Dead or Alive? New Confirmatory Test Using Quantitative Analysis of Computed Tomographic Angiography

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BACKGROUND

-Brain death (BD) diagnosis relies heavily on clinical examination, but in absence of a reliable exam ancillary tests may be required. [1-4]

-Confirmatory tests demonstrate the absence of cerebral electrical activity or cerebral blood flow (CBF).

-Four-vessel cerebral angiography (FVCA) has traditionally been considered the goal-standard to demonstrate absence of CBF.

-At our institution, nuclear medicine perfusion test (NMPT) has become the standard confirmatory test.

-Computed tomographic angiography (CTA) has been recognized in detecting CBF arrest in BD, but no standard has been established. [5-16]

Stasis Filling:

-Minimal, weak, and delayed persistent opacification of proximal intracranial arterial segments on cerebral angiography of BD patients. [5,18-20]

-A consequence of increased intracranial pressure, high cerebrovascular resistance, and altered cerebral autoregulation mechanisms resulting in cessation of capillary circulation while proximal arterial segments remain patent. [20,21]

-Incidence of 5-28% on FVCA and 30-59% on CTA. [9,18,21,22]

OBJECTIVE

1. Quantitatively analyze CTA and compare its accuracy to NMPT in its ability to diagnose BD

2. Determine a Hounsfield unit (HU) threshold that discriminates between stasis filling and preserved cerebral perfusion

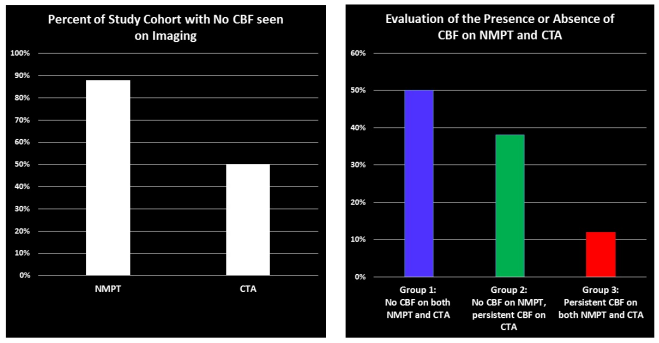
METHODS

Prospective clinical study, from 2007-2014, evaluating a consecutive series of clinically BD patients (n=60) and randomly selected control group with normal CTAs (n=20). NMPT, used as the reference standard, was performed followed immediately by CTA. Assessment of NMPT and quantitative CTA HU analysis of the horizontal segment of middle cerebral artery (M1), precommunicating segment of anterior cerebral artery (A1), and basilar artery (BA) was performed.

RESULTS

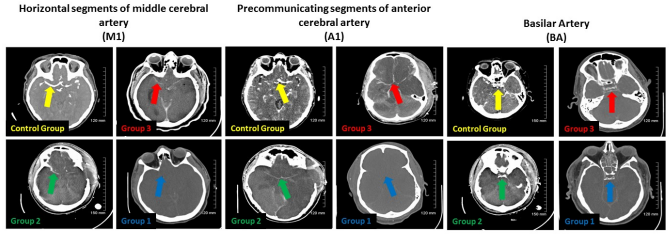
-Demographics: Only motor vehicle collision as the mechanism of injury was significantly different between groups (p = 0.030)

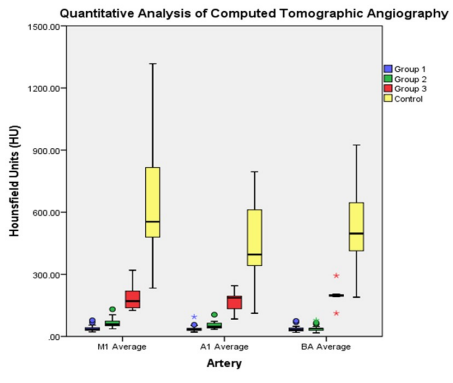
Qualitative CTA and NMPT Analysis



-Using NMPT as a reference standard, the amount of CBF seen on CTA in Group 2 is not consistent with preserved cerebral perfusion and represents stasis filling while the amount of CBF seen on CTA in Group 3 is consistent with preserved cerebral perfusion.

