



The utility of perfusion CT and CT angiography on early diagnosis and the management of vasospasm after subarachnoid hemorrhage

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ABSTRACT

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Subarachnoid hemorrhage is one of the most important and dangerous neurologic emergencies worldwide. It is characterized by a sudden and severe headache caused most commonly by the rupture of intracranial aneurysm. Cerebral vasospasm is the most important cause of disability and death in whom survived from the first event. Early diagnosis and management of cerebral vasospasm could prevent and reduce its morbidity and mortality. Thus, an ideal technique must be able to detect the vasospasm before the occurrence of neurological deficits. Perfusion computed tomography could assess vascularity of brain including cerebral blood flow, cerebral blood volume, time to peak and mean transit time. For this application, perfusion computed tomography and computed tomography angiography techniques offer significant advantages and can result in early diagnosis of vasospasm. In this review, we discuss the utility of these two techniques and their safety in the diagnosis and the management of vasospasm following subarachnoid hemorrhage.

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Introduction

Subarachnoid hemorrhage (SAH) is one of the most important neurologic emergency worldwide that characterized by a sudden and severe headache due to the extravasation of blood into the subarachnoid space caused most commonly by the rupture of intracranial aneurysm. Aneurysmal subarachnoid hemorrhage (aSAH) accounts for about 10-30% mortality rate (1,2). Subsequent complications include symptomatic vasospasm (46 percent of patients), hydrocephalus and rebleeding; in descending order (3). Many of these patients suffer from various complications over time, ranged from long-term cognitive impairment, functional disability and reduced quality of life (4). Cerebral vasospasm

remains the important cause of disability and death in whom survived from the first event. Cerebral vasospasm develops in the first two weeks following SAH in 70% of cases (5) and about 50% of patients, who show vasospasm in angiographic evaluation, will eventually suffer from neurologic ischemic deficits. The clinical diagnosis of cerebral vasospasm can be made based on the new focal neurologic deficits, however are nonspecific. But the diagnosis will be difficult due to the presence of neurologic deficits at baseline (6). Furthermore, most of the patients receive sedation therapy in intensive care unit, which may lead to delayed diagnosis and losing the benefit of prompt treatment.

Current techniques of diagnosis vasospasm follow-

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ing aSAH are transcranial doppler ultrasonography (TCD), digital subtraction angiography (DSA), perfusion computed tomography (PCT) and computed tomography angiography (CTA). The ideal technique must be able to detect the vasospasm before the occurrence of neurological deficits. For this application, PCT and CTA techniques offer significant advantages over the first two aforementioned techniques.

In this review, we discuss the PCT and CTA techniques utility and differences in the diagnosis and the management of vasospasm following subarachnoid hemorrhage.

In this review article, we searched PubMed database with the following search terms: subarachnoid hemorrhage (OR cerebral vasospasm) AND CT angiography (OR perfusion CT). All the related English-language articles using CTA and PCT for the evaluation of cerebral vasospasm following SAH were extracted and summarized. The last search was performed on February 2014.

Literature review

As previously mentioned, cerebral vasospasm is one of the most noticeable devastating complications of aneurysmal SAH. Based on various studies, different factors can play a role as predictors of increased rate of occurrence in SAH patients. There are some controversies in the literature considering the role of increased age in the higher incidence of vasospasm following aSAH. Some studies indicated that advanced age increased the incidence of vasospasm (7), while some suggested increased risk in younger age (8-10) or no association between age and vasospasm (11).

Smoking is also an important risk factor in SAH and in the subsequent vasospasm (12).

Cocaine use can also cause artery vasospasm especially in coronary arteries. Nevertheless, there is controversy in the literature regarding the effect of cocaine use. In 2010, Alaraj et al. found no association between symptomatic vasospasm and neurologic deficits or between vasospasm severity and treatment response in cocaine users and nonusers (13). In 2001, Conway and Tamargo revealed the higher prevalence of vasospasm in aSAH patients with recent cocaine use but there was no difference in clinical outcome (14).

