



CT angiography in patients with acute spontaneous intracranial hemorrhage: detection and characterization of intracranial aneurysms: comparison of Volume Rendering and Maximum Intensity Projection algorithms – Part One

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KEYWORDS :

Introduction

Computed Tomography (CT) is the best diagnostic modality for the evaluation of intracranial hemorrhage. CT determines both the size and location, as well as, suggests an etiology of the intracranial hemorrhage.¹

Intracranial hemorrhage is one of the most often causes of acute neurological deficiency and it is an indication for urgent diagnostics. Rupture of a cerebral aneurysm is the most common cause of non-traumatic intracranial hemorrhage.

Cerebral aneurysm is a localized, pathological dilatation of brain blood vessels. There is many types of cerebral aneurysms, characterized by their shape, localization, size and cause.

The aim of this study is to compare maximum intensity projection (MIP) and volume rendering (VR) CT angiography in detection and characterization of intracranial aneurysms in patients with acute non-traumatic hemorrhage, using surgical finding or digital subtraction angiography (DSA) as the “gold standard”, to reduce need for invasive procedures.

Materials and methods

Patients

Study included 150 patients with acute non-traumatic intracranial hemorrhage.

All patients diagnosed with intracranial hemorrhage by non-contrast CT, underwent CT angiography of the cerebral vessels using MIP and VR reconstruction scans.

Patients with positive findings by one and/or other method were sent directly to surgery or to DSA.

74 patients with aneurysm as the cause of bleeding, underwent surgery on the basis of the CT angiography findings. Total of 96 patients were operated. 80 patients underwent DSA, and 21 had normal DSA findings.

Methods

All patients with non-traumatic intracranial hemorrhage were determined by age and gender.

CT angiography was performed on the multilayer and multi-detector machine (Radiology department): 4-layer Volume Zoom Siemens, Erlangen, Germany, and 64-layer Light Speed GE, USA. Conventional angiography was performed at the Department of Radiology, machine Axiom Artis, Siemens, Erlangen, Germany, by the Seldinger method.

All patients were operated at the Neurosurgical Clinic, Clinical Center Sarajevo.

MIP and VR reconstruction of CT angiography of the cerebral vessels were especially interpreted for the presence, location and aneurysm size.

Statistical analysis

The methods of statistical analysis used:

- Methods of descriptive statistics in form of data presentation through the frequencies, percentages, mean values, proportions (especially the proportions related to the sensitivity and specificity of each method), and the average rank scores (ranks related to size).

Following methods of inferential analysis are used: The McNemar test, Cohen kappa coefficient and ROC curve.

To test the accuracy of the tests the following statistical methods were used: sensitivity, specificity, positive predictive value and negative predictive value.

Results

Of the 150 patients with non-traumatic intracranial hemorrhage 121 (81%) were diagnosed with aneurysm, 8 (5%) with arteriovenous malformations, in 29 (14%) bleeding cause not found.

Intracranial aneurysms

In 121 patients, 90 females (63.4%) and 52 males (36.6%), aged 19-77, mean age 53.57, 150 aneurysms were diagnosed: 101 patients had 1 aneurysm (83%), 14 patients two (12%), 4 patients three (3%), 1 patient four (1%) and 1 patient 5 aneurysm (1%).

Sex	Number of patients	Percentage (%)
Female	95	63,4
Male	55	36,6
Total	150	100

Table 1 Structure of patients by gender

The largest number of aneurysms was found on medial cerebral artery (MCA) 62 (41%), anterior cerebral artery (ACA) 47 (31%), internal carotid artery (ICA) 33 (22%), vertebral basilar artery (VBA) 7 (5%) and on posterior cerebral artery (PCA) 1 (1%).

Artery	Number of aneurysm	Percentage (%)
MCA	62	41
ACA	47	31
ICA	33	22
VBA	7	5
PCA	1	1
Total	150	100

Table 2 Number of aneurysms on arteries

The largest number of aneurysms were medium size 90 (60%), 30 (20%) large aneurysms were found, small aneurysms 27 (18%) and giant (≥ 25 mm) 3 (2%).

Aneurysm	Number	Percentage (%)
Small (≤ 3 mm)	27	18
Medium (4-10mm)	90	60
Large (11-24mm)	30	20
Giant (≥ 25 mm)	3	2
Total	150	100

Table 3 Size of aneurysm

All aneurysms larger than 3 mm were diagnosed using MIP reconstruction of CT angiography.

