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Research article

Risk prediction of postoperative permanent stroke in acute type A aortic dissection patients with severe common carotid artery stenosis using brain CT perfusion

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A R T I C L E I N F O

Keywords:
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A B S T R A C T

Rationale and objectives: To explore the feasibility and predictive utility for neurological outcomes of brain computed tomography perfusion (CTP) for surgically treated acute type A aortic dissection patients with severe common carotid artery stenosis.
Materials and methods: Consecutive acute type A aortic dissection patients with severe common carotid artery stenosis undergoing preoperative brain computed tomography perfusion and surgery at our center were examined in retrospect. Brain perfusion was assessed using parameters including cerebral blood flow, cerebral blood volume, mean transmit time, time to maximum, penumbra volume and infarct core volume. Univariable and multivariable regression analyses were performed to identify clinical and imaging predictors associated with postoperative permanent stroke.
Results: Out of 44 patients included, 19 patients (43.2 %) presented with postoperative permanent stroke. Univariable analysis revealed that internal carotid artery dissection, cerebral blood flow of the affected side, cerebral blood volume of the affected side, and penumbra volume were implicated in postoperative permanent stroke. Multivariable analysis further showed that cerebral blood flow of the affected side was an independent indicator of a permanent stroke following surgery (odds ratio: 0.820, 95 % confidence interval: 0.684–0.982; $p = 0.012$). The area under the receiver operating characteristic curve was 0.867 (95 % confidence interval: 0.764–0.970), and the optimal cut-off value was 45.6mL/100 mL/min.
Conclusion: Cerebral blood flow of the affected side was an independent indicator of permanent stroke following surgery in acute type A aortic dissection patients with severe common carotid artery stenosis. Brain CTP could be a helpful modality for quantitative evaluation of cerebral malperfusion and neurological prognostication.

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Non-standard abbreviations and acronyms:

CTP	computed tomography perfusion
ATAAD	acute type A aortic dissection
CTA	computed tomography angiography
aAO	ascending aorta
CCA	common carotid artery
GCS	Glasgow Coma Scale
CTP	computed tomography perfusion
CBF	cerebral blood flow
CBV	cerebral blood volume
Tmax	time to maximum
MTT	mean transit time.

1. Introduction

Cerebral malperfusion complicating acute type A aortic dissection (ATAAD) significantly worsens surgical outcomes, being associated with higher mortality and permanent neurological impairment [1,2]. However, the satisfactory treatment of ATAAD patients with cerebral malperfusion is still uncertain; surgical decision making suffers from lack of guidelines stating when surgery should be avoided or how to modify the surgical approach. Quantitative and objective evaluation of cerebral malperfusion before surgery would be helpful for neurological prognosis and critical decision making for this high-risk patient population, but this evaluation remains challenging in the setting of ATAAD. Firstly, cerebral malperfusion in ATAAD is hard to diagnose because of the urgent surgery. Secondly, cerebral malperfusion in patients with ATAAD is essentially determined by symptoms, which are biased [3–5].

To evaluate cerebral malperfusion in ATAAD patients, objective assessment of cervical arteries by computed tomography angiography (CTA) has been explored [3,5–8], but their utilities have not yet been established. Besides, these modalities cannot provide direct imaging evidence of cerebral malperfusion. Multiparametric magnetic resonance imaging (MRI) has been applied to quantify brain ischemia [9]. However, this modality is not effective or accessible in emergencies.

Brain computed tomography perfusion (CTP) may improve the situation, which has been advocated by the American Heart Association/American Stroke Association guidelines to assess cerebral malperfusion quantitatively [10]. Recently, two studies explored the applicability of CTP in the quantitative evaluation of cerebral malperfusion in ATAAD, though both with limited cases (2 and 14 cases), and suggested the predictive value of brain CTP in the neurological prognosis after surgery [5,11]. So far, the efficacy of CTP in the ATAAD patient population and its clinical significance are still uncertain. Given that the severity of common carotid artery (CCA) true lumen flow impairment may be an indicator for cerebral malperfusion [12,13], we applied brain CTP to ATAAD patients complicated with severe CCA true lumen stenosis or occlusion (70%–100 %) who were surgically treated [14]. Our goal was to examine the feasibility and neurological prognostic usefulness of brain CTP for this patient cohort.

2. Materials and methods

Ethical statement

This single-center, retrospective study was approved by the institutional review board of Xijing Hospital (KY20222142), and the requirement for informed written consent was waived. Additional informed consent was obtained for publication of the images of human participants.

2.1. Study design

Medical records were analyzed for consecutive patients with ATAAD and severe CCA true lumen stenosis (70%–100 %) who had surgery at our center between August 2018 and March 2020. All these patients underwent brain CTP before surgery because of severe stenosis in unilateral or bilateral CCA true lumen, which may be a marker of cerebral malperfusion [12,13]. Exclusion criteria were as follows: (1) aortic surgical history; (2) previous old cerebral stroke; (3) unsatisfactory CTP images. We reviewed and recorded patient demographics, preoperative status, imaging data, and perioperative data. Laboratory results including D-dimer, brain natriuretic peptide, troponin and creatinine were also regained. All patients included had emergent total arch replacement. Primary outcome was permanent stroke following surgery. Baseline characteristics, surgical details, aorta and neck CTA findings, and brain CTP findings were compared between patients with and without permanent stroke following surgery.

