Intravenous Thrombolysis in Posterior Cerebral Artery Infarctions

L. Breuer a H.B. Huttner a K. Jentsch a C. Blinzier a K. Winder b T. Engelhorn b M. Köhrmann a

Departments of a Neurology and b Neuroradiology, University of Erlangen-Nuremberg, Erlangen, Germany

Key Words
Ischemic stroke · Intravenous thrombolysis · Posterior cerebral artery

Abstract
Background: Approximately 5–10% of all acute ischemic strokes (AIS) occur in the territory of the posterior cerebral artery (PCA). Little is known about intravenous thrombolysis (IVT) in this infarct subgroup in terms of outcome and intracerebral hemorrhage rates. The aim of our study was to evaluate differences between supratentorial PCA infarcts and anterior circulation infarcts regarding baseline characteristics, stroke severity, outcome, safety and clinical findings, which would implicate a change in the existing thrombolysis practice in patients with PCA stroke. Methods: All patients with AIS in the supratentorial PCA territory receiving IVT between 01/2006 and 01/2010 were selected from the Erlangen Thrombolysis Database (group 1, n = 21). They were compared to all IVT patients with strokes in other supratentorial vascular territories over the same period of time (group 2, n = 398). Baseline demographic data, as well as clinical and laboratory findings were analyzed. The outcome was assessed using the modified Rankin Scale at 3 months. Results: Only serum glucose levels at baseline (110.5 ± 36.1 vs. 127.2 ± 48.2 mg/dl; p = 0.036) and the baseline National Institutes of Health Stroke Scale score (median 6.5 vs. 9; p = 0.016) were significantly lower in group 1 compared to group 2. Favorable clinical outcome (57.1 vs. 48.6%; p = 0.445) and intracerebral hemorrhage rates (4.8 vs. 4%; p = 1.000) were comparable in both groups. Conclusions: No substantial differences were found between supratentorial PCA and anterior circulation infarcts. Our data on safety and efficacy support the present common thrombolysis practice in supratentorial PCA infarct patients, though an indication for IVT should rather be based on the existence of functionally disabling deficit than merely on the National Institutes of Health Stroke Scale.

Introduction
Infarcts in the territory of the posterior cerebral arteries (PCA) constitute for approximately 5–10% of all ischemic infarcts [1]. Up to two thirds of all PCA infarcts (PCAI) are pure superficial infarcts [2–5], while thalamic involvement is expected in 20–30% [6–12]. Several studies have analyzed the variety of neurological symptoms caused by PCAI as well as differing etiological mechanisms and clinical outcome in this infarct subgroup [2, 4, 5, 13, 14]. Yet, data on patients with PCAI re-
ceiving intravenous thrombolysis (IVT) is limited, for
different reasons. First, previous randomized IVT stroke 
trials focused on patients with anterior circulation stroke 
and ischemic strokes in the posterior circulation are
still excluded from many acute treatment trials. Sec-
ond, typical functional deficits of PCAI are often consid-
ered not disabling in the acute phase and the National 
Institutes of Health Stroke Scale (NIHSS) score underes-
timates the severity of PCAI symptoms, as complete 
homeomorphic hemianopia accounts for only 2 NIHSS 
points but severely affects the quality of life (e.g. driving,
reading, watching TV). For these reasons, IVT is often
not initiated. However, if IVT is applied, differentiation
is rarely made between supratentorial PCAI and anterior 
circulation strokes in the present clinical routine. This
retrospective study compared IVT patients with ischemic
infarcts in the supratentorial PCAI territory to those with
anterior circulation infarcts. We aimed to evaluate wheth-
er differences exist between these 2 groups regarding
baseline characteristics, stroke severity, outcome, safety,
mortality, clinical and imaging findings, which would
implicate a change in the existing thrombolysis practice
in patients with PCA stroke.

Methods

Patient Selection and Treatment

The Erlangen Stroke and Thrombolysis Database is a prospec-
tive database of all patients with acute ischemic stroke (AIS) at our
institution (University Hospital Erlangen, Erlangen, Germany). It
contains baseline demographic and stroke-related data as well as
treatment specifics and imaging information for each stroke pa-
tient who underwent thrombolysis. All patients treated with IVT
between 01/2006 and 01/2010 were analyzed (n = 457). In this
study, we compared patients with AIS in the supratentorial PCA
territory (cortical infarctions with and without sole additional
thalamic involvement; group 1, n = 21) to all patients with AIS in
the anterior circulation [middle cerebral artery (MCA) territory
and anterior cerebral artery (ACA) territory] receiving throm-
bolysis over the same period of time (group 2, n = 398). The study
focused on isolated supratentorial PCAI since clinical differentia-
tion from anterior circulation strokes can be difficult and treat-
ment is similar. In contrast, infratentorial strokes involving the
midbrain as well as cerebellar and brainstem infarcts are clini-
cally distinct and often lead to other treatment approaches. There-
therefore, they were excluded from this study (n = 38). Differences
between group 1 and group 2 regarding demographics, cerebrovas-
cular risk factors, etiological stroke causes (TOAST classification)
[18], clinical features, laboratory and neuroimaging data, compli-
cations and outcome were analyzed.

