The Hyperdense Posterior Cerebral Artery Sign
A Computed Tomography Marker of Acute Ischemia in the Posterior Cerebral Artery Territory

Timo Krings, MD; Dagmar Noelchen, MD; Michael Mull, MD; Klaus Willmes, PhD; Ingo G. Meister, MD; Peter Reinacher, MD; Rudolf Toepper, MD; Armin K. Thron, MD

Background and Purpose—In the anterior circulation, the hyperdense middle cerebral artery (MCA) sign is a well-established marker for early ischemia. Similarly, the hyperdense basilar artery sign or the MCA “dot” sign may be a diagnostic clue for basilar artery or distal MCA branch thrombosis. The purpose of this study was to define the hyperdense posterior cerebral artery (PCA) sign and determine its incidence, diagnostic value, and reliability as a marker for ischemia in the territory of the PCA.

Methods—Cranial computed tomographies (CCTs) of 48 patients with proven acute ischemia (<12 hours) in the PCA territory were compared by 3 independent and blinded readers to the CCTs of 86 age-matched patients without PCA infarction. Using follow-up imaging, the correlation of the hyperdense PCA (HPCA) with infarct size, thalamic infarction, and bleeding were investigated.

Results—An HPCA was found in 35.4% of all patients with PCA infarction, typically within the ambient cistern, with a specificity of 95.4%. The thalamus was affected significantly more often (P=0.009) and the size of the infarct was significantly more often large than medium (P=0.018) or small (P<0.001) when an HPCA was present. Hemorrhagic transformation tended to occur more often when the HPCA was present.

Conclusions—An HPCA was detected in more than one third of all patients with PCA ischemia, suiting the incidence of the hyperdense MCA. Based on our results, this sign may not only be helpful in the early diagnosis of PCA infarction but might also act as a prognostic marker in acute PCA territory ischemic stroke. (Stroke. 2006;37:399-403.)

Key Words: computed tomography ▶ posterior cerebral artery ▶ stroke, ischemic

Even in the era of diffusion and perfusion-weighted MRI, cranial computed tomography (CCT) plays a major role in the evaluation of early ischemic stroke because in the emergency setting, CCT is still the first diagnostic step after physical examination in many hospitals. The early diagnosis of stroke is important for the further management, and, therefore, a number of authors have looked at hyperacute findings on CCT in stroke victims. The majority of these studies focused on the middle cerebral artery (MCA) territory, where most strokes occur. Unilateral hyperdensity of the MCA, the so-called “hyperdense MCA sign” (HMCAS) was recognized as one of the earliest signs of ischemic stroke and has been reported to be present within 90 minutes after onset of neurological symptomatology.1,2 This sign is recognized on non–contrast-enhanced CT as an area of increased attenuation when compared with the contralateral hemisphere along the course of the first and second segment of the MCA.3 The hyperattenuating component represents an intraluminal clot from a thrombus or an embolus. Whereas flowing blood has an attenuation of ≈40 Hounsfield units, the attenuation of thrombus is close to 80 Hounsfield units, most likely because of the extrusion of serum in the thrombus with the subsequently increased hemoglobin concentration.4 The HMCAS is associated with a large MCA territory infarction, severe neurological deficit, and poor clinical outcome.5–7 Apart from the HMCAS, hyperdensities along the course of other cerebral vessels have been described for the basilar artery and for the more distal vessel segments of the MCA, the so-called hyperdense sylvian fissure “dot” sign,8 and more recently, in a case of a hyperdense posterior cerebral artery (PCA) as a marker for PCA territory ischemic stroke.9 Concerning this latter sign, it is as yet unknown in what frequency it appears and in how far the presence of such a sign might provide information about the prediction of neurological deficits, the size of the affected brain tissue, and possible hemorrhagic transformation. Therefore, the purpose of this study was to determine the incidence, diagnostic value, and reliability of the HPCA sign (HPCAS) as a marker for ischemia in the PCA territory.
Methods

Study Group
This is a retrospective study of 48 patients who experienced an acute infarction (ie, <12 hours old) in the PCA territory between April 1995 and April 2004 and who were evaluated with emergency non–contrast-enhanced CT. Patients were included in the study: (1) if a PCA territory ischemia was proven either by follow-up MRI or CT; (2) if the exact onset of symptoms was recorded within the patient’s chart; and (3) if CCT was performed within the first 12 hours after symptom onset. There was a male preponderance of 31 to 17 patients. Patient age ranged between 38 and 81 years, with a mean age of 61. In 38 patients, a follow-up CT was performed, and in the other 10 patients, a follow-up MRI was available.