2.2. Definition of clinical parameters

ATAAD was defined as any non-traumatic dissection of the aorta proximal to the left subclavian artery presenting within 14 days of symptom onset [3], and there were no non-A non-B in this study. Preoperative hypotension was defined as systolic blood pressure <90 mmHg or requiring catecholamines to maintain blood pressure for any reason. The presence of non-cerebral other-organ malperfusion was evaluated by CTA scan, physical examination, laboratory values and electrocardiography. Postoperative permanent stroke was defined as permanent loss of neurological function confirmed by brain injury detected by CT or MRI.

2.3. Neurologic, radiographic and ultrasonographic evaluation

Our surgery team implemented neurological examination upon patient arrival. Glasgow Coma Scale (GCS) was obtained on patients with neurological symptoms to assess the severity of the symptoms [15]. Coma was defined as neurological deficits with a GCS score of ≤8. At our center, all patients suspected of ATAAD first underwent echocardiography, as well as carotid artery ultrasound to detect any CCA true lumen flow impairment. Fortunately, thanks to the "green channel" of ultrasonography for ATAAD patients at our center, ultrasonography is readily accessible. Then, all patients had preoperative neck and aorta CTA imaging. Brain CTP was also applied, with a time-delay of 60 s, if CCA true lumen was severely stenosed detected by carotid artery ultrasound.

2.4. Imaging acquisition and post-processing

A dual-source CT scanner (SOMATOM Definition Flash, Siemens Healthineers, Forchheim, Germany) was used to get the CTA. In the cranio-caudal orientation, patients had simultaneous neck and aorta CTA imaging. The following were the scanning parameters: 100 kV tube voltage, 3.0 pitch, 2 × 128 × 0.6 mm slice collimatio, and reference tube current of 300 mAs. A 70 mL injection of iopromide (Ultravist 370, 370 mg I/mL, Bayer Schering Pharma, Berlin, Germany) was administered to each patient at a flow rate of 5 mL/s. Next, 40 mL of saline solution were administered. The suprarenal descending aorta was used for bolus monitoring, with an attenuation threshold of 100 HU.CTP was then acquired in a total of 30 cycles with a 1.5 s acquisition interval following CTA acquisition, if necessary. At a rate of 8 mL/s, 40 mL of contrast and 40 mL of saline solution were injected. The scanning parameters included an 80 kV tube voltage, a 32 × 1.2 mm slice collimation, and an 80 mA tube current. An on-site computer running Siemens Healthineers' VB10 software (syngo.via) was used for post-processing. The "CT Neuro Perfusion" module was used to create perfusion maps, including time to maximum (Tmax) and cerebral blood flow (CBF).

2.5. Image analysis

All image analyses were independently carried out in a double-blind fashion by two skilled radiologists (each with 18 and 10 years of experience in cardiovascular imaging), and any disagreements were settled by consensus. The true lumen diameter of aAO was defined as the minimum diameter of the true lumen of aAO in the section orthogonal to the centerline. The aAO diameter was defined as the diameter of aAO at the largest slice. Diameter ratio of the true lumen in aAO was defined by dividing the diameter of the true lumen over that of the involved aAO.

Although CCA dissection was suggested as predictive of postoperative stroke, the impacts of different CCA impairments were controversial in terms of its location (unilateral or bilateral) and severity (stenosed or occluded) [12,13]. Moreover, an assessment of the detailed damaged condition of a compromised CCA was rare. Therefore, we further analyzed the comprehensive status of the CCA dissection, such as its extent (entire CCA dissection), and if there was re-entry in the impaired CCA.

We depicted CTP images at basal ganglia, beside the body of lateral ventricle, and centrum semiovale. We draw by hand to encompass the brain parenchyma of one side as the regions of interest (ROIs). Then, the software would create the mirror images on the other hemisphere correspondingly. The CBF, cerebral blood volume (CBV), mean transit time (MTT) and Tmax of each side was designated as the average value of the corresponding parameter at the three sections of each hemisphere. The affected side of brain was defined as the same side of which CCA was severe stenosis. If both sides of CCA saw severe stenosis or occlusion, the affected side was defined as the side with the lower CBF. The software determined the volume of brain tissue with malperfusion based on previous criteria [16,17]. Specifically, salvageable "penumbra" was designated as spital area Tmax> 6 s, and irreversible "ischaemic core" was defined as regional cerebral blood flow <30 % of contralateral hemisphere median.