Moreover, hypertension and alcohol abuse (15), positive history of first-degree relative SAH (16), inherited connective tissue disorders associated with intracranial aneurysm (17) are the risk factors that may increase the risk of SAH itself.

Computed tomography angiography

Multi-slice computed tomography is a useful technique to investigate the cause of SAH by injection of contrast medium. CTA is a minimally invasive technique, which can be performed in the emergency setting for vascular imaging, when urgent treatment

decisions are necessary. Moreover, in uncooperative and critically ill patients, CTA evaluation can be significantly useful because patients receive minimal sedation due to the rapid acquisition of CT data. Its sensitivity in the detection of aneurysm larger than 3 mm is 96%, while the detection rate decreases to 61% for the aneurysm less than or equal to 3 mm (18).

In Binaghi and colleagues study, who evaluated symptomatic patients with vasospasm after aSAH, they determined that CTA accurately detected all the vasospasms located on the distal intracranial segments, in contrast to the carotid siphon. In the presence of severe vasospasm, CTA showed the sensitivity of 76.5%, specificity of 99.5% and accuracy of 97.5% in comparison to mild-moderate vasospasm with 86.8%, 96.8%, and 95.2%, respectively (19).

Perfusion computerized tomography

This method evaluated the perfusion hemodynamics of selected region in the brain during the injection of contrast material by repeated sequential scanning. PCT can calculate the perfusion parameters of cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT). Thus, the data can give useful information on CBF throughout the territory of each cerebral artery in patients with ischemic cerebral stroke or aSAH.

In a study by Killeen (2013), done on ninety-seven patients with SAH, they found the sensitivity of 97% and specificity of 76% for PCT diagnosing vasospasm. Compared to patients who had DSA, PCT deficits were detected in 70%, occurring in 97% of patients with vasospasm and 23% without vasospasm. They concluded that positive PCT findings deserved serious consideration in these patients (20).

A retrospective study of Killeen et al on fifty-seven aSAH patients with delayed cerebral ischemia (DCI), demonstrated that PCT was capable of detecting DCI in 80% of cases compared to DSA ability to demonstrate 73% of vasospasms. There was a significant difference in CBF in patients with and without DCI. The PCT showed the sensitivity of 0.80 (95% CI 0.68-0.92) and specificity of 0.67 (95% CI 0.40-0.93), while they were 0.73 (95% CI 0.60-0.86) and 0.75 (95% CI 0.50-0.99) for DSA, respectively (21).

Wintermark and colleagues illustrated that those patients with suspected vasospasm after aSAH could benefit from the combination of CTA and PCT (with a corresponding MTT threshold of 6.4 seconds) as an accurate screening test with the accuracy of 93% (22).

In the meta-analysis carried out by Greenberg et al., CTA and PCT were potentially beneficial techniques with the high diagnostic accuracy in patients with vasospasm after aSAH (CTA= 98 ± 2.0% and CTP=97 ± 3.0%). Their results showed that the higher patients' risks of CTA and PCT were associated with the intravenous contrast administration (e.g., hypersensitivity,

nephrotoxicity) and radiation exposure (23).

In Binaghi study, in the presence of severe vasospasm, PCT showed the sensitivity of 90%, specificity of 100% and the accuracy of 92.3%% in comparison to mild-moderate vasospasm with 20%, 100%, and 38.5%, respectively (19).

In prospective clinical trial by Westermaier, the value of TCD, PCT and neurological examinations was compared considering the predication of DCI following aSAH. TCD had an accuracy of 0.65 compared to the accuracy of 0.63 for PCT to forecast DCI. While DCI prediction accuracy was 0.96 for delayed ischemic neurological deficits to predict DCI. They assumed that neurological evaluation was most accurate method to detect DCI in first 3 days if done at close interval. Moreover, combining PCT and TCD had a higher sensitivity and negative predictive value than TCD alone, which

improved the number of detected cases of vasospasm (24). Therefore, PCT data might increase the clinical long-term outcome of patients with SAH based on its higher diagnostic accuracy (25).