Thrombolysis and Neuroimaging Protocol

All patients were treated and monitored in our stroke unit ac-
cording to European guidelines [19]. According to international
guidelines [19, 20], IVT was not restricted by a certain lower
NIHSS limit. Independent of the NIHSS score at admission, pa-
tients needed to have a disabling syndrome in the judgment of the
 treat ing stroke physician in order to be eligible for IVT [21]. Sim-
ple functional tests (i.e. walking, buttoning up trousers, reading,
writing, phoning) are carried out in the emergency room to de-
termine the functional impact of the symptom in borderline cas-
es. In addition to standard CT-based treatment within the 3-hour
time window, multimodal CT and an MRI mismatch-based algo-

Evaluation of Outcome and Safety

The NIHSS score was recorded by a stroke neurologist certi-
fied for NIHSS evaluation at baseline and 3 times per day through-
out the hospital stay. The outcome at 90 days was assessed using
the modified Rankin Scale (mRS) evaluated by a neurologist as
part of the general database independently from the present study
using a semi-structured interview either in person or by tele-
phone. A considerable proportion of patients receiving throm-
bolysis had a pre-stroke mRS >1. Therefore, favorable clinical out-
come was defined as an mRS of 0–2 and/or clinical recovery to the
pre-stroke mRS. Asymptomatic (aICH) and symptomatic intra-
cranial hemorrhage were defined according to the Euro-

Statistical Analysis

Statistical analyses were performed using the ‘SPSS’ software
package (version 18.0, SSPS Inc.). All data were tested for normal-
ity and are given as median and range or the mean ± SD, as ap-
appropriate. Categorical variables are presented as frequencies
and percentages. Groups of patients with AIS in the PCA territory
and patients with AIS in other territories were compared using the
Mann-Whitney U test, χ² test and Fisher’s exact test.

Results

During the time period of this study, 457 patients re-
ceived IVT. A total of 59 (12.9%) patients had posterior
circulation strokes partly involving the midbrain as well as
the cerebellum or brainstem. The PCA territory was
involved in 38 (8.3%) patients, and supratentorial PCA
occurred in 21 (4.6%) patients (group 1).

PCAl: Clinical Symptoms and Baseline Characteristics

The frequency of different clinical symptoms of the
PCAl patients treated with IVT is given in table 1. Char-
acteristics for all patients (PCAl/MCA/ACA infarcts) and
for groups 1 and 2 are presented in table 2. The median
age was 73 years (interquartile range 63–81), and 55.4%
were men. The prevalence of cardiovascular risk factors
was high. There were no statistically significant differ-

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ences between the 2 groups regarding age, sex, cardiovascular risk factors, blood pressure, cholesterol, international normalized ratio, platelet count, hemoglobin A1c and inflammation markers such as C-reactive protein and white blood cell count at baseline. Furthermore, both groups were comparable regarding stroke etiology, previous prophylactic treatment and time from symptom onset to thrombolysis. The median baseline NIHSS score was significantly lower in group 1 than in group 2 (6.5 vs. 9; p = 0.016). The median NIHSS at 24 h still showed a trend towards less neurological impairment in group 1 (3.5 vs. 5; p = 0.079), and at discharge, no statistically significant difference could be detected (median NIHSS, 3 vs. 4; p = 0.202). Further, serum glucose levels at baseline [110.5 ± 36.1 mg/dl (group 1) vs. 127.2 ± 48.2 mg/dl (group 2); p = 0.036] between the 2 groups were significantly different. A fetal origin of the PCA was identified in 4 patients (19%) of group 1.

**Outcome, Safety and Mortality**

The length of hospital stay (8 days, range 6.5–10, vs. 8 days, range 6–12; p = 0.477), favorable clinical outcome at day 90 (57.1 vs. 48.6%; p = 0.445), intracranial bleeding rates (sICB: 0 vs. 3.5%, p = 0.632; aICH: 9.5 vs. 6.8%, p = 0.649) and mortality (0 vs. 8.8%; p = 0.240) were comparable in group 1 and group 2 (table 3).

