Fluoroscopic angiography quantifies delay in cerebral circulation time and requires less radiation in carotid stenosis patients: A pilot study

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Abstract

Background: Quantitative digital subtraction angiography (DSA) facilitates in-room assessment of flow changes in various cerebrovascular diseases and improves patient safety. The purpose of this study was to compare the diagnostic accuracy of quantitative fluoroscopic angiography (FA) and DSA.

Methods: Twenty-two patients with >70% carotid stenosis according to NASCET criteria were prospectively included in the study. All patients received DSA and FA (ArtisZee, Siemens Healthcare, Forchheim, Germany) before and after carotid stenting in the same angiosuite. The regions of interest (ROIs) included the extracranial internal carotid artery (eICA), first segment of the middle cerebral artery (MCA1), and sigmoid sinus in the anterior–posterior view; cavernous portion of the ICA (cICA), parietal vein, and jugular vein in the lateral views. The time-to-peak (TTP) for all ROIs and cerebral circulation time (CCT) were measured from FA and DSA scans. TTP, CCT, and radiation doses from DSA were compared with those from FA.

Results: The mean age of the patients were 69 ± 9.5 years old. The average stenosis was 89.7% ± 7.8% before stenting and 31% ± 3.6% after stenting. No patient suffered from periprocedural stroke. The intermethod correlation for TTP for all ROIs except the eICA and cICA ranged from 0.46 to 0.65 before stenting and 0.57 to 0.73 after stenting, and that for CCT was 0.65 before stenting and 0.57 after stenting. The radiation doses were significantly lower for FA than for DSA regardless of views or periprocedural timing ($p < 0.001$).

Conclusion: Stenosis facilitated the creation of a bolus by manual injection and therefore increased the accuracy of cerebral flow quantification in FA. Cerebral hemodynamic assessment by FA is quicker and associated with less radiation.

Keywords: Carotid stenosis; Cerebral circulation time; Fluoroscopic angiography; Radiation dose

1. INTRODUCTION

Angiographic cerebral circulation time (CCT) is defined as the time difference between time to peak (TTP) for the cavernous internal carotid artery (cICA) and the parietal vein (PV), and represents the time needed for blood to pass the brain parenchyma.[1] CCT has proven to be robust in monitoring peritherapeutic intracranial hemodynamic changes in several kinds of cerebrovascular disease such as stenotic-occlusive disease, vasospasm, carotid-cavenous fistula, and dural arteriovenous fistula.[2,3,4–8] The major advantage of CCT is that it can be obtained rapidly within the same angiosuite. Previously acquired standard digital subtraction angiography (DSA) series can be used for analysis, eliminating the radiation exposure and contrast medium administration of yet another series.

Fluoroscopy is often used to facilitate real-time appreciation of angiographic anatomy as well as hemodynamics, but its use is most often qualitative.[9] Recent studies showed moderate to high correlation between quantitative fluoroscopic angiography (FA) and DSA used to assess hepatic tumor embolization.[10] Because of the invisibility of current embolization agents, interventionists intermittently hand-inject contrast to observe hemodynamics: the optimal endpoint of embolization is defined as approximately the point just before blood flow reflux. FA helps to determine the endpoint and, compared to repeated DSA, saves time and contrast.

Carotid stenosis accounts for 3% to 5% of patients referred for vascular imaging and carries an increased risk of stroke.[11] It can be treated by carotid artery stenting (CAS) or carotid endarterectomy. CAS shows equivalent therapeutic efficacy compared to carotid endarterectomy.[12] During CAS, postdilatation after stent deployment ensures adequate flow augmentation but also carries a potential risk of hyperperfusion as well as thromboembolic events.[13,14] Appropriate dilatation of stenotic vessels conventionally depends on the interventionist's intuition and rarely on objective determination. We expected that FA could provide a fast in-room assessment without interrupting therapeutic procedure. Our purpose was to determine the accuracy of FA relative

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to DSA in evaluating CCT in patients with stenosis. The radiation doses associated with FA and DSA were also compared.

2. METHODS

2.1 Patient selection

Thirteen patients were prospectively included in this study, if they had >70% carotid artery stenosis according to North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria. Exclusion criteria were creatinine clearance rate <60 mL/min or any known coronary heart disease. The protocol of this study was approved by the Institutional Review Board of Taipei Veterans General Hospital (IRB: 2014-090912BC; title: Finding the Optimal Parameter for the DSA Time Density Curve When Evaluating Cerebral Flow Changes in Patients with Cerebrovascular Disorders).