The control group consisted of 86 patients (61 males, with a mean age between 24 and 83 years; mean age 62 years) who were studied under the clinical question “Rule out PCA ischemia” but in whom imaging studies and the further clinical course ruled out an ischemia in the PCA territory as studied by their clinical charts.

CT Data
All CT examinations were performed on a high-resolution tomograph (between 1995 and 1999 Somatom DR; after 1999 Somatom Plus 4; Siemens). The scanning protocol consisted of axial 4-mm-thick orbitomeatal sections from the occipital foramen to the sellar region (including the posterior fossa and the transition to the diencephalon as the site of interest for the present study) and of 8-mm-thick sections from the sellar region to the vertex.

Data Analysis
All 134 CT scans were independently reviewed by 3 clinicians experienced in interpreting CT ischemic changes (T.K., D.N., M.M.), with the researchers blinded to the affected hemisphere but, in an effort to reproduce daily practice, knowing that all patients had neurological symptoms suiting acute PCA ischemia. Each scan was assessed for the presence of the following signs: (1) HPCA. According to criteria defined previously for the HMCA,10 an HPCA was present if the PCA was denser than its counterpart on the presumably nonaffected hemisphere and denser than any other visualized vessel of comparable size. (2) Presence and size of other ischemic signs were reported in 2 patients, resulting in a specificity of this sign of 95.4%. Fisher’s exact test revealed a highly significant difference in the incidence of the HPCA in patients with PCA infarction compared with those without PCA infarction (P<0.001).

In 31 of the 48 patients with a PCA infarction, ischemic signs other than the HPCA were present, resulting in an incidence of 64.6%; in the control group, false-positive early ischemic signs were reported in 2 patients, resulting in a specificity of 97.7% (1 patient had a post-traumatic edema, and 1 experienced reversible posterior leukencephalopathy). Of the 31 CCTs without an HPCA, no other early markers of ischemia were visible in 11 cases; of the 17 patients with an HPCA, 13 CCTs showed also other early markers of cerebral ischemia, resulting in a total of 4 patients (8.3%) in whom the HPCA was the only and first CT marker of ischemia in the PCA territory (Figure 2).

Table 1 provides the values expressing inter-rater agreement between the 3 pairs of observers for the HPCA: (1) in all 134 CTs, (2) in the patient group, (3) in the control group, and (4) for the early ischemic signs in all 134 CTs. The statistic is a measure of agreement of 2 observers; a value of 0 indicates chance agreement, and a value of 1 indicates perfect agreement. Values of 0 to 0.2 indicate poor agreement, 0.21 to 0.4 fair agreement, 0.41 to 0.6 moderate agreement, 0.61 to 0.8 good agreement, and 0.81 to 1 excellent agreement.

Timing of the HPCA
CCTs were performed between 1 hour and 12 hours between symptom onset (mean 5.8 hours; SD 3.1 hours); 13 patients were scanned within the first 3 hours, 15 patients between 3 and 6 hours after symptom onset, and the remaining 20 patients between 6 and 12 hours. In the patient group that was scanned within the first 3 hours, the HPCA was present in 7
of 13 patients (53.8%); in the second group, a positive HPCAS was seen in 7 of 15 patients (46.6%), whereas in the group of patients scanned after 6 hours, the sign was only present in 3 of 20 (15%). Significant differences between the 3 groups were only present between the 2 early groups and the late group (Fisher's exact test \( P = 0.005 \) and 0.01, respectively; Pearson's correlation coefficient was \( r = -0.31 \). This finding is further underlined when looking at the follow-up CTs, which were available in 12 of the 17 patients with an HPCAS. These follow-up CTs were performed between 48 and 96 hours after the onset of neurological symptoms (mean 67 hours; SD 17.3 hours) and demonstrated that in 9 patients, the HPCAS was no longer present. In those patients who had no HPCAS on their initial scan, follow-up CT did not show an HPCAS either. When taking these data into the Pearson statistic, a highly significant correlation coefficient of \( r = -0.89 \) was calculated, indicating that the hyperdensity most likely is an early and transient phenomenon, similar to the HMCAS.\(^1\)

