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Brief Report

Relationships among language ability, the arcuate fasciculus and lesion volume in patients with putaminal hemorrhage: a diffusion tensor imaging study

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Relationships among language ability, arcuate fasciculus and lesion volume were investigated by use of diffusion tensor tractography in patients with putaminal hemorrhage. Thirty-three right-handed patients within six weeks of hemorrhage onset were recruited. Correlation of the aphasia quotient with subset (fluency, comprehension, repetition, naming) scores, diffusion tensor tractography parameters and lesion volume of patients, aphasia quotient (r = 0.446) with subset (naming: r = 0.489) score had moderate positive correlations with fractional anisotropy of the left arcuate fasciculus. The aphasia quotient subset (repetition) score had a strong positive correlation with fractional anisotropy of the left arcuate fasciculus (r = 0.520), whereas, aphasia quotient subset (fluency and comprehension) scores had no significant correlations with fractional anisotropy of the left arcuate fasciculus after Benjamini–Hochberg correction. Aphasia quotient (r = 0.668) with subset (fluency: r = 0.736, comprehension: r = 0.739, repetition: r = 0.649, naming: r = 0.766) scores had strong positive correlations with the tract volume of the left arcuate fasciculus and strong negative correlations with lesion volume (r = –0.521, fluency: r = –0.520, comprehension: r = –0.513, repetition: r = –0.518, naming: r = –0.562). Fractional anisotropy of the left arcuate fasciculus had a moderate negative correlation with lesion volume (r = –0.462), whereas the tract volume of the left arcuate fasciculus had a strong negative correlation with lesion volume (r = –0.700). According to the result of mediation analysis, tract volume of the left arcuate fasciculus fully mediated the effect of lesion volume on the aphasia quotient. Regarding the receiver operating characteristic curve, the lesion volume cut-off value was 29.17 cm^3 and the area under the curve (0.74), sensitivity (0.77) and specificity (0.80) were higher than those of fractional anisotropy, tract volume and aphasia quotient cut-off values. It was found that level of language disability was related to lesion volume as well as to injury severity of arcuate fasciculus in the dominant hemisphere of patients with putaminal hemorrhage. In particular, the tract volume of the arcuate fasciculus in the dominant hemisphere fully mediated the effect of lesion volume on language ability. Additionally, a lesion volume of approximately 30 cm^3 was helpful in discriminating arcuate fasciculus discontinuation in the dominant hemisphere.

Keywords

Arcuate fasciculus; Lesion volume; Language ability; Diffusion tensor tractography; Diffusion tensor imaging

1. Introduction

The arcuate fasciculus (AF), an important neural tract for language, connects the posterior superior temporal cortex and posterior part of the inferior frontal gyrus, often referred to as Wernicke's and Broca's areas [1]. Injury of the AF such as discontinuation causes various language deficits, including conduction aphasia [2–6]. Approximately 24–38% of acute stroke patients and 10–18% of chronic stroke patients have been reported to exhibit aphasia [7–12]. Therefore, precise estimation of the AF state (preserved, discontinued, or non-reconstructed) during the early stage of a stroke is clinically important as it would help clinicians design rehabilitative strategies and predict aphasia outcome. Additionally, such estimates provide useful data for determining the necessity of surgical intervention during the acute stage of intracerebral hemorrhage. Putaminal hemorrhage is the most common type of intracerebral hemorrhage as the putamen is the site most involved with that type of hemorrhage as a hematoma can expand to the internal capsule, corona radiata, centrum semiovale, or temporal lobe [13]. Conservative treatment is considered when a hematoma is smaller than 10 cm^3, whereas surgery such as craniotomy and ventriculoperitoneal shunt is considered with moderate neurologic deficits or a hematoma larger than 30 cm^3 [14]. Putaminal hemorrhage with large lesion volume (LV) in the dominant hemisphere may cause both language deficits including conduction aphasia and effect change in the microstructure of the AF [15, 16]. However, precise estimation of the AF affected by the LV of putaminal hemorrhage had been limited because conventional brain imaging techniques, such as computed tomography or magnetic resonance imaging, do not clearly discriminate the AF from adjacent white matter [1, 17].

The development of diffusion tensor imaging, which produces images based on measurements of the diffusion of water molecules in structures, has allowed investigation of the overall microstructural characteristics of brain white matter. In particular, diffusion tensor tractography in human brain tissue, derived from diffusion tensor imaging, enables three-dimensional reconstruction and visualization of structures, including the AF [18, 19]. Several diffusion tensor tractography based studies have demonstrated relationships between language ability and the severity of AF injury in the dominant hemisphere in stroke patients [20–24]. However, currently those relationships have not been fully elucidated. In particular, the relationships between LV, language ability and the state of the AF in the dominant hemisphere require characterization.

In this study, by using diffusion tensor tractography, the relationships among language ability, the AF state in the dominant hemisphere and LV were investigated in patients with putaminal hemorrhage.