2.2. Imaging protocol

DSA acquisitions with a standard, clinically routine protocol were carried out in all 42 cases. A power injector (Liebel-Flarsheim Angiomat, Illumena, San Diego, California) was used to create a contrast bolus after a 4-French angiocatheter was placed in the common carotid artery at the C4 vertebral body level. A bolus of 12 to 14 mL of 60% diluted iodine contrast (Iopamiro, Bracco, Italy) was administered within 1.5 seconds. Neither extra contrast medium nor extra radiation was used. The acquisition parameters were 7.5 frames/s for the first 5 seconds, followed by 4 frames/s for 3 seconds, 3 frames/s for 2 seconds, and finally 2 frames/s for 2 seconds. The entire DSA acquisition lasted for 12 seconds but was manually prolonged to visualize internal jugular vein (IJV) opacification in cases of slow intracranial circulation.[15] FA acquisition was stopped as soon as the density of the contrast medium in the JV started to decay. The 12-mL bolus of contrast was manually injected through a syringe at the maximum achievable speed. The same biplane angiosuite (Artis zee, Siemens Healthcare, Forchheim, Germany) was used in FA and DSA for all cases. The field of view and source-to-object distance were the same between FA and DSA but could be modified to facilitate the intervention by the interventionist.

2.3. Data analysis

Extracranial ICA (eICA), middle cerebral artery (MCA), and IJV were chosen as regions of interest (ROIs) in the anterior–posterior (AP) view; the cavernous portion of the ICA (cICA), and PV were chosen as ROIs in the lateral views (Fig. 1). TTP was defined as the time point at which contrast concentration in the ROI reached a maximum during the angiographic series. The TTPs of all ROIs were assessed by iFlow (Siemens Healthcare, Germany) and compared between FA and DSA. CCT was defined as the difference in TTP between the cICA and PV. CCT has been validated as a successful surrogate for the pathologic hemodynamics of cerebrovascular disease.[7,15–17]

Table 1

Patient characteristics

Number of patients	22
Age, y	69 ± 9.5
Average stenosis before stent, %	89.7 ± 7.8
Average stenosis after stent, %	31 ± 3.6
Hypertension, %	72
Diabetes mellitus, %	36
Hyperlipidemia, %	32
Smoking, %	54
Peripheral arterial disease, %	32
Prior radiation in head and neck, %	14

2.4. Radiation dose

The dose × area product was used to compare radiation dose between DSA and FA series. The dose × area product was defined as absorbed dose multiplied by the area irradiated, and expressed in microgray meters squared ($\mu Gy \cdot m^2$). These data were retrieved from the dose information page and automatically generated by the angiosuite system.

2.5. Statistical analysis

All statistical analysis was performed using SPSS 20 (2010; IBM-SPSS, Chicago, IL). We used Pearson correlations to determine the relationships between TTPs of individual ROIs and CCT measured on DSA and FA. We used the Student's *t* test to compare the dose area products measured on DSA with those measured on FA. The statistical significance level was set at $p < 0.05$.

3. RESULTS

The patient characteristics are listed in Table 1. The mean age of the patients were 69 ± 9.5 years old. The average stenosis was 89.7% ± 7.8% before stenting and 31% ± 3.6% after stenting. No patient suffered from periprocedural stroke. The TTP of contrast enhancement in the eICA was not significantly correlated between FA and DSA either before or after stenting, while that of cICA was only moderately correlated ($\rho = 0.62$) before stenting but not significantly correlated after stenting.