2.6. Surgical approach

We implement sternotomy with cardiopulmonary bypass and hypothermic circulatory arrest with antegrade cerebral perfusion as described previously [18]. In short, patients with severe CCA true lumen stenosis at our center had total arch replacement with our institutional strategy of extra-anatomic revascularization and cannulation. A standard cardiopulmonary bypass was established with femoral arterial cannulation. Then, innominate artery and/or CCA revascularization and cannulation were performed according to preoperative CTA findings. Specifically, if the right CCA or left CCA was severely stenosed or occluded, the impaired artery was fully exposed above the normal vessel beyond the distal limit of the dissection, and end-to-end anastomosed to an 8–10 mm prosthetic graft through which arterial cannulation was achieved. Myocardial protection was achieved through antegrade and/or retrograde delivery of cold blood cardioplegia. Cerebral oximetry by Near-infrared spectroscopy (NIRS), as well as bladder and nasopharyngeal temperatures, were routinely monitored. The flow rate for antegrade cerebral perfusion was 5–10 mL/kg/min during hypothermic circulatory arrest when patients were cooled to 24–25 °C. Mean arterial pressure during cerebral perfusion was maintained at around 60 mmHg (50–70 mmHg). The decision-making for unilateral or bilateral cerebral perfusion was based on preoperative evaluation, intraoperative monitoring and surgeon preference at our center. Specifically, if one side of carotid common artery was free of dissection and without internal carotid artery stenosis, unilateral cerebral perfusion was applied. Cerebral oximetry by Near-infrared spectroscopy was monitored to ensure cerebral perfusion was satisfying. On the other hand, if both sides of carotid common artery were with severe stenosis, bilateral cerebral perfusion was preferable. For patients who were started on unilateral perfusion, if the Near-infrared spectroscopy value on either side reduced by >20 % of the baseline value during the procedure, cerebral perfusion was then switched to bilateral.

2.7. Statistical analysis

For categorical data, summary statistics are shown as counts with percentages; for continuously distributed continuous data, they are shown as means and standard deviations; and for non-normally distributed continuous data, they are shown as medians with quartiles. The Shapiro-Wilk test was used to examine the distribution of the data. Unpaired t-tests were used to compare continuous variables with normal data distributions; non-parametric Mann-Whitney U-tests were used to compare data with skewed distributions; $\chi 2$ statistics were used to compare categorical variables; and the Fisher's exact test was employed if observed frequencies were less than five. Multiple logistic regression analysis was used to determine the indicators of permanent stroke following surgery. Variables with a univariable value of P-value <0.05 were added to the multivariable model. The results are reported as odds ratios (ORs) with 95 % confidence intervals (CIs). Using MedCalc Software, receiver operating curves were examined to determine the optimal cut-off value of the continuous variables to predict postoperative persistent stroke with the highest degree of accuracy. The Youden index was used to establish the ideal cut-off value. P-values less than 0.05 were regarded as statistically significant in all two-tailed analyses. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS Statistics 24; IBM Corp., Armonk, NY, USA).

3. Results

3.1. Patient characteristics and surgical details

Between August 2018 and March 2020, 312 patients underwent emergency open surgery for ATAAD at our hospital. Medical records were analyzed for 51 consecutive ATAAD patients with severe CCA true lumen stenosis or occlusion undergoing standard surgery, and 44 eligible patients were enrolled (Fig. 1). The demographics, clinical characteristics, and surgical details of all included patients with and without postoperative permanent stroke are shown in Table 1. Nineteen patients (43.2 %) were diagnosed with postoperative permanent stroke. The mean age of all patients included was 53.1 ± 9.7 years, and 68.2 % was male. A total of 31 patients (70.5 %) presented new onset neurological symptoms at arrival, including vertigo in 12 patients, syncope in 5 patients, sensomotoric deficit in 9 patients, and coma developing independent of the haemodynamic instability in 5 patients. There was no significant difference between the patients with and without postoperative permanent stroke in terms of baseline characteristics, major

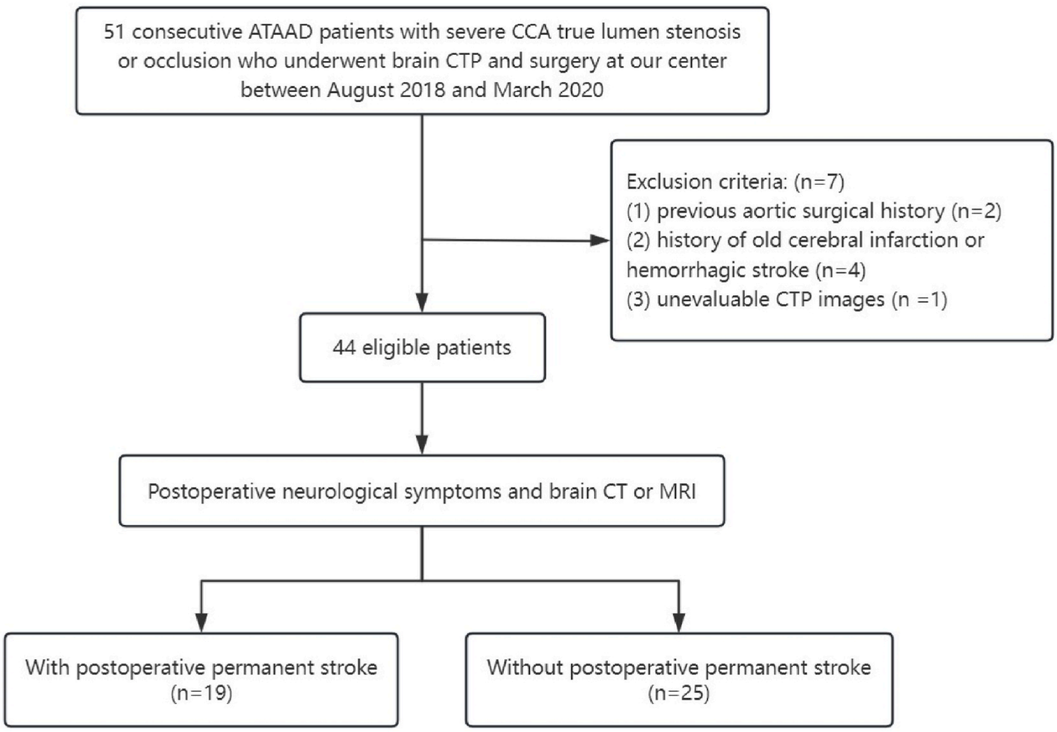

Fig. 1. Study flowchart. ATAAD = acute type A aortic dissection, CCA = common carotid artery, CTP = computed tomography perfusion.