Similarly, Kunze et al. revealed that neurological assessment at close interval had the highest sensitivity and specificity to detect cerebral vasospasm and they found higher accuracy, sensitivity and negative predictive value for PCT compared to TCD (26). PCT will be helpful to detect vasospasm if patients are not amenable to detailed neurological evaluation.

Sanelli and colleague showed that the diagnostic accuracy of CBF was 94% compared to mean transit time (MTT) diagnostic accuracy of 85% for DCI, with the optimal threshold values of 36.5 mL/100 g/min for CBF and 5.4 seconds for MTT during PCT technique (27).

We summarize the aforementioned studies in table 1.

Table 1. Characteristics of studies evaluating perfusion computed tomography and computed tomography angiography on the diagnosis of vasospasm following subarachnoid hemorrhage

Author Year Reference	Patients	Diagnostic procedures	Results
Wintermark 2006 (22)	27 patients with acute SAH*	CTA**/PCT***, DSA****, TDC*****	Significant higher PPV***** in PCT (89.9%) compared to TCD (62.9%). CTA qualitative assessment and PCT-derived mean transit time had the most accurate combination in vasospasm diagnosis (93%)
Greenberg 2010 (23)	literature data bases (PubMed, Embase, Cochrane Database of Systematic Reviews, and the Web of Science) from 1996 to 2009 with SAH patients	CTA or CTP as the index test, DSA as the reference standard	CTA had a pooled sensitivity of 79.6% and pooled specificity of 93.1%. CTP pooled sensitivity and specificity were 74.1% and 93%, respectively. Overall DORs were 124.5 for CTA and 43 for CTP.
Binaghi 2007 (19)	27 patients with symptomatic cerebrovascular vasospasm (retrospective cohort study)	CTA, PCT	MSCTA with the sensitivity of 86.8% and specificity of 96.8% for mild-moderate vasospasm and sensitivity of 76.5% and 99.5% for severe vasospasm against 38.5%. PCT had a sensitivity and specificity of 20% and 100% for mid-moderate and 90% and 100% for severe vasospasms respectively
Killeen 2014 (20)	97 patients with SAH	PCT	Sensitivity of 97% and specificity of 76%
Killeen 2011 (21)	57 patients with aneurysmal SAH	CTP, DSA	Sensitivity of 80% and specificity of 67% for CTA and 73% and 75% for DSA respectively
Westermaier 2013 (22)	61 patients with aneurysmal SAH	PCT and TCD	Sensitivity of 93% for PCT and 81% for TCD
Kunze 2012 (26)	53 patients with aneurysmal SAH no longer than 96 hours ago	PCT and TCD	Sensitivity of 93% and specificity of 27% for PCT and 74% and 57% for TCD respectively
Sanelli 2011 (27)	97 patients with SAH (prospective cohort study)	PCT (Quantitative cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) values were obtained)	Diagnostic accuracy was 93% CBF, 88% MTT and 72% CBV

* SAH: Subarachnoid hemorrhage; ** CTA: Computed tomography angiography; *** PCT: Perfusion computed tomography; **** DSA: Digital subtraction angiography; ***** TCD: Transcranial doppler sonography; ***** PPV: Positive predictive value

Limitations

There are some limitations of applying PCT including contrast material administration and subsequent radiation exposure. Secondly, PCT cannot provide whole-brain coverage in a single scan, except for modern new scanners. The last limitation goes to posterior fossa evaluation due to adjacent bone, which produces beam-hardening artifact.

Conclusion

In attempts to improve SAH ultimate outcomes, earlier and more precise diagnosis of vasospasm plays an inevitable role in preventing the devastating sequel of permanent neurologic deficits or death in addition to initiation of immediate treatment. PCT with CTA is a valuable and safe tool for the early diagnosis of vasospasm following aSAH, especially in very critical patients. Further studies are required to better define the implication of these modalities in aSAH.

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Conflict of Interest

The authors declare no conflict of interest.

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