	4-10mm	11-24mm	≥ 25 mm					
ACA	33	5	0	47	32%			
CMA	36	13	1	62	42.5%			
PCA	0	1	0	1	1%			
ICA	15	11	2	30	20.5%			
VBA	6	0	0	6	4%			
	90	62%	30	20%	3	2%	146	100%

Table 4 Number of aneurysms estimated by MIP reconstruction of CTA

The area under the ROC curve for MIP method was 0.916 meaning that the MPI method has very good separation power (discriminatory power) of positive and negative findings ($p < 0.001$):

- Sensitivity: 95.30% (92 - 97%).
- Specificity: 87.9% (74.6 - 95.5%).
- Positive predictive value: 97.3% (94.4 - 99%).
- Negative predictive value: 80.6% (68.4 to 87.6%).
- Positive likelihood ratio (+ LR) = Sensitivity / (1 - specificity): 7.865 (3.6 - 21.7). This test is 8 times more likely to detect aneurysms in patients than in healthy subjects.
- Negative likelihood ratio (-LR) = (1 - sensitivity) / specificity: 0.053 (0.031 to 0.102). This test is 0.05 times less likely to show the negative results in the sick compared to healthy subjects.
- Youden's J = Sensitivity + Specificity - 1: 0.832 (0.670 - 0.925).
- Test accuracy = Really positive + Really negative / Total = 143 + 29 / 183 = 93.9%. MIP method has accuracy of total 93.9%, or accuracy index 0.832.
- Number Needed to Diagnose (NND) = 1 / (Sensitivity - (1 - specificity)) = 1 / (Youden's J): 1.2 (1.081 to 1.492).
- Diagnostic Odds Ratio = (Sensitivity / (1 - Sensitivity)) / (1 - Specificity) / Specificity: 148.1 (35.77-693,570).
- Kappa: 0.804 (0.647 to 0.894). Precision and affordability of this test is 0.80.

All aneurysms larger than 3 mm were diagnosed VR reconstruction.

	4-10mm	11-24mm	≥ 25 mm					
ACA	33	5	0	47	31%			
MCA	36	13	1	65	43%			
PCA	0	1	0	1	1%			
ICA	15	9	2	31	21%			
VBA	6	0	0	6	4%			
	90	60%	30	20%	3	2%	150	100%

Table 5 Aneurysms diagnosed with VR reconstruction of CTA

The area under the ROC curve for the VR method is 0.945 proving VR method having very good separation power of positive and negative findings ($p < 0.001$), being better than MIP method.

- Sensitivity: 98% (from 95.0 to 99.3%).
- Specificity: 90.92% (from 79.1 to 96.7%).
- Positive predictive value: 98% (from 90.4 to 99.3%).
- Negative predictive value: 90.9% (79.1 to 96.7%).
- Positive likelihood ratio (+ LR) = Sensitivity/(1-specificity):

10.780 (4.575 - 30.434). This test has 11 times greater chance in detecting aneurysm in patients, than in healthy subjects.

- Negative likelihood ratio (-LR) = (1 - Sensitivity) / Specificity: 0.022 (0.007 - 0.058). This test is 0.022 times less likely to show negative test result (denying disease) in diseased compared to healthy subjects.
- Test accuracy = Really positive + Really negative / Total = 147 + 30/183 = 96.7%
- Youden's J (Test accuracy Index) = Sensitivity + Specificity - 1: 0.889 (0.746 - 0.960). VR method has accuracy total of 96.7%, or index of accuracy is 0.889.
- Number Needed to Diagnose (NND) = 1 / (Sensitivity - (1 - specificity)) = 1 / (Youden's J): 1.125 (1.041 to 1.341).
- Diagnostic Odds Ratio (DOR) = (Sensitivity / (1 - sensitivity)) / ((1 - specificity) / Specificity): 490 (78.9 - 4102).
- Kappa: 0.889 (0.746 to 0.960) kappa indicates accuracy and repeatability of results. In this case, the repeatability is high, 89%. Intervals in brackets were determined with 95% of confidence.

	MIP	VR	MIP + VR
Sensitivity (%)	95.54 (91 - 98)	98.03 (94 - 99)	98.03 (94 - 99)
Specificity (%)	87.87 (71 - 96)	90.62 (74 - 98)	85.29 (68 - 95)
Positive predictive value (%)	97.4 % (93 - 99 %)	98.03 % (94 - 99 %)	96.77 % (92 - 98 %)
Negative predictive value (%)	80.55 % (63 - 91 %)	90.62 % (74 - 98 %)	90.62 % (74 - 98 %)
Prevalence (%)	82.63	82.7	82.81
Accuracy (%)	94.21	96.76	95.72
*Intervals in brackets are determined with 95% confidence			

Table 6 VR reconstruction vs MIP reconstruction

The area under the ROC curve for the MIP method is 0.916 and 0.945 for the VR method compared to the gold standard representing very high overall accuracy of both diagnostic tests (VR and MIP). There is no significant differences between the two methods in comparison to the golden standard $p = 0.18$. The area under the ROC curve was greater in VR reconstruction compared to MIP reconstruction.

