Vasospasm after subarachnoid hemorrhage: utility of perfusion CT and CT angiography on diagnosis of delayed cerebral ischemia

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**Aims and objectives**

Cerebral vasospasm is a major cause of delayed neurologic morbidity after a subarachnoid hemorrhage (SAH). Cerebral ischemia secondary to vasospasm occurs in 20%-30% of these patients and has been correlated with a 1.5-3 fold increase in mortality in the first two weeks after SAH.

The etiology of cerebral ischemia after SAH is complex, and its pathophysiology is poorly understood, often leading to indeterminate diagnoses and delayed treatments.

Delayed cerebral ischemia (DCI) has been defined as new focal neurologic impairment or worsening on the Glasgow Coma Scale, after other possible causes of clinical deterioration have been eliminated, and/ or new infarction on imaging attributed to vasospasm.

Early recognition and prompt treatment of vasospasm can improve neurologic outcomes(3) however, aggressive treatment of vasospasm increases the risk of hemorrhage and brain edema, consequently a noninvasive yet reliable, fast, and accurate diagnostic work-up is necessary to discern those patients who are in need of such an active therapy (4).

Perfusion CT imaging provides an accurate noninvasive survey of the hemodynamics effects of vasospasm on the brain parenchyma.

The aim of this study was:

- To evaluate the utility of perfusion CT (PCT) combined with CT angiography (CTA) for the diagnosis of vasospasm and the delayed cerebral ischemia (DCI), by using conventional digital subtraction (DSA) as the gold standard.
- To correlate PCT maps with the territory of the vessels affected with vasospasm in DSA and with the final territories infarcted on the follow-up Non-contrast CT (NCT).
Methods and materials

Patients:

We retrospectively reviewed every patient arrived with acute subarachnoid hemorrhage that stayed at least seven days in the neurosurgical intensive care unit at our institution from 2012 to 2015.

Every patient included arrived with Acute Subarachnoid Hemorrhage (ASH) following aneurysmal rupture. We excluded from the study the patients under 18 or older than 85 year old and also pregnant women.

We performed Non-enhanced computed tomography (NECT) using the Fisher scale to quantify the amount of subarachnoid Hemorrhage Fig. 1 on page 11.
Fig. 1: Fisher Scale grading system used to quantify the amount of subarachnoid hemorrhage and intraventricular hemorrhage (IVH). The percentages in the blue circles refers to the risk of vasospasm. Grade III and IV in the scale are the ones with the higher risk to develop "symtomatic vasospasm". Department of Neuroradiology at Virgen de la Salud Hospital Toledo (Spain).

References: - Toledo/ES

The relationship between cerebral vasospasm and a high density of blood in the basal subarachnoid cisterns on the initial CT scan was first described by Takemae (6). Based on a multivariate logistic regression model in which CT scans and clinical variables were used, Claassen, et al. found four independent predictors of delayed cerebral ischemia: mean arterial pressure greater than 112 mm Hg, intraventricular hemorrhage (IVH) in both lateral ventricles, mean blood flow velocities greater than 140 cm/sec on TCD ultrasonography studies obtained within 5 days of SAH, and thick SAH in any cistern or fissure. Of these predictors, IVH was the strongest and was associated with a threefold increase in the risk of delayed cerebral ischemia. They believe the increased risk in patients with IVH were due to a higher load of spasmogens in the cerebrospinal fluid (CSF) and to stagnation of CSF (6).

Many scales have been proposed to grade the amount of cisternal subarachnoid blood in the hopes of more accurately determining which patients are at highest risk. The most well-known scale that continues to be used is the one created by Fisher, et al. (Fig 1) The Fisher grade, developed in 1980, is commonly used to predict the risk of cerebral vasospasm after subaracnoid hemorrhage (SAH) based on the amount of blood shown on initial CT scans.

Fisher Scale:

- **Grade I:** no hemorrhage evident.
- **Grade II:** Subaracnoide hemorrhage less than 1 mm thick (interhemispheric, insular or ambient cisterns).
- **Grade III:** Localized clot and/or layers of blood greater than 1 mm thick in the vertical plane.
- **Grade IV:** intracerebral or intraventricular clots with diffuse or absent blood in basal cisterns.