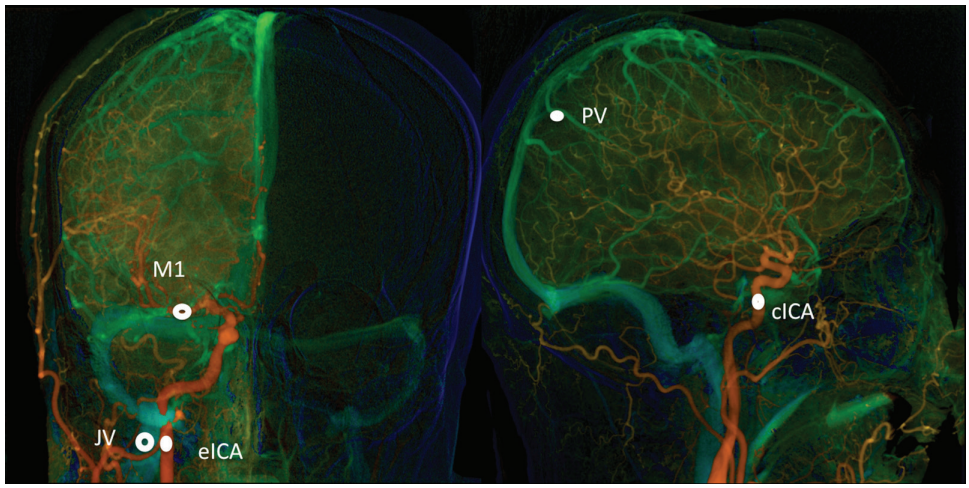

Fig. 1 Regions of interest in the (A) anterior–posterior (AP) and (B) lateral views of fluoroscopic angiography. CCT, cerebral circulation time; cICA, cavernous segment of ICA; eICA, extracranial internal carotid artery, 2 cm below carotid canal; JV, jugular vein; M1, first segment of middle cerebral artery; PV, parietal vein.

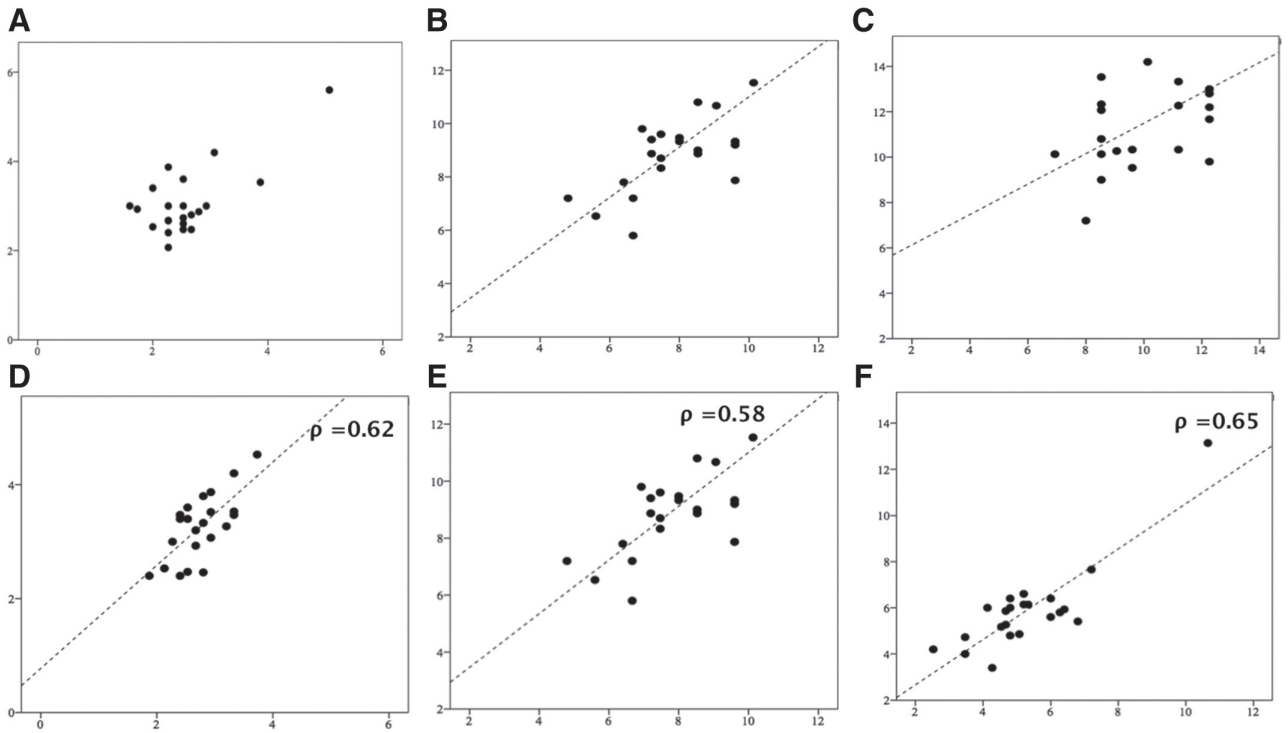

Fig. 2 Correlation of (a) TTPs at eICA; (b) TTPs at M1; (c) TTPs at JV; (d) TTPs at cICA; (e) TTPs at PV, between DSA (*x*-axis) and quantitative fluoroscopy angiography (*y*-axis) before stenting; (f) CCTs between DSA (*x*-axis) and quantitative fluoroscopy angiography (*y*-axis) before stenting. CCT, cerebral circulation time; DSA, digital subtraction angiography; eICA, extracranial internal carotid artery; JV, jugular vein; M1, first segment of middle cerebral artery; PV, parietal vein; TTP, time-to-peak.