Statistical comparison of results using McNemar's χ^2 test.

- Statistical comparison of the results: MIP vs. VR $p = 0.371$. Since $p > 0.05$, there is no statistically significant differences in detection of aneurysms between MIP and VR methods.
- Statistical comparison of the results: MIP vs. the golden standard $p = 0.549$. Since $p > 0.05$, there were no statistically significant differences in detection of aneurysms between the MIP and the golden standard method.
- Statistical comparison of the results: VR vs. golden standard $p = 0.1$. Since $p > 0.05$, there were no statistically significant differences in detection of aneurysms between MIP and VR methods.

Discussion

Spontaneous non-traumatic intracranial hemorrhage is significant cause of morbidity and mortality in the world.

Indication of DSA as a method of choice and ability to find the cause of bleeding is still controversial. Instructions of American Association of stroke suggest that diagnostic DSA should definitely be done in patients with unclear cause of intracranial bleeding, being potential candidates for surgical treatment, particularly for young patients not having hypertension and are clinically stable.

CT is highly sensitive method for diagnosing bleeding representing golden standard. Bleeding is observed as a hyper-dense change in relation to the brain parenchyma or in sub-arachnoid space. Gradient-echo T2* or susceptibility MRI sequence is as sensitive as CT scan, but examination duration, anesthetic monitoring, screening cost, patient's clinical status and lack of access to MRI

diminish the importance of MRI examinations in emergency cases. According to Rinkelu et al. 15 to 20% of patients with non-traumatic intracranial hemorrhage, the presence of aneurysm or vascular malformation was not proved completely, correlating with our findings of 14% of patients with no aneurysm or vascular anomalies. CT angiography may be the first choice method for diagnosing the cause of intracranial bleeding in patients with non-traumatic intracranial hemorrhage.

Argid R. et al., in a series of 193 patients suffering from sub-arachnoid hemorrhage (SAH) with negative CT angiography findings, subsequently underwent DSA, where only 1 aneurysm was diagnosed, so we can rely on the CT angiography findings even in negative findings case.

Intracranial aneurysms

a) Incidence of aneurysms

In our study middle patients' age was 53.6, at Numminen et al. was 48.4, at Zhang et al. 52 and at Hwang et al. 54.6 respectively.

Aneurysms are more common in female population, being 75% of cases at Osborn et al., at Zhang et al. 60% 9, at Menke et al. 59% and in our study 63% cases.

In our study, 83% of patients had solitary aneurysm, 17% had more than one, where 70% had two and 30% more than two aneurysms (14 patients two, four patients three, one patient with four and one patient with five).

According to Bonneville et al., multiple aneurysms were found in 20-30% of patients, being higher than in our study. Bonneville et al. had two aneurysms in 75% cases, three in 15%, and 10% more than three. Papke et al. diagnosed 84 aneurysms in 63 patients, 48 (76%) patients had 1, 15 had over one, 9 (60%) had 2 and 6 (30%) 3 aneurysm.

At Zhang et al.9 in 60 patients, 70 aneurysms were diagnosed, solitary aneurysm had 51 patients (85%), more than one aneurysm had 15% of patients: two aneurysms 8 (89%), and three 1 (11%) patients. At Menke et al.12, out of 3643 patients in the meta-analysis, 84% had an aneurysm, 11.2% had two, and 4.5% had three or more than three aneurysms.

b) The incidence of aneurysms by localization

The most frequent localization of aneurysms according to the literature is anterior circulation area-90%, while 10% is in the posterior circulation.

In our study, 41% of aneurysms were diagnosed in artery cerebral media (MCA), 31% on anterior cerebral artery (ACA), on the intern carotid artery (ICA) 22% (Table 7).

The comparison to studies of Osborn11, Numminen8, Zhang, Hwang10, Donmaz and Merhemic is shown in Table 7.

In study of Li et al.2 118 of 128 patients, a total of 145 aneurysms were detected on 3D DSA. No aneurysm was detected in 10 patients. The aneurysms were located at the anterior communicating artery (n=37, 25.5%), the posterior communicating artery (n=36, 24.8%), the internal carotid artery (n=48, 33.1%), the middle cerebral artery (n=22, 15.1%), and the basilar artery (n=2, 1.3%).