Quantitative CTA Analysis





-Omnibus ANOVA analysis demonstrated that all groups varied significantly for M1, A1, and BA ($p < 0.001$).

-One-to-one evaluation between the groups also revealed a significant difference between all groups, except for the BA when comparing Group 1 and Group 2 (mean HU of 35.68 vs. 39.74, $p = 0.778$), indicating that the BA may be the most sensitive for BD diagnosis.

-To insure 100% specificity, we set out to establish a HU threshold that would not exceed the minimum HU values of Group 3 and control group.

CTA HU Evaluation for BD Confirmation

All Vessels (M1, A1, and BA)

HU	Sens	Spec	PPV	NPV	LR+	LR-
35	0.377	1.000	1.000	0.154	N/A	0.623
40	0.572	1.000	1.000	0.209	N/A	0.428
45	0.642	1.000	1.000	0.240	N/A	0.358
50	0.723	1.000	1.000	0.280	N/A	0.277
55	0.786	1.000	1.000	0.346	N/A	0.214
60	0.830	1.000	1.000	0.400	N/A	0.170
65	0.862	1.000	1.000	0.459	N/A	0.138
70	0.899	1.000	1.000	0.529	N/A	0.101
75	0.937	1.000	1.000	0.641	N/A	0.063
80	0.969	1.000	1.000	0.783	N/A	0.031
85	0.975	0.944	0.994	0.810	17.547	0.027
90	0.975	0.944	0.994	0.810	17.547	0.027
95	0.981	0.944	0.994	0.850	17.660	0.020
100	0.981	0.944	0.994	0.850	17.660	0.020
105	0.987	0.944	0.994	0.895	17.774	0.013
110	0.994	0.944	0.994	0.944	17.887	0.007
115	0.994	0.889	0.988	0.941	8.943	0.007
120	0.994	0.889	0.988	0.941	8.943	0.007
125	0.994	0.889	0.988	0.941	8.943	0.007
130	0.994	0.833	0.981	0.938	5.962	0.008
135	1.000	0.778	0.975	1.000	4.500	0
140	1.000	0.722	0.970	1.000	3.600	0
145	1.000	0.667	0.964	1.000	3.000	0
150	1.000	0.667	0.964	1.000	3.000	0
155	1.000	0.667	0.964	1.000	3.000	0
160	1.000	0.667	0.964	1.000	3.000	0
165	1.000	0.667	0.964	1.000	3.000	0
170	1.000	0.667	0.964	1.000	3.000	0
175	1.000	0.667	0.964	1.000	3.000	0
180	1.000	0.667	0.964	1.000	3.000	0
185	1.000	0.667	0.964	1.000	3.000	0
190	1.000	0.556	0.952	1.000	2.250	0
195	1.000	0.500	0.946	1.000	2.000	0
200	1.000	0.333	0.930	1.000	1.500	0

CTA: computed tomographic angiography; M1: Horizontal segment of middle cerebral artery; A1: Precommunicating segment of anterior cerebral artery; BA: Basilar artery; Sens: sensitivity; Spec: specificity; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio; N/A: not applicable, these values could not be calculated due to a denominator of 0.

CONCLUSION

-No CBF seen on CTA is consistent with BD, with 100% sensitivity and specificity

-We established criteria that differentiates persistent CBF on CTA as either preserved cerebral perfusion or stasis filling.

-We propose that a CTA HU less than 80 in M1, A1 and BA is concordant with no CBF on NMPT, therefore indicative of a lack of physiologic cerebral perfusion, thus allows the confirmation of BD with 97% sensitivity and 100% specificity.

-Despite the good results obtained in our study, a large prospective multi-institutional study must be performed to confirm our findings and standardize our defined criteria

References available upon request