The majority of current evidence seems to support the suggestion that the presence of significant IVH is also a risk factor for vasospasm; intracerebral hematomas (ICH), on the other hand, have consistently been shown not to be a risk factor (6).

CT angiography was used for screening of intracranial aneurysm. A caudocraneal scanning direction was performed, covering the whole brain down to 4 cm below the foramen magnum, to encompass the posteroinferior cerebellar arteries in the volumen
analysis. CTA raw data were reformatted in axial, sagittal and coronal 3-mm-thick maximal intensity projection (MIP) images and volumen rendering (VR) in 3D.

**Fig. 2**: Fig. 2 - Analysis of CT angiography data with thin-section axial and coronal MIP images in a 40 year-old patient. She arrived to the emergency service with ASH grade IV in the Fisher Scale. Note the big sacular aneurysm (red arrows) which is more clearly demonstrated on the 3D images (green arrows) in the bifurcation of the middle cerebral artery (M1 to M2) on the right side. Department of Neuroradiology at Virgen de la Salud Hospital Toledo (Spain).

**References**: - Toledo/ES

**CT imaging protocol:**

Perfusion CT was performed, mostly during the typical time period for delayed cerebral ischemia (DCI) [between the sixth to eighth days from ASH] (Fig 3) and when the patients showed new onset of clinical deterioration or high velocities in transcranial Doppler ultrasound (TCD), particularly in unconsciousness patients.
Fig. 3: Delayed cerebral ischemia manifests in approximately 30% of patients with acute subarachnoid hemorrhage and typically occurs between days 6 and 8 after the initial hemorrhage, where there is a peak of "symptomatic vasospasm" (red line), though it can range from 3 to 13 days as described in the graphic below. Department of Neuroradiology at Virgen de la Salud Hospital Toledo (Spain).

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There is a standard scanning protocol for Perfusion CT at our institution by using LightSpeed 64-row CT (General Electric Healthcare) with a scanning volume of 8.0 cm selecting the territory affected by clinical criteria. Fig. 4 on page 13
Fig. 4: Sample of normal Perfusion CT maps in a patient with frontoparietal craniotomy obtained after postprocessing the software. Note in red circles the different maps: cerebral blood volume (CBV), Tmax, mean transit time (MTT) and cerebral blood flow (CBF). Department of Neuroradiology, Virgen de la Salud Hospital Toledo (Spain).

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PCT data acquisition consisted of a 45-second series, with 45 gantry rotations performed in cine mode during intravenous administration of iodinated contrast material. A bolus of 40mL of iohexol was administered into an antecubital vein (right arm preferred) by using a power injector at an injection rate of 4mL per second. The acquisition parameters for both PCT series included 80KVp and 120mAS.

Digital Subtraction Angiography (DSA) was performed in selected cases for endovascular embolization of the aneurysm and also for endovascular therapy (nimodipine) in cases with "angiographic vasospasm" refractory to medical treatment. Fig. 5 on page 14.
Fig. 5: DSA was used for aneurysm and vasospasm treatment. Note the saccular aneurysm (red arrows) in the anterior communicating artery in the upper images and the severe vasospasm (narrowing >75% of the diameter of the vessel) in the anterior and middle cerebral arteries (red arrows) in the lower images, both successfully treated, as shown on the right images. Department of Neuroradiology, Virgen de la Salud Hospital Toledo (Spain).

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Three- or 4 vessels DSA was performed via transfemoral approach under monitored sedation or general anesthesia. Conventional angiographic views (frontal, lateral, oblique) were obtained, as were dedicated magnified and focused views on the treated aneurysmal sites.

Non-enhanced CT was performed in every patients on the following days to evaluate possible infarcted cerebral areas in the corresponding territory at risk on PCT maps or if clinical deterioration was observed.
The CT protocol consisted of a baseline unenhanced cerebral CT with approximately 5mm transverse sections acquired at 120 kVp and 200mA.
**Fig. 1:** Fisher Scale grading system used to quantify the amount of subarachnoid hemorrhage and intraventricular hemorrhage (IVH). The percentages in the blue circles refer to the risk of vasospasm. Grade III and IV in the scale are the ones with the higher risk to develop "symptomatic vasospasm". Department of Neuroradiology at Virgen de la Salud Hospital Toledo (Spain).