Author	ACA	MCA	ICA	PCA	VBA
Merhemic Z	31%	41%	22%	1%	5%
Ruptured aneurysm	35.5%	37%	21.5%	1%	5%
Osborn A ¹¹	30-35%	20%	30-35%		10%
Nuuminen et al ⁸	22%	39%	31%	3%	5%
Zhang et al ¹⁶	29%	16%	48%	1%	6%
Hwang et al ¹⁰	36.5%	28.5%	28%	0.5%	6.5%
Donmez et al ¹⁷	30%	32%	30%		8%
Merhemic et al ¹⁸	26.5%	34.5%	28%	3%	8%

Table 7 Results displayed in percentage (%) by varies authors regarding

localization of the intracranial aneurysm

x) Aneurysms Size

According to the gold standard (operative findings or DSA), most aneurysms in our study are medium size (4-10 mm), 90 (60%), corresponding to study from Donmez et al.¹⁷ where out of 164 aneurysms, medium were found in 53% (132), in a study by Merhemic et al.⁵⁶ were found 18, and Ramasundara et al. found 68% out of 36 aneurysms¹⁹.

Aneurysms larger than 10 mm were found in 22% in our study, at Donmez et al.¹⁷ 23%, Merhemic et al.¹⁷ 31% and Ramasundara et al.19.9%.

The largest number of ruptured aneurysms is medium size aneurysm 67% (11/121). Aneurysms bigger than 10 mm participated with 24% (29/121).

Medium size of ruptured aneurysms was 8.16 to 8.27 mm found by golden standard (DSA and operation findings), while the size of non-ruptured intracranial aneurysms according to the golden standard is between 3.13 to 3.62 mm.

According to Yue W. size of non-ruptured intracranial aneurysms was 12.5 ± 8.0 mm showing our results not being in correlation to this.

According to Numminen et al.8 the average size of non-ruptured aneurysms was 4.5 mm correlating with our findings.

CTA findings

CTA is a noninvasive diagnostic method, simple to perform, extremely fast and convenient, extremely important for patients with acute intracranial hemorrhage.

Nagai et al.²¹ presented a series of 25 patients being successfully operated on the basis of CT angiography, confirming that the CTA were sufficient for surgery.

Bleeding occurring during angiography, significantly worsens a patient's condition and overall treatment outcome. Much better for the patient is to perform surgery by placing pistons on aneurysm, if accessible without classic angiography findings (DSA) ^{22,23,24}.

In our study, out of 121 patients with aneurysm rupture, 96 were treated, of which 74 patients had surgery according to CTA findings. In our study of 150 aneurysms, all were larger than 3 mm and were diagnosed with MIP and VR reconstruction thus for aneurysms larger than 3 mm sensitivity, specificity, PPV, NPV, and accuracy is 100%.

Finding of MIP reconstruction provides 95.3% of sensitivity, 87.9% of specificity, 97.3% of PPV, NPP of 80.6%, and accuracy of 93.9%. Positive and negative likelihood ratio is 7.865 and 0.053.

Finding of VR reconstruction has 98% of sensitivity, 90.9% of specificity, 98.0% of PPV, NPP of 90.9% and 96.7% of accuracy. Positive and negative likelihood ratio is 10.780 and 0.022.

Common findings of MVP and VR reconstructions have 98% of sensitivity, 84.8% of specificity, 96.7% of PPV, 90.3% of the NPP, and accuracy of 95.6%. Positive and negative likelihood ratio was 6.468 and 0.024.

There was no statistically significant difference (McNemar's test) in detection of aneurysms between MIP and VR findings of CTA, nor between the findings of the MIP and the golden standard (DSA, OP), nor between the VR and the golden standard (p>0.05).

The area under the ROC curve for both MIP and VR reconstructions (0.91 and 0.95), and compared to the gold standard is great, being very high diagnostic accuracy of both tests, although the finding of

VR reconstruction is more accurate than of MIP reconstruction. Sufficient is to evaluate the findings of VR reconstruction for the presence, location and size of aneurysm.