2. Methods

2.1 Subjects

Thirty-three right-handed consecutive subjects with putaminal hemorrhage (23 men, 10 women; mean age 50.49 ± 9.68 years; range, 28~67 years) were recruited according to the following inclusion criteria: (1) first-ever stroke; (2) age: 20–69 years; (3) spontaneous putaminal hemorrhage confirmed by a neuroradiologist; (4) diffusion tenor imaging scanning and language evaluation performed within six weeks of hemorrhage onset; and (5) no previous history of psychiatric or neurological disease [25]. The left hemisphere is assumed to be the language dominant hemisphere in right-handed subjects [26]. Table 1 summarizes the demographic and clinical characteristics of the subjects. This study was performed retrospectively and the study protocol was approved by the institutional review board of the Yeungnam University Hospital (YUMC 2021-03-014).

Table 1. Demographic and clinical characteristics of subjects.

	Subjects
Age (years)	50.49 ± 9.68
Number (*n*)	33
Male:Female	23:10
Mean duration to AQ (days)	18.36 ± 9.03
Mean duration to DTI (days)	18.36 ± 9.03
AQ value	47.38 ± 36.78
FA	0.42 ± 0.04
TV	832.12 ± 488.06
LV (cm^3)	29.1 ± 20.38

AQ, aphasia quotient; DTI, diffusion tensor imaging; FA, fractional anisotropy; TV, tract volume; LV, lesion volume; Values presented are mean ± standard deviation.

2.2 Language evaluation

The aphasia quotient (AQ) of the Western Aphasia Battery was used to assess the language ability of subjects (range, 0–100 percentiles). The AQ value comprises four subset scores (fluency, comprehension, repetition and naming) and higher scores indicate better function [27]. The reliability and validity of the Western Aphasia Battery has been well established [27, 28]. Subject AQ scores were obtained at an average of 18.4 ± 9 days after putaminal hemorrhage onset.

2.3 Lesion volume measurement

Brain LV was determined by examination of a T2-weighted turbo single echo (TSE) sequence in brain magnetic resonance images (18.4 ± 9 days after onset) and each subject LV was calculated by applying the following formula: [A (cm) × B (cm) × C (cm)]/2 (A: lesion length; B: width at the largest cross-sectional area; C: total height from the bottom to top slices showing the hematoma) [29]. Representative LV measurement images are presented in Fig. 1.

2.4 Diffusion tensor imaging and tractography

Diffusion tensor imaging data were acquired on the same day as the language (AQ) evaluation (18.4 ± 9 days after PH onset). Diffusion tensor imaging was performed using a sensitivity-encoding head coil on a 1.5 T Philips Gyroscan Intera (Hoffman-LaRoche Ltd, Best, Netherlands) scanner with single-shot echo-planar imaging and navigator echo. Sixty contiguous slices (acquisition matrix = 96 × 96; reconstruction matrix = 192 × 192; field of view = 240 mm × 240 mm; TR = 10.726 ms; TE = 76 ms, b = 1000 s/mm^2, NEX = 1 and thickness = 2.5mm) were acquired for each of the 32 non-collinear diffusion-sensitizing gradients. Eddy current image distortion, head motion effects and B0 inhomogeneity distortion were corrected using affine multi-scale two-dimensional registration with the Oxford Centre for Functional Magnetic Resonance Imaging of Brain (FMRIB) Software Library (FSL: www.fmrib.ox.ac.uk/fsl) [30]. Evaluation of the AF was obtained with DTI Studio software (CMRM, Johns Hopkins Medical Institute, Baltimore, Maryland) based on the fiber assignment continuous tracking (FACT) algorithm. For tracking of the AF, the seed region of interest was assigned manually to the posterior parietal area of the superior longitudinal fascicle where the longitudinal aspect of the AF is expected, while the target region of interest was located in the posterior temporal lobe [1, 17, 31, 32]. The color map of the seed region of interest was green (rostral–caudal) and the target region of interest was blue (superior–inferior). Termination criteria used for fiber tracking were fractional anisotropy (FA) $<$0.2 and angle $<$60° [31, 32].

2.5 Statistical analysis

Statistical analysis was performed using SPSS 21.0 for Windows (SPSS, Chicago, IL, USA). Multiple comparisons were corrected by the Benjamini–Hochberg (BH) procedure to control the false discovery rate [33]. Pearson correlation analysis was used to estimate the significance of the correlations among AQ values with subset (fluency, comprehension, repetition, and naming) scores, diffusion tensor tractography parameters (FA: fractional anisotropy; TV: tract volume) and LV; $p < 0.05$ and false discovery rate cut off $<$0.05 were considered statistically significant. The correlation coefficient indicates the strength (0.1–0.29: weak correlation; 0.3–0.49: moderate correlation; more than 0.50: strong correlation) and direction (positive or negative) of the relation-