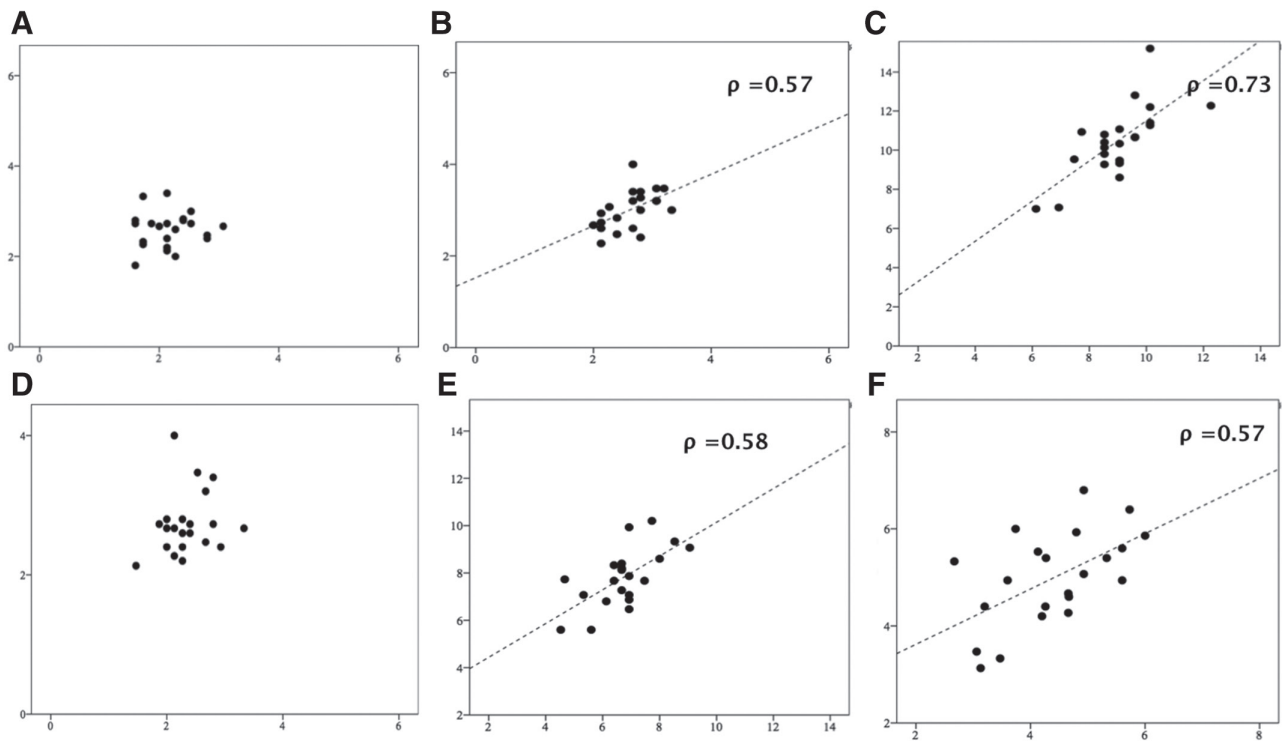

Fig. 3 Correlation of (a) TTPs at eICA; (b) TTPs at M1; (c) TTPs at JV; (d) TTPs at cICA; (e) TTPs at PV, between DSA (*x*-axis) and quantitative fluoroscopy angiography (*y*-axis) after stenting; (f) CCTs between DSA (*x*-axis) and quantitative fluoroscopy angiography (*y*-axis) after stenting. CCT, cerebral circulation time; DSA, digital subtraction angiography; eICA, extracranial internal carotid artery; JV, jugular vein; M1, first segment of middle cerebral artery; PV, parietal vein; TTP, time-to-peak.