Table 1
Baseline characteristics and surgical details of patients with acute type A aortic dissection with and without postoperative permanent stroke.

Variables	All patients (n = 44)	Postoperative permanent stroke (−) (n = 25)	Postoperative permanent stroke (+) (n = 19)	P value
Baseline characteristics				
Age (yrs)	53.1 ± 9.7	53.4 ± 9.3	52.5 ± 11.0	0.785
Sex (male)	30 (68.2)	18 (72.0)	12 (63.2)	0.533
Hypertension	25 (56.8)	15 (60.0)	10 (52.6)	0.625
Diabetes	2 (4.6)	1 (4.0)	1 (5.3)	>0.99
Hypotension	5 (11.4)	2 (8.0)	3 (15.8)	0.744
Moderate-severe AR	7 (15.9)	2 (8.0)	5 (26.3)	0.219
Pericardial effusion	12 (27.3)	6 (24.0)	6 (31.6)	0.576
Interval from symptom to imaging (hours)	12 (9.0–20.0)	12 (5.0–24.0)	12 (10.5–16.0)	0.454
Neurological symptoms				
Vertigo	12 (27.3)	7 (28.0)	5 (26.3)	0.901
Syncope	5 (11.4)	3 (12.0)	2 (10.5)	>0.99
Sensomotoric deficit	9 (20.5)	5 (20.0)	4 (21.1)	>0.99
Coma	5 (11.4)	2 (8.0)	3 (15.8)	0.744
Laboratory results				
D-dimer, mg/L	11.5 (4.7–26.7)	10.3 (3.4–24.7)	13.7 (7.1–52.2)	0.470
Creatinine, μmol/L	69.0 (52.0–100.0)	72.0 (52.0–107.0)	67.0 (51.0–80.5)	0.732
BNP, pg/mL	449.9 (221.7–1205.0)	398.8 (218.9–672.9)	1205 (236.2–2343)	0.845
Troponin, ng/mL	0.05 (0.02–0.07)	0.05 (0.02–0.07)	0.07 (0.03–0.11)	0.083
Surgical details				
Branch vascular revascularization site				
Only innominate artery	13 (29.6)	7 (28.0)	6 (31.6)	0.797
Innominate artery + right common carotid artery and/or right subclavian artery	7 (15.9)	3 (12.0)	4 (21.1)	0.691
Only left common carotid artery	9 (20.5)	5 (20.0)	4 (21.1)	1.000
Bilateral common carotid artery	10 (22.7)	7 (28.0)	3 (15.8)	0.552
Aortic root repair	11 (25.0)	4 (16.0)	7 (36.8)	0.219
Aortic root replacement	6 (13.6)	2 (8.0)	4 (21.1)	0.420
CABG	7 (15.9)	3 (12.0)	4 (21.1)	0.691
Antegrade cerebral perfusion				
Unilateral	23 (52.3)	15 (60.0)	8 (42.1)	0.239
Bilateral	21 (47.7)	10 (40.0)	11 (57.9)	
Operative time (min)	404.2 ± 77.3	398.3 ± 62.1	412.0 ± 94.9	0.566
CPB time (min)	229.5 ± 42.2	229.2 ± 35.9	229.9 ± 50.2	0.956
Aortic cross-clamp time (min)	96.0 (80.5–107.5)	93.0 (79.0–102.5)	98.0 (83.0–109.0)	0.361
Time of DHCA (min)	32.9 ± 6.4	32.0 ± 6.1	34.1 ± 6.7	0.303

Note. Data are means ± standard deviations or median (interquartile range). Unless otherwise specified, data are numbers of participants, with percentages in parentheses.
AR = aortic valve regurgitation, BNP = brain natriuretic peptide, CABG = coronary artery bypass grafting, CPB = cardiopulmonary bypass, DHCA = deep hypothermic circulatory arrest.

laboratory results and neurological symptoms.

All patients included underwent emergent total arch replacement with our institutional extra-anatomic revascularization and cannulation strategy. Surgical details are also shown in Table 1. There was no statistically significant difference in surgical details including branch vascular reconstruction site, aortic root procedure, and concomitant coronary artery bypass grafting. Unilateral or bilateral antegrade cerebral perfusion was applied during deep hypothermic circulatory arrest and there was no significant difference between the patients with and without postoperative permanent stroke. Duration times of operation, cardiopulmonary bypass, aortic cross-clamp and deep hypothermic circulatory arrest were also similar.