**Lesion Volume and the HPCAS**

In our group of 48 patients with an acute PCA infarction, there were 7 patients with a small infarct comprising less than one third of the PCA territory. Typically, these infarctions were located in cortical territories of the calcarine branch of the PCA. In none of these patients was an HPCAS present. Eighteen patients had medium-sized infarcts, 6 of whom had an HPCAS (33.3%), and 23 patients had large infarctions, with 11 demonstrating an HPCAS (47.8%). The probability of having a large infarction versus a medium-sized infarction when an HPCAS was present was marginally statistically significant (Fisher’s exact test \( P = 0.018 \)); the probability of having a large infarction versus a small-sized infarction when an HPCAS was present and the probability of having a medium-sized infarction versus a small sized infarction were highly statistically significant (\( P > 0.001 \)). Similarly, the probability of a thalamic affection when an HPCAS was present was determined. Of the 17 patients with an HPCAS, 10 had thalamic involvement (58.8%), whereas thalamic involvement of the remaining 31 patients without HPCAS was only present in 8 cases (25.8%), resulting in a statistically significant difference for the probability of thalamic involvement of Fisher \( P = 0.009 \).

**Clinical Symptoms, Hemorrhagic Transformation, and Etiology and the HPCAS**

A complete hemianopia was present in 14 of the 17 patients with an HPCA (82.3%), whereas the remaining 3 patients experienced an incomplete hemianopia. In the 31 patients without an HPCA, complete hemianopia was present in 17 cases (54.8%), indicating a statistically significant frequency for having a complete hemianopia if the HPCAS is present of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Interobserver Agreement Using ( \kappa ) Statistics</th>
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<tbody>
<tr>
<td></td>
<td>Presence of HPCAS in All 134 CCTs</td>
</tr>
<tr>
<td>Observer 1 vs observer 2</td>
<td>0.881</td>
</tr>
<tr>
<td>Observer 1 vs observer 3</td>
<td>0.795</td>
</tr>
<tr>
<td>Observer 2 vs observer 3</td>
<td>0.782</td>
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</tbody>
</table>
Table 2. Etiology of PCA Infarction

<table>
<thead>
<tr>
<th>Etiology of PCA Infarction</th>
<th>Patients Without HPCAS</th>
<th>Patients With HPCAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presumed cardiac emboli</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Presumed arterio-arterial emboli (atherosclerotic disease of supplying artery, as determined by angiography)</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>After coronary angiography</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>17</td>
</tr>
</tbody>
</table>

Discussion

The incidence of the HMCAS as a marker for early ischemia in the MCA territory has been described to vary between 5% and 75% of patients with acute ischemic stroke; however, these differences are attributable to a number of factors, including varying numbers of included patients, varying stroke locations (only MCA strokes versus all strokes), and varying timing of investigation, to name a few. In the largest study, which included only MCA strokes, an incidence of 41.2% was found, which roughly suits our incidence of 35.4%. Interobserver variability was good to excellent for the patient group but showed considerable variation in the control groups, which indicated that additional training is required to obtain reasonable accuracy and reproducibility between readers.

A thrombus or an embolus is considered to be the most likely explanation for a hyperdense artery sign based on indirect evidence such as disappearance of the hyperdensity over time or after thrombolysis. Moreover, in a case report, the radiologic–pathologic correlation of an HMCAS demonstrated an embolus as the substrate of the hyperdensity. The authors found a clot consisting of fibrin, erythrocytes, some neutrophils, and cellular debris, whereas the adjacent arterial wall showed no abnormalities. Based on these observations, there are several possible reasons why the incidence of the hyperdensity within an artery is lower than other early CT signs in acute cerebral infarction. Hemodynamic infarctions or, at the time of the CCT, already resolved clot or clots with low attenuation attributable to different components, will not demonstrate the typical hyperdensity along the course of a vessel. Moreover, if slices are too thick in relation to the affected vessel, a hyperdense artery will not be present. This was presumably the case in those 7 patients included in our study who had a small cortical infarct within distal branches of the PCA.