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Results

Of the fifty-five patients analysed with acute subarachnoid hemorrhage in the neurosurgical intensive care unit, only ten were eligible for evaluation and only nine received endovascular treatment with nimodipine.

The data of the eligible 10 patients was analysed. Six (60%) were female and 4 (40%) were male with an average age of 43 years (range: 40 - 68 years). Between the younger patients in this study, three of them, (30%) required several intra-arterial administration of nimodipine, and all of them were women and active smokers.

Seven (70%) had subarachnoid hemorrhage grade IV and three (30%) had ASH grade III according to Fisher scale in the initial non-enhanced CT.

As far as Perfusion CT is concerned, nine patients (90%) had prolongation of the mean transit time (MTT) with +/- cerebral blood flow abnormalities in rCBF maps. Only in one patients perfusion maps were normal although he had clinical deterioration. The Perfusion CT was performed the ninth day by average since the acute subarachnoid hemorrhage (range: 3rd to 15th days from the initial ASH).

In our study PCT detected vasospasm in all but one patient, in which vasospasm wasn't clearly confirmed. 30% was severe and 70% moderate. In patients with moderate vasospasm only MTT was increased, however in patients with sever vasospasm not only MTT but also CBF were altered. These facts suggests that MTT prolongation alone may suggest mild-moderate asospasm, whereas an MTT prolongation associated with CBF and/or CBV abnormalities may suggest severe vasospasm. (4). In most cases PCT maps were normal when vasospasm was absent, suggesting that an abnormal PCT in particular patients with ASH secondary to aneurysmal rupture could be associated with vasospasm until proved otherwise.

Value of PCT in cerebral Vasospasm: PCT allows the assessment of cerebral auto regulation and some reports have already discussed the use of perfusion studies in cerebrovascular vasospasm. We use a visual grading system to classify the severity of the vasospasm. Fig. 6 on page 22
Fig. 6: Axial Cerebral blood flood (CBF), cerebral blood volume (CBV) and mean transit time (MTT) maps. Visual Grading system for Vasospasm: The upper images (A) showed normal PCT maps where the B images showed prolongation of mean transit time (red arrow) whereas the images in C showed CBF, CBV and MTT altered maps (purple arrows). Department of Neuroradiology at Virgen de la Salud Hospital. Toledo (Spain).

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Delayed cerebral ischemia (DCI) occurred mostly between the sixth and eighth days since ASH and 70% of our patients, did it the typical period of time when "symtomatyc vasospasm" is more often. 90% of them, occurred in the brain hemisphere with the lowest initial perfusion according to CBF maps and in the region with higher density of blood in the subaracnoid space. This area at risk of ischemia was later confirmed as an hypodensity in the corresponding territory on the follow-up Non-enhanced CT in 80% of the cases, shown as an established infarction. Fortunately, in most cases it was smaller than the corresponding territory with MTT prolongation.
Fig. 7: Sample of patient in our study: 49 year old female with ASH grade III in the Fisher scale secondary to aneurysmal rupture. We identified a saccular aneurysm on the right posterior communicating artery which was successfully embolized as showed in the Digital Subtraction angiography (DSA) (yellow arrows) on the upper right side of the image. On the 7th after ASH she started with clinical deterioration so CTP was performed. On the CTP maps we can observed prolongation of MTT compared with the contralateral side, and subtle decreased on the CBF maps on the right middle and part of the anterior cerebral arteries territories (ACM and ACA) (red circles). No CBV abnormalities were observed. Due to the suspecte vasospasm following the CTP maps and clinical deterioration, DSA was performed. Note in the images before-nimodipine administration (red arrows) the severe narrowing of the right ACM and ACA (>75% of the diameter of the vessel) with good angiographic result on the images after nimodipine administration(green arrows). Nevertheless the efficacy of intra-arterial nimodipine administration is temporary and on the non-enhanced CT follow up images we observed hypodensities in the MCA and CAA territories that suggest delayed cerebral infarcts (yellow circles) however those are smaller than the corresponding territory at risk of ischemia shown on CTP maps. Department of Neuroradiology and interventional neuroradiology of the Virgen de la Salud, Hospital . Toledo (Spain).