3.2. Preoperative CTA findings of aorta and neck

Comprehensive CTA findings that were likely considered to indicate postoperative permanent stroke are presented in Table 2. Dissection of internal carotid artery was more common in patients with postoperative permanent stroke ($p = 0.016$). This may be because end-to-end anastomosis between surgical graft and normal vessel beyond the dissection in the internal carotid artery is not possible at our center. Beyond that, we observed no significant difference in terms of other CTA characteristics, including aortic sinus involvement, true lumen diameter of ascending aorta, entry tear in the aortic arch, retrograde dissection, intimal flap plaque, unilateral and bilateral CCA dissection, CCA true lumen occlusion, entire CCA dissection with and without re-entry (all $p > 0.05$).

3.3. Preoperative brain CTP parameters

Detailed preoperative brain CTP findings are presented in Table 3. For all patients included, mean CBF of the affected side was 42.7

Table 2
Aorta CTA findings in patients with acute type A aortic dissection with and without postoperative permanent stroke.

CTA findings	All patients (n = 44)	Postoperative permanent stroke (−) (n = 25)	Postoperative permanent stroke (+) (n = 19)	P value
Aortic sinus involvement	17 (38.6)	8 (32.0)	9 (47.4)	0.300
The true lumen diameter of aAO (mm)	15.5 ± 7.2	15.6 ± 7.3	15.5 ± 7.2	0.969
The aAO diameter (mm)	44.0 (41.1–48.0)	44.0 (40.5–50.5)	44.0 (42.0–46.0)	0.943
True lumen ratio of aAO	0.3 ± 0.2	0.3 ± 0.2	0.3 ± 0.1	0.955
Entry tear in the aortic arch	14 (31.8)	8 (32.0)	6 (31.6)	0.976
Retrograde dissection	2 (4.6)	1 (4.0)	1 (5.3)	1.000
Intimal flap plaque	9 (20.5)	5 (20.0)	4 (21.1)	1.000
Severe luminal stenosis of major branches				
Coronary involvement	7 (15.9)	3 (12.0)	4 (21.1)	0.691
Renal artery	9 (20.5)	3 (12.0)	6 (31.6)	0.223
Femoral artery	6 (13.6)	4 (16.0)	2 (10.5)	0.936
CCA dissection				
Right	25 (56.8)	13 (52.0)	12 (63.2)	0.649
Left	9 (20.5)	5 (20.0)	4 (21.1)	
Both	10 (22.7)	7 (28.0)	3 (15.8)	
CCA true lumen occlusion	17 (38.6)	7 (28.0)	10 (52.6)	0.096
Entire CCA dissection without re-entry	10 (22.7)	6 (24.0)	4 (21.1)	0.391
Entire CCA dissection with re-entry	15 (34.1)	10 (40.0)	5 (26.3)	0.343
ICA dissection	8 (18.2)	1 (4.0)	7 (36.8)	**0.016**

CTA = computed tomography angiography, aAO = ascending aorta, CCA = common carotid artery, ICA = internal carotid artery.

mL/100 mL/min, median penumbra volume was 32.2 mL, and median infarct core volume was 0 mL. CBF of the affected side ($p < 0.001$) and CBV of the affected side ($p = 0.003$) were significantly lower in patients with postoperative permanent stroke, while penumbra volume ($p < 0.001$) was significantly higher in these patients. There were no significant differences in MTT of each hemisphere, Tmax of each hemisphere and infarct core volume (all $p > 0.05$).

4. Outcome characteristics

Neurologic evaluation could be performed in all patients because there were no early postoperative deaths (within 24 h after surgery). Incidence of postoperative permanent stroke was 43.2 % (n = 19), including coma in 2 patients demonstrating large cerebral infarction on CT, paresis in 11 patients, dysphagia in 3 patients, dysarthria in 2 patients, and paresthesia in 1 patient. Overall in-hospital mortality was 13.6 % (6 patients), and the reason for death was coma in 2 patients, multiorgan failure in 3 patients and myocardial infarction in 1 patient. In-hospital mortality was higher in patients with postoperative permanent stroke (6 patients versus 0 patients; $p = 0.01$).

4.1. *Risk factors of postoperative permanent stroke*

Univariable analysis revealed that internal carotid artery dissection, CBF of the affected side, CBV of the affected side, and penumbra volume were implicated in postoperative permanent stroke. Multivariable logistic regression analysis further showed that CBF of the affected side was an independent predictor of postoperative permanent stroke (OR: 0.820, 95 % CI: 0.684–0.982; $p = 0.012$) (Table 4). A receiver operating characteristic curve was used to find the cut-off point of CBF of the affected side for predicting postoperative permanent stroke. The results revealed that the area under the receiver operating characteristic curve was 0.867 (95 %

Table 3
Cerebral CTP findings in patients with acute type A aortic dissection with and without postoperative permanent stroke.

