risk factors and small vessel disease.

	Risc HA	Risc DM	Risc HLP		P
Small vessel disease	78	33	62	0,39	0,822
No small vessel disease	142	55	99		

	Risc HA	Risc DM	Risc HLP		P
Perforator	46	25	34	2,30	0,316
No perforator	175	63	127		

Table 11. Differences between initial NIHSS of PCS and ACS patients.

N=246 PCS	median	Mode	First quartiles	Third quartiles	Standard deviation
NIHSS	4,5	3	3	8	6,24
N=1549 ACS					
NIHSS	8	6	5	14	5,95

If we look back to NIHSS values in our cohort there was a substantial difference between the two stroke groups. (Table 11.) Following median and mean NIHSS values for PCS, most of those patients wouldn't be eligible for revascularization treatment. Our experience is quite disappointing, while our rt-PA rates are up to 9,7% of ischemic stroke, only 3,7% (n. 9) of PCS patients were treated with rt-PA, none with MT. According to a larger collaborative study, minor PCS are significantly more often associated with disability at 3 months compared to minor ACS (16). We also had similar conclusions: out of 121 patients with NIHSS ≤ 4 , 33 or 28% had a poor outcome, meanwhile 65 of 339 or only 19% from the ACS group also had a poor outcome.

DISCUSSION

We wanted to compare our results with previously published studies regarding this still challenging part of cerebral ischemia research, the posterior circulation stroke. During these five years, we have seen a small but increasing number of strokes in the posterior circulation. These epidemiological data, although in many aspects not statistically significant, can definitely predict a new trend and show that it is necessary to pay more attention to the differentiation of this type of stroke. We demonstrated that the posterior circulation stroke is more likely to affect younger patients, another reason to put more effort into not underestimating the clinical presentation. As we know from other studies, this clinical presentation can vary and usually leads to the misinterpretation of a mild stroke. The NIHSS values in PCS patients are shown to be lower than in ACS. According to our finding more PCS patients with low initial NIHSS scoring (≤ 4) had a worst outcome (mRS ≥ 3) compared to ACS patients. Although, in general, we had better outcomes and lower mortality rates in PCS group. Atrial fibrillation as a major cause of embolic stroke was not as prominent in our study as expected or observed in other studies. This may be because our posterior circulation strokes occurred in the proximal territory rather than in the distal territory, where they have been mostly shown to originate from embolic propagation. In our study, the cerebellum was the most common site, especially the PICA, although with a particularly high rate of atrial fibrillation, leading to the conclusion that etiologically these strokes also had a cardioembolic etiology, after all. This statement differs from data from other studies, and the reason could perhaps be a combined lesion in the proximal part of the vertebrobasilar territory. Reviewing our medical records, we weren't able to capture all planned data, therefore there is a possibility of bias in data collection. According to our data 76% of our patients had angiography performed (MRIA or MSCTA) and only 45% had an MRI performed during the inpatient stay. We should have performed more neuroradiological and vascular examinations to clearly define any large vessel disease, especially in the ICVA and PICA, to determine the exact extent of LVD. Given the emerging therapeutic options, these patients should

receive a detailed clinical evaluation and complete imaging of the brain and vessels, regardless of severity. Neurosonologic evaluation should be performed as soon as possible but not delaying therapy. In our study 75% of our PCS patients had a neurosonologic workup done. In view of the more frequent cardioembolic strokes in the posterior circulation, a complete cardiac evaluation is essential. Medical care should be particularly careful to assess dysphagia in order to prevent aspiration (17).

Finally, it should be said at the outset that it is critical to change the way we perform initial scoring to assess the severity of posterior circulation stroke. So far, there have been attempts to assign some value to certain signs such as dysphagia, abnormal coughing and gait ataxia but so far such ideas have not been broadly accepted. Perhaps with further adaptation of the NIHSS, we might reach a generally accepted consensus.

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none

CONFLICT OF INTEREST

None to declare.

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