References: - Toledo/ES
Much work has been done to elucidate factors that are predictive of cerebral vasospasm. The ability to predict vasospasm would be a powerful tool for the neurointensivist. Variable predictive of vasospasm can be categorized as modifiable or nonmodifiable. The nonmodifiable variables that have been investigated include patient age, race, site of the aneurysm, preexisting hypertension, cocaine or cigarette use, neurological grade and the amount of hemorrhage on CT scans. In cases with big aneurysm and cardiovascular risk factors as hypertension, complications are more frequently observed.

**Fig. 8:** Another sample was a 33 year old female that arrived to the emergency service with ASH grade IV (short red arrow) on the axial non-enhanced CT and a hyperdense big nodular image on the left hemisphere (red long arrow) that at first impress to be an intracranial hematoma but finally turned to be a huge saccular aneurysm (yellow arrows) of the left distal CMA demostrated on the DSA images(Fig A). Her aneurysm was clipped by the neurosurgical team and she started with clinical deterioration shortly afterwards so CTP was peformed without evidence of vasospasm, only postsurgical changes (craniectomy) and sign of hyperaemia in the herniated brain parenchyma (red circle in C) were observed. Few days later she started with aphasia and seizures and new CTP showed more extracranial herniation of brain parenchyma and a established
infarcted area in the left CMA territory (red circle in D) that was confirmed on the axial non-enhanced CT performed few days later (red circle in E) with hemorrhagic transformation (yellow arrow in E). Department of Neuroradiology of Virgen de la Salud Hospital Toledo (Spain).

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And finally the last case with good correlation between the localization of aneurysm (distal right M1), sign of vasospasm on CTP (right hemisphere at first) and final infarcted areas predominantly on the right hemisphere in a 39 year old female.

Fig. 9: Finally the last case is a 39 year old female that starts with headache and dizziness. Non-enhanced CT was performed showing ASH grade IV (A). Saccular aneurysm was demonstrated on CT angiography on the right side (B yellow arrows) that was successfully embolized (C) as seen in DSA before and after treatment (C). Fifth day after ASH high velocities were observed in the Transcranial Doppler, so CTP was performed showing only subtle prolongation on MTT maps on the right side (yellow arrows in D). She received medical treatment (oral nimodipine) and endovascular treatment and apparently when better. Unfortunately the eighth day after ASH she
started with new neurological focal onset and as shown on the CTP images in E, extensive area of both CMA, CCA and part of the cerebral posterior arteries territory (yellow arrows in E) were at risk of ischemia secondary to severe vasospasm. Note that on CBV maps sign of established infarcted areas were already seen were observed on both CCA and in part of the right CMA territory (yellow circles in CBV maps). She received a second nimodipine intra-arterial administration but unfortunately on the follow-up non-enhanced CT (F) performed a few days later a vast area of edema was observed in the right hemisphere and cortical hypodensities were observed in the CMA and CCA right territories (purple arrows in F). Department of Neuroradiology of Virgen de la Salud Hospital Toledo (Spain).

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Conclusion

In patients with clinical signs of cerebrovascular vasospasm, CT angiography and Perfusion CT data were of great help no only in defining anatomic location and the severity of vasospasm but also in assessing the related risk o cerebral ischemia to try to improve poor outcomes in such as patients.

In our study, correlation was observed between abnormalities on the MTT and CBF maps with arterial narrowing in the corresponding artery supplying territory on Digital Substraction angiography.

Final areas of infarction observed in the follow-up non-enhanced CT matched with the territories at risk of ischemia in the Perfusion CT maps and fortunately in most patients the final infarcted areas were smaller than the territory with MTT prolongation on Perfusion CT maps.

CT adds important pysiologic data to the clinical information and anatomic imaging of patients with subarachnoid hemorrhage. Therefore, future steps must be done by using a large prospective clinical trial study design.
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References