**Discussion**

Little is known about IVT in patients with supratentorial PCAI in terms of baseline characteristics, stroke severity, clinical outcome, ICH rates and length of hospital stay. Pivotal randomized IVT stroke trials focused on anterior circulation stroke [15–17] and there is no systematic analysis of thrombolysis in isolated PCAI. Therefore, it is unknown whether IVT in this infarct subgroup differs from treatment of anterior circulation infarcts. Several authors have investigated the heterogeneous clinical patterns, topography, etiological causes, long-term functional outcome, intracerebral bleeding and mortality of PCAI in larger case series [1, 4, 6, 8, 11, 12, 23–25]. However, none of these authors clearly differentiated between PCAI patients who received tissue plasminogen activator and those who were not treated with thrombolysis.

Our findings with 8.3% overall PCA involvement and 4.6% isolated supratentorial PCAI correspond well with pre-existing data (5–10%) [1]. Thrombolysis in supratentorial PCAI is rare because the corresponding symptoms are often underestimated and not primarily considered for IVT by the treating physician. Furthermore, affected patients are frequently not aware of their symptoms, or symptom recognition is delayed. On the other hand, unintentional IVT in PCAI patients can occur because differentiation between posterior infarctions and anterior circulation infarcts in the primary emergency room setting may be difficult (see case presentation in fig. 1). Maulaz et al. [26] described PCA strokes mimicking anterior stroke in 17.8%. Especially in the case of combined superficial and deep PCA strokes which occur in up to 38% [3, 6, 12, 23, 27, 28], differentiation from MCA/ACA strokes remains challenging because of existing aphasic symptoms, predominant hemiparesis, neglect and sensory deficits. Additional affection of lateral thalamic structures, sometimes combined with thalamocapsular edema, can cause hemiparesis via (reversible) impairment of the pyramidal tracts [6–8, 12]. Moreover, memory dysfunction and other neurophysiological defects may complicate the examination of these patients [2, 3, 14].

In our study, most analyzed aspects like age, sex, cerebrovascular risk factors, vital parameters and laboratory results did not show significant differences between groups 1 and 2. Only glucose level at baseline which is known as an independent predictor for higher bleeding risk and worse clinical outcome [29–32] was lower in PCA stroke patients. However, sICH/aICH rates and good clinical outcome were similar in both groups and comparable to the large randomized trials [17, 33, 34]. None of the PCA stroke patients died during the hospital stay, which is consistent with PCA stroke mortality rates (0–7%) in the literature [3, 6, 14, 23, 28, 35].

Four of our PCA stroke patients (19%) showed a fetal origin of the PCA, and as such, the infarction was attributable to the anterior circulation. This is comparable to the results of de Monyé et al. [36] who reported this vessel

### Table 1. Clinical symptoms in PCA patients (n = 21)

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>PCA strokes</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
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<tr>
<td>Homonymous hemianopia</td>
<td>14</td>
</tr>
<tr>
<td>Facial palsy</td>
<td>11</td>
</tr>
<tr>
<td>Aphasia</td>
<td>8</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>6</td>
</tr>
<tr>
<td>Head deviation and/or gaze palsy</td>
<td>4</td>
</tr>
<tr>
<td>Neglect</td>
<td>2</td>
</tr>
</tbody>
</table>

Patients can have combinations of symptoms.
variant in 17% of 82 PCAI patients. Examination of this variant is important since secondary prophylaxis, e.g. in case of a higher-grade symptomatic stenosis of the internal carotid artery feeding the fetal PCA, is affected.

Patients with supratentorial PCAI had a significantly lower baseline NIHSS score compared to group 2, while rates of independent and favorable clinical outcome at 3 months did not differ between the 2 groups. This may be explained by the fact that symptoms of supratentorial PCAI are undervalued by the NIHSS but nevertheless influence functional outcome, comparable to symptoms caused by anterior circulation strokes. Thus, even though