CTP findings	All patients (n = 44)	Postoperative permanent stroke (−) (n = 25)	Postoperative permanent stroke (+) (n = 19)	P value
CBF of the affected side (mL/100 mL/min)	42.7 ± 9.9	48.0 ± 7.7	35.7 ± 7.8	<**0.001**
CBF of the contralateral side (mL/100 mL/min)	53.8 ± 6.7	53.1 ± 6.9	54.8 ± 6.4	0.420
CBV of the affected side (mL/100 mL)	3.1 ± 0.4	3.3 ± 0.4	2.9 ± 0.4	**0.003**
CBV of the contralateral side (mL/100 mL)	3.6 ± 0.4	3.5 ± 0.4	3.6 ± 0.4	0.335
MTT of the affected side (sec)	6.2 ± 1.9	6.0 ± 2.0	6.5 ± 1.8	0.425
MTT of the contralateral side (sec)	4.9 ± 0.7	4.9 ± 0.7	4.9 ± 0.6	0.884
Tmax of the affected side (sec)	4.6 ± 1.4	4.4 ± 1.4	4.8 ± 1.4	0.371
Tmax of the contralateral side (sec)	2.6 ± 0.6	2.6 ± 0.7	2.7 ± 0.6	0.748
Penumbra volume (mL)	32.2 (8.5–84.1)	10.7 (4.9–28.8)	84.2 (53.8–186.5)	<**0.001**
ICV (mL)	0 (0–6.2)	0 (0–3.7)	2.2 (0–14.9)	0.077

CTP = computed tomography perfusion, CBF = cerebral blood flow, CBV = cerebral blood volume, MTT = mean transit time, Tmax = time to maximum, ICV = infract core volume.

CI: 0.764–0.970), and the positive predictive value and negative predictive value were 63.3 % and 100.0 %, respectively. The optimal cut-off value of CBF of the affected side was 45.6 mL/100 mL/min (Fig. 2). A representative example of an ATAAD patient with postoperative permanent stroke is given in Fig. 3 (a, b) and Fig. 4(a–d). Fig. 3 shows the images of preoperative aortic CTA and postoperative brain CT, and Fig. 4 shows preoperative brain CTP images of the same patient.

5. Discussion

To the author's knowledge, this is the first study of its size to examine the applicability and prognostic usefulness of CTP in ATAAD patients combined with severe stenosis of CCA undergoing surgery. The findings of our study suggested that brain CTP may be an applicable and useful modality, helping to assess cerebral malperfusion objectively and quantitatively, in anticipating neurological outcomes in this patient cohort, with CBF of the affected side being indicated as an independent indicator of permanent stroke following surgery.

Cerebral malperfusion secondary to ATAAD has been suggested as a sign of adverse prognosis [1,2]. To improve outcomes of ATAAD patients with cerebral malperfusion, exclusive attention has been paid to surgical issues, such as timeliness of operation, surgical techniques of aortic arch reconstruction, and cerebral perfusion strategy during hypothermic circulatory arrest. Despite this, postoperative cerebrovascular accident remains frequent (from 9.5 % to 47 %) and negatively prognostic [6,7,19,20]. Frequently, patients are referred for emergent operations but despite the lack of a clear evidence of cerebral malperfusion they develop neurological symptoms postoperatively [21]; however, it is also true that patients with symptoms of cerebral malperfusion do not have permanent neurological deficits after surgery [22]. What we should know is how much the aortic dissection itself has impaired cerebral perfusion and functions at the time of surgery. Therefore, an objective and quantitative evaluation modality for cerebral malperfusion in ATAAD patients is highly warranted.

So far, different modalities including magnetic resonance perfusion, xenon CT, positron emission tomography, and single photon emission computed tomography have been applied to assess cerebral perfusion directly [23]. However, these modalities were not regarded as readily accessible for ATAAD patients in emergencies. On the other hand, there have been also indirect ways to evaluate cerebral malperfusion by involvement of CCA and/or internal carotid artery (ICA) on CTA [5,12,13]. However, the utility of these evaluations has not yet been established. For example, the Penn-Saitama-Freiburg registry for CCA dissection in type A aortic dissection, the largest series so far, included 279 patients with unilateral CCA dissection and 161 patients with bilateral CCA dissection and showed that unilateral CCA involvement was predictive of in-hospital stroke, whereas bilateral CCA involvement was paradoxically not [13]. Another study derived from the same registry further explored the impact of severity of CCA true lumen impairment and indicated that CCA occlusion was predictive of in-hospital stroke, whereas CCA true lumen flow impairment (true lumen compressed >50 %) was not [12]. Based on these mixed results, it seems conceivable that a static CTA image may not naturally mirror flow impairment and cerebral malperfusion, given that many cases of malperfusion syndromes were ascribed to dynamic obstruction [24].

As such, we have focused on CTP mainly because of its two strengths: its applicability in emergencies and the quantitative evaluation. Firstly, CTP is regarded as an easier and faster method to get information about cerebral perfusion before an emergent surgery for aortic dissection [25,26].The added perfusion CT scan caused no significant delay, which can be completed in 2–3 min and could easily be added to a screening CT angiogram, as observed in our application and the cases series of Inoue et al. [11]. The safe application of preoperative CTP was showed in 6 patients with stable haemodynamics, but they also suggested that all ATAAD patients combined with cerebral malperfusion should have preoperative CTP [11]. In our study, not only all haemodynamically stable patients but also 5 patients (11.4 %) with hypotension on arrival safely underwent preoperative CTP and CTA scan without significant delay. Admittedly, for the few extremely unstable patients warranting immediate surgery, not only CTP but also CTA was inapplicable. This limitation is common for all time-consuming preoperative modalities.