Table 2

Comparison of dose area product between digital subtraction angiography and fluoroscopy angiography

	DSA (μGy·m²)	FA (μGy·m²)	*p*
Pre stenting			
AP view	1228.76 ± 238.46	88.65 ± 23.84	0.0001
Lateral view	1380.39 ± 402.31	106.44 ± 59.41	0.0001
Post stenting			
AP view	1246.70 ± 294.23	52.15 ± 15.07	0.0001
Lateral view	1386.46 ± 591.02	56.73 ± 12.16	0.0001

AP = anterior–posterior; DSA = digital subtraction angiography; FA = fluoroscopic angiography.

The correlations of TTPs in other ROIs were all significant between DSA and FA, and ranged from 0.46 to 0.73 before stenting (Fig. 2) and after stenting (Fig. 3). The correlation of CCTs from DSA and FA was 0.86 before stenting and 0.67 after stenting. The CCT before stenting was significantly shortened after stenting when measured on DSA (5.29 ± 1.14 seconds to 4.39 ± 0.64 seconds) and on FA (5.68 ± 0.96 seconds to 4.98 ± 0.71 seconds).

The dose area products calculated from FA images in the AP view (88.65 ± 23.84) and lateral views (106.44 ± 59.41) were both significantly less than those of DSA (1228.76 ± 238.46 in the AP view and 1380.39 ± 402.31 in the lateral views, $p < 0.001$) in prestenting series. The dose area products calculated from FA images in the AP view (52.15 ± 15.07) and lateral view (56.73 ± 12.16) were also both significantly less than those of DSA (1246.70 ± 294.23 in the AP view, 1386.40 ± 591.02 in lateral views, $p < 0.001$) in poststenting series (Table 2).

4. DISCUSSION

Although the shape of the bolus created by manual contrast injection during FA was more variable compared to that created by the power injector during DSA, our result still showed a moderate correlation of TTPs in most ROIs between DSA and FA peritherapeutically. In both DSA and FA, CCTs reflected the restoration of blood flow after stenting, which confirmed the feasibility of using FA as an alternative DSA to monitor cerebral hemodynamic changes. The advantage of FA is that it substantially decreases radiation exposure, which is a concern in DSA. Meanwhile, the overall procedural time would be theoretically shortened because FA preparation time is shorter than DSA.

According to Lieber et al.,[18] the contrast was well mixed with the blood in the ROI and extended from the injection site a distance of eight times the vessel diameter in clinical protocols. TTPs in the eICA and cICA were not correlated between DSA and FA before stenting, and only TTP in the cICA was correlated between DSA and FA after stenting. Our explanation was that both eICA and cICA were upstream from the ICA and closer to the injection site than the other ROIs. Meanwhile, the vessel lumen was also widened after stenting, and therefore the contrast bolus took longer to mix well with the blood flow and travel through a wider vessel lumen. The similarity of two waveforms between FA and DSA was higher before stenting than after stenting. This finding was consistent with the finding of Lin et al. that the correlation of TTPs between DSA and FA was higher after embolization of the arterial segment because reducing the tumor load slowed blood flow to allow better mixing of contrast with blood.

Several parameters are used to describe waveforms: area under the curve, maximum slope, peak density, arrival time, minimum slope, and full width half maximum. Although these parameters more or less reflect the cerebral hemodynamic changes due to disease progression or vascular hemodynamic change, TTP is the most robust parameter for clinical scenario evaluation regardless of the vascular location or injection protocol.[19,20]

There were some limitations of this study: first, a certain amount of variability is associated with manual injection, and variation between individuals was not evaluated owing to the relative small sample size. A power-injector could have been used in both FA and DSA for comparison but it did not fit the clinical scenario. Second, one of the effects of overlapping vasculature on the time density curve profile is to shift the TTP. It is therefore important to use previously validated, relatively robust ROIs, eg, cICA and PV to minimize this effect.[1] Third, the time density curve approach merely provides a surrogate hemodynamic marker, ie, TTP instead of velocity. It is clinically feasible but not the best parameter to characterize pulsatile flow in the arterial system. On the contrary, computer fluid simulation or optic flow methods might improve flow estimation but both demand intensive computation and are time consuming.[21,22] Further evaluation of FA applied to high flow diseases such as arteriovenous malformation or fistula is warranted.

In conclusion, time density curve analysis of a contrast bolus created by manual injection was feasible. CCT measured on FA can reflect the severity of blood disturbance in carotid stenosis and can be used to evaluate the therapeutic effects of carotid stenting. FA provides a quicker cerebral hemodynamic assessment with less radiation exposure.

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