The reason why the HPCAS compared with the HMCAS has only been described in a single case report but not in larger previous studies may have different reasons. The frequency of PCA territory infarcts is between 5% and 10%, therefore, only few large PCA stroke series exist that have mainly studied clinical features and etiology but that did not specifically look for imaging findings. However, there are other potential reasons. Standard slice orientation in CCT is orbitomeatal, therefore, the cistern of the MCA is typically displayed in a single slice, which enables easy detection of the MCA, especially when atrophic changes in the brain are present. A MCA hyperdensity can therefore be visualized well. The course of the PCA is more complex. Typically, the P1 segment ascends laterally around the cerebral peduncles to reach the ambient cistern, where it courses horizontally, medial to the temporal lobe, and in close proximity to the tentorium. The pars circularis (or P1 and P2 segment) ends in the quadrigeminal cistern with the branch of the lateral occipital artery where the pars corticalis (P3 and P4 segment) starts. Because of this course, only the P2 segment is running parallel to the cutting plane within a cistern (the ambient cistern); a hyperdensity, if present, can therefore most easily be detected in that region.

In 4 patients of the control group, all readers diagnosed a false-positive HPCAS. In retrospect, these cases were reanalyzed. In 3 patients, we were able to identify the hyperdensities as calcified PCAs (by evaluating follow-up CCTs); in 1 case, the hyperdensity was identified as a tentorial calcifica-
tion in direct proximity to the PCA. Calcifications typically demonstrate a higher density than thrombus; however, in the rather small vessels and the curved course of the PCA, partial volume effects can lead to signal attenuation of these calcifications and might therefore render differentiation from real thrombus in the artery difficult or even impossible.

It has been reported that the arterial density depends on the timing between the onset of symptoms and the CCT. It has been described that the HMCAS is present in 75% of the infarctions in the first 90 minutes and in 15% from hour 12 to hour 24,11 that it is the most early sign for an ischemia in the MCA territory,16 and that it demonstrates a negative linear dependency with time.17 Our results concerning the HPCAS are comparable to the results obtained in the anterior circulation. In a number of patients, the HPCAS was the first sign of ischemia in the PCA territory, and in the majority of patients for whom a follow-up CCT was available, the HPCA was no longer visible. The majority of HPCAS was found in those patients scanned early after symptom onset, whereas in those patients in whom the CT scan was delayed, the HPCAS was less often encountered.

In the anterior circulation, an HMCAS is a marker of poor prognosis.17 Similarly, more often we found in our group of patients large infarctions and thalamic ischemia. We presume that this was attributable to the fact that, as explained above, the PCA could only be evaluated in its proximal portion (P2 segment). Because the thalamogeniculate arteries that supply the lateral thalamus originate from this segment, involvement of the thalamus in addition to the hemispheral territory is more likely, and the more proximal arterial occlusion predicts a larger size of the infarcted tissue, a more severe clinical symptomatology, including alterations in consciousness, the tendency toward a complete hemianopia, and hemorrhagic transformation.

Summary
The characteristics of the HPCAS have not been described previously in a large series of patients. We defined this sign as the hyperdensity within the ambient cistern, medial to the tentorium cerebelli that is typically visualized in 1 or 2 adjacent slices and that can extend into the quadrigeminal cistern. This sign is detected with good interobserver reliability in more than one third of all patients with PCA ischemia, suiting the incidence of the HMCAS in MCA stroke. The HPCA is often associated with thalamic infarction, large PCA territory ischemia, more severe neurological symptomatology, and a higher risk of hemorrhagic transformation. Therefore, this sign may not only be helpful in the early diagnosis of PCA infarction but might also act as a prognostic marker in acute PCA territory ischemic stroke.

References
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