The other strength of CTP is the quantitative evaluation of cerebral malperfusion and its neurologically prognostic value. CTP has been recommended guidelines to assess cerebral malperfusion [10], providing quantitative analysis of CBV, CBF, Tmax, and MTT. Patients with mismatch ratios>1.8 have been considered as good candidates for endovascular thrombectomy in patients with acute ischaemic stroke [27]. On the other hand, an ischaemic core of >53 mL was suggested as an indicator for intracranial hemorrhage following interventional treatment [28]. Although it remains uncertain if these criteria were suitable for ATAAD patients with cerebral malperfusion, quantitative assessment with CTP should be useful in decision-making and predicting outcomes based on some preliminary evidence. For example, in the case series of ATAAD patients reported by Inoue et al. though small in size (6 patients), the neurological outcomes after surgery supported the aforementioned criteria [11].

Table 4
Risk predictors for postoperative permanent stroke in patients with acute type A aortic dissection.

Variables	OR	95 % CI	P value
CTA characteristics			
ICA dissection	3.459	0.297–40.330	0.322
CTP characteristics			
CBF of the affected side (mL/100 mL/min)	0.820	0.684–0.982	**0.012**
CBV of the affected side (mL/100 mL)	0.330	0.021–5.153	0.429
Penumbra volume (mL)	1.004	0.995–1.014	0.379

CTA = computed tomography angiography, ICA = internal carotid artery, CTP = computed tomography perfusion, CBF = cerebral blood flow, CBV = cerebral blood volume.

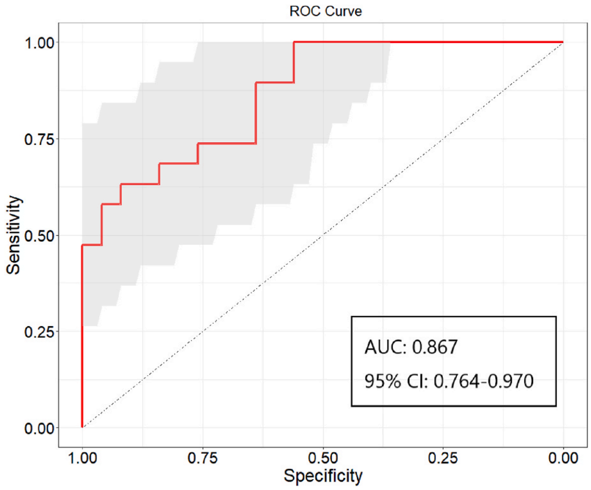

Fig. 2. Receiver operating characteristic curve of cerebral blood flow of the affected side to predict postoperative permanent stroke. The area under the receiver operating characteristic curve was 0.867, and optimal cut-off value was 45.6mL/100 mL/min.

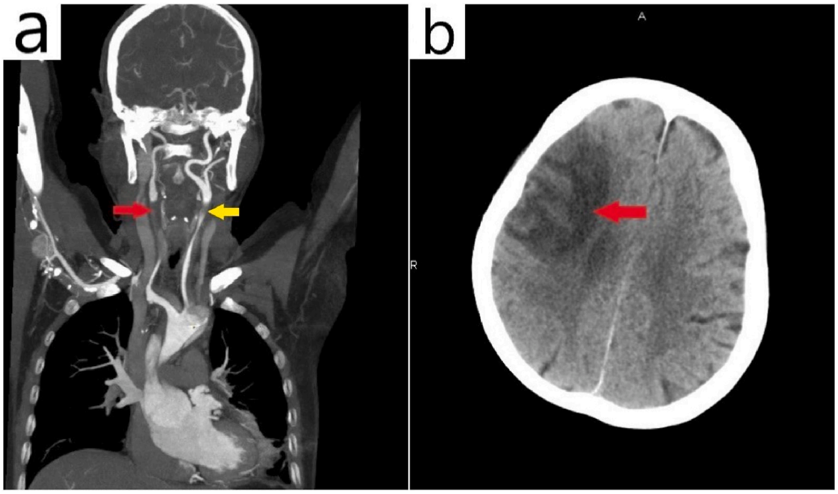

Fig. 3. A 61-year-old woman presented with thoracic and back pain for 10 h and no neurological symptoms before admission. Aortic CTA showed ATAAD with occlusion of right CCA (red arrow) and severe true lumen stenosis of left CCA (yellow arrow) (a). Brain CT on the fifth day after the emergency surgery showed an infarct in the right parietal lobe (b, red arrow). CTA = computed tomography angiography, ATAAD = acute type A aortic dissection, CCA = common carotid artery.