<table>
<thead>
<tr>
<th>Table 2. Baseline and outcome characteristics</th>
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<tbody>
<tr>
<td>All infarcts (PCA/MCA/ACA) (n = 419)</td>
</tr>
<tr>
<td>Sex, male</td>
</tr>
<tr>
<td>Risk factors</td>
</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>Hypercholesterolemia</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Coronary artery disease</td>
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<tr>
<td>Atrial fibrillation</td>
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<tr>
<td>Previous stroke</td>
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<tr>
<td>Nicotine</td>
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<tr>
<td>Previous myocardial infarction</td>
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<tr>
<td>Peripheral artery disease</td>
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<tr>
<td>Systolic blood pressure, mm Hg</td>
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<tr>
<td>Diastolic blood pressure, mm Hg</td>
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<tr>
<td>Temperature, °C</td>
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<tr>
<td>Blood parameters</td>
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<tr>
<td>Glucose at baseline, mg/dl</td>
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<tr>
<td>Cholesterol at baseline, mg/dl</td>
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<tr>
<td>International normalized ratio</td>
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<tr>
<td>White blood cell count, ×10³/µl</td>
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<tr>
<td>Platelet count, ×10³/µl</td>
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<tr>
<td>Hemoglobin A1c</td>
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<tr>
<td>C-reactive protein at baseline, mg/l</td>
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<tr>
<td>Previous prophylactic treatment (n = 415)</td>
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<tr>
<td>ASA</td>
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<tr>
<td>Clopidogrel</td>
</tr>
<tr>
<td>ERDP/ASA</td>
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<tr>
<td>Oral anticoagulation</td>
</tr>
<tr>
<td>No previous antiplatelet treatment</td>
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<tr>
<td>Median NIHSS score [range]</td>
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<tr>
<td>Baseline</td>
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<tr>
<td>24 h</td>
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<tr>
<td>Discharge</td>
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<tr>
<td>TOAST criteria</td>
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<tr>
<td>Large vessel</td>
</tr>
<tr>
<td>Embolic</td>
</tr>
<tr>
<td>Micro/lacunar</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

Figures are numbers with percentages in parentheses or means ± SD unless otherwise stated.
ASA = Acetylsalicylic acid; ERDP = extended-release dipyridamole.
patients with PCAI had lower NIHSS scores, this does not mean that they were functionally less affected. Often, treating physicians are hesitant to perform IVT in the case of low NIHSS scores. However, taking the disabling character of e.g. isolated complete hemianopia into account, treatment decision should be based on considerations regarding functional impairment of the symptoms rather than solely on a particular NIHSS score [21]. This also applies to the design of inclusion criteria of acute stroke studies.

Our study has obvious limitations, most notably the retrospective, observational design. Furthermore, the investigated number of IVT-treated PCAI is small. In addition, since according to international guidelines [19] treatment was based on non-contrast CT only in the majority of cases, we could not assess recanalization data. Because of the differing sample size, statistical comparisons between group 1 and group 2 are difficult and results must be interpreted with caution. However, to our knowledge, this is the first systematical analysis of IVT in supratentorial PCA strokes.

In conclusion, our results do not suggest any substantial differences regarding safety and outcome between IVT in PCAI and anterior circulation infarcts. Thus, di-

### Table 3. Outcome and safety data

<table>
<thead>
<tr>
<th></th>
<th>All infarcts (PCA/MCA/ACA) (n = 419)</th>
<th>PCAI (n = 21)</th>
<th>MCA/ACA infarcts (n = 398)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome at 3 months</td>
<td></td>
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<tr>
<td>Favorable clinical outcome</td>
<td>203 (49.0)</td>
<td>12 (57.1)</td>
<td>191 (48.6)</td>
<td>0.445</td>
</tr>
<tr>
<td>Hemorrhagic complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aICH</td>
<td>29 (6.9)</td>
<td>2 (9.5)</td>
<td>27 (6.8)</td>
<td>0.649</td>
</tr>
<tr>
<td>sICH</td>
<td>14 (3.3)</td>
<td>0</td>
<td>14 (3.5)</td>
<td>0.632</td>
</tr>
<tr>
<td>Median length of hospital stay, days</td>
<td>8 [6–12]</td>
<td>8 [6.5–10]</td>
<td>8 [6–12]</td>
<td>0.477</td>
</tr>
<tr>
<td>Mortality at 3 months</td>
<td>49 (11.6)</td>
<td>0</td>
<td>49 (12.3)</td>
<td>0.153</td>
</tr>
</tbody>
</table>

Figures in parentheses are percentages; figures in brackets are ranges.

### Fig. 1. Case presentation.

- **a**–**c** Pretreatment CT (**a**) of an 82-year-old man presenting to the emergency room with clinically suspected left-sided MCA territory stroke (severe aphasia, right-sided facial palsy and hemiparesis). Further examination revealed complete hemianopia to the right side. CT angiography (**b**) and CT perfusion imaging (**c**) demonstrate left-sided PCA occlusion and a corresponding extended perfusion deficit. **d** Post-treatment CT after unsuccessful thrombolysis with 63 mg tissue plasminogen activator (within 100 min of symptom onset) showing ischemic infarction in the left PCA territory.
agnostics to firmly identify those patients do not seem required before IVT. Taking the naturally lower NIHSS scores in PCAI with nevertheless functionally disabling syndromes into account, indication for IVT and inclusion into clinical trials should be considered on the functional impact of PCAI symptoms rather than solely on a specific NIHSS score.

Disclosure Statement

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References