Authors	Sensitivity (%)	Specificity (%)	PPD (%)	NPD (%)	Accuracy Test (%)
<i>Merhemic MIP</i>	95.3	87.9	97.3	80.6	83.2
VR	98	90.9	98	90.9	96.7
MIP+VR	98	84.8	96.7	90.3	95.6
<i>Ruptured MIP</i>	96.7	74.4	99.2	87.9	96.7
VR	97.5	96.7	99.2	90.6	97.3
MIP+VR	97.5	96.7	99.2	90.6	97.3
<i>McKinney et al¹⁵</i>	97.4	90	97.4	90	95.8
<i>Donmez et al¹⁷</i>	95.1	94.1			95
<i>Yoon et al⁶</i>	92.5	93.3			92.6
<i>Zhang et al¹⁶</i>	91.5	95	97.7	82.6	92.5
<i>Bone removed CTA</i>	95.7	95	97.8	90.5	95.5
<i>Ramasudara et al¹⁹</i>	94	80	94	80	
<i>Li et al²⁵</i>	98.1	100	100	85.7	
<i>Li et al²⁶</i>	99	100	100	92.3	
<i>Ramgren et al²⁷</i>	91.6	100	100	77	
<i>Cheng et al²⁸</i>	94.4	87.9	94.6	82.1	90.5
<i>Hiratsuka et al²⁹</i>	87	79			85
<i>Aulbach P et al³⁰</i>	99	98	99	98	

Table 8 Results of studies by different authors for the presence of aneurysms in CTA in %

Mc Kinney et al¹⁵ study examined 63 patients with suspected presence of intracranial aneurysms on 64-layer CT machine and compared findings with DSA. 37 aneurysms were found in 28 patients, a 2 mm size aneurysm on the internal carotid artery was not diagnosed by CTA, while 6 mm aneurysm in medial cerebral artery was diagnosed by CTA, but not confirmed by DSA examination (false positive result). The author emphasizes the presence of venous plexus in the region leading to false positive finding. Our findings are bit better than McKinney et al¹⁵, but this difference can be considered insignificant. We emphasize that the majority of our patients were examined on a 4-layer CT machine resulting in lower results compared to 64-layer machine, but in our study findings were written by two experienced radiologists.

In Ramgren et al²⁷ study 285 aneurysms in 235 patients were detected by DSA, 19 aneurysms were missed on CTA, and 223 aneurysms were classified as ruptured. 91 patient had no aneurysm. Ramasundara et al¹⁹ have compared the findings of the CT VR reconstruction with findings of DSA as golden standard and got the sensitivity and specificity (94% and 80%), while finding of VR with subtraction of bones gave 91% sensitivity and specificity of 90%.

Zhang et al¹⁶ evaluated dual-energy CTA allowing automatic removal of bone with a single scan, while subtraction CT angiography takes two scans to clear the bone. They compared the findings of detection and characterization of aneurysms to conventional CT angiography, while DSA was used as the golden standard. According to findings of dual-energy CTA 45 aneurysms were found at 41 patients, two false-negative findings and one false-positive result, which obtained the sensitivity, specificity, PPV, NPV and accuracy of 95.7%, 95%, 97.8%, 90.5% and 95.5%.

In Zhang et al¹⁶ study 46 patients with suspected presence of intracranial aneurysms underwent the CT angiography on dual-source dual-energy CT camera, 3D DSA. 40 aneurysms were found in 35 patients. By Dual-energy CT angiography 38 aneurysms were found in 34 patients. Two aneurysms were not diagnosed, so the sensitivity, specificity, PPV and NPV were 95%, 100%, 100% and 99.7%, which is the best score in relation to other literature and to

our results.

In Li et al²⁵ study performed on 64-layer CT machine, 108 patients with suspected presence of an aneurysm, underwent CT angiography and DSA. At 96 patients 106 aneurysms were diagnosed and obtained a sensitivity, specificity, PPV and NPV for the first radiologist of 98.1%, 100%, 100% and 85%, and for second radiologist of 99%, 100%, 100% and 92.3%.

In Hiratsuka et al²⁹ study 34 patients with 47 aneurysms and 8 without aneurysms were presented, being reviewed by CT angiography on 64-layer CT machine, 3D TOF magnetic resonance imaging using intra-arterial angiography to confirm aneurysm presence. Three radiologist diagnosed 6 false-positive aneurysms (three on the internal carotid artery and three on vertebral artery), and 18 false negative (14 on ICA of which 3 less than 3 mm, 4 in ACA, two of which less than 3 mm). Sensitivity, specificity, and accuracy of CTA were 87%, 79% and 85%, being in comparison with our findings and those of other authors' weaker result.

Conclusion

CTA examination is essential for diagnosing the cause of intracranial bleeding. In comparison CTA vs. DSA, there was significant difference in findings MIP vs. DSA, but there was no significant difference in findings VR vs. DSA. It is enough to evaluate only volume rendering (VR) reconstruction for detection and characterization of intracranial aneurysms. All aneurysms larger than 3 mm were diagnosed on CT angiography. Ruptured aneurysms are much larger than non-ruptured, and in surgery, size of aneurysms was significantly larger than on CTA.

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