In light of previous evidence, we applied preoperative CTP and explored its neurologically prognostic value in a larger cohort of ATAAD patients who were surgically treated (44 patients). Given that the severity of CCA true lumen flow impairment may be a surrogate marker for cerebral malperfusion [12,13], we applied CTP to patients combined with severe stenosis of CCA true lumen (70–100 %) [14]. Because CCA impairment was also identified as an indicator of stroke following surgery [12,20], the rate of post-operative permanent stroke in our study seemed unsurprisingly high (43.2 %), which was comparable to those of previous studies (18–51 %) in the similar setting [12,13]. Furthermore, we analyzed major risk factors associated with postoperative stroke, based on previous studies, including age, hypotension at arrival, detailed status of impaired CCA, malperfusion syndrome, internal carotid artery involvement, retrograde dissection, and entry tear in the aortic arch [5–7,12,29,30]. Our multivariable analysis suggested that CBF may be an independent indicator of postoperative permanent stroke. The optimal cut-off value should be 45.6mL/100 mL/min. Interestingly, all patients in our cohort were categorized as benign in terms of cerebral malperfusion according to the aforementioned criteria of ischaemic core volume. Unsurprisingly, there was no severe neurological event after surgeries such as cerebral edema, herniation syndrome, or intracranial hemorrhage. It was notable that, however, 2 patients presented coma after surgery. Besides, the overall in-hospital mortality (13.6 %) in our study was comparable with previous studies, but the in-hospital mortality of the patients with postoperative permanent stroke (31.6 %, 6 of 19 patients) was higher than that of a previous study of Dumfarth et al. (22.9 %) [29]. This could be partly explained by the severe CCA impairment and the consequent ischaemic stroke burden in patients included in

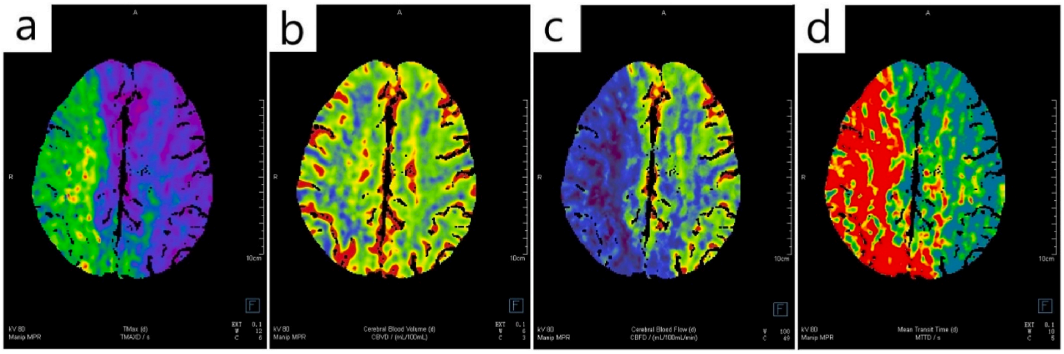

Fig. 4. Preoperative brain CTP images of the same patient as Fig. 2.Tmax of the affected side (right) was 4.97s, and Tmax of the contralateral side was 2.11s (a). CBV of the affected side (right) was 3.05mL/100 mL, and CBV of the contralateral side was 3.40 mL/100 mL (b). CBF of the affected side (right) was 23.41 mL/100 mL/min, and CBF of the contralateral side was 54.23 mL/100 mL/min (c). MTT of the affected side (right) was 9.45s, and MTT of the contralateral was 4.35s (d). CTP = computed tomography perfusion, Tmax = time to maximum, CBV = cerebral blood volume, CBF = cerebral blood flow, MTT = mean transit time.

our study, given that cerebral malperfusion is associated with elevated mortality [2].

Our study has several limitations. First, in this retrospective study, the fact that patients not having CTP or CTA were not included may cause selection bias. In this study, only 2 patients failed to have CTP scan due to unstable haemodynamics indicating emergency surgery. The majority of patients (>90 %) completed CTP scan. Furthermore, all patients included in our study could be categorized as benign in terms of cerebral malperfusion according to the aforementioned criteria. Though we suggested the prognostic value of CBF in our cohort, our finding warrants further validation in a larger population with a wide spectrum of severity (mismatch ratio >1.8 or ischaemic core >53 mL). Besides, infarct core may not be accurately diagnosed, which is premised on the normal blood flow in the contralateral hemisphere, in some ATAAD patients, such as those with both sides of CCA involvement or with hypotension. Further studies are warranted to explore the specific criteria for ATAAD patients. Moreover, we got CTP images at variant time points which could affect the assessment of CTP parameters. Finally, the averaged CBF was decided by manually drawn ROIs, leading to deviation. We tried to lessen this by having two capable radiologists with disagreement resolved by consensus. Further studies following a prospective design and defined approach are necessary to validate the findings of this investigation.

6. Conclusion

In conclusion, our study identified CBF of the affected side on preoperative brain CTP as an independent indicator of permanent stroke following surgery in ATAAD patients with severe stenosis of CCA. Brain CTP may be a valuable modality for quantitative evaluation of cerebral malperfusion and neurological prognostication in ATAAD patients. Integrating these insights into the preoperative evaluation may contribute to personalized treatment strategies and improved outcomes in this challenging patient population.

Data availability statement

The data associated with this study has not been deposited into a publicly available repository. The data underlying this article will be shared on reasonable request to the corresponding author.

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CRediT authorship contribution statement

Chengxiang Li: Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization. **Jing Yu:** Writing – review & editing, Resources, Formal analysis, Data curation, Conceptualization. **Lei Shang:** Software, Methodology, Investigation, Formal analysis. **Ziqi Yang:** Validation, Resources, Investigation. **Xiwei Deng:** Validation, Resources, Investigation. **Rui An:** Supervision, Resources. **Jian Xu:** Supervision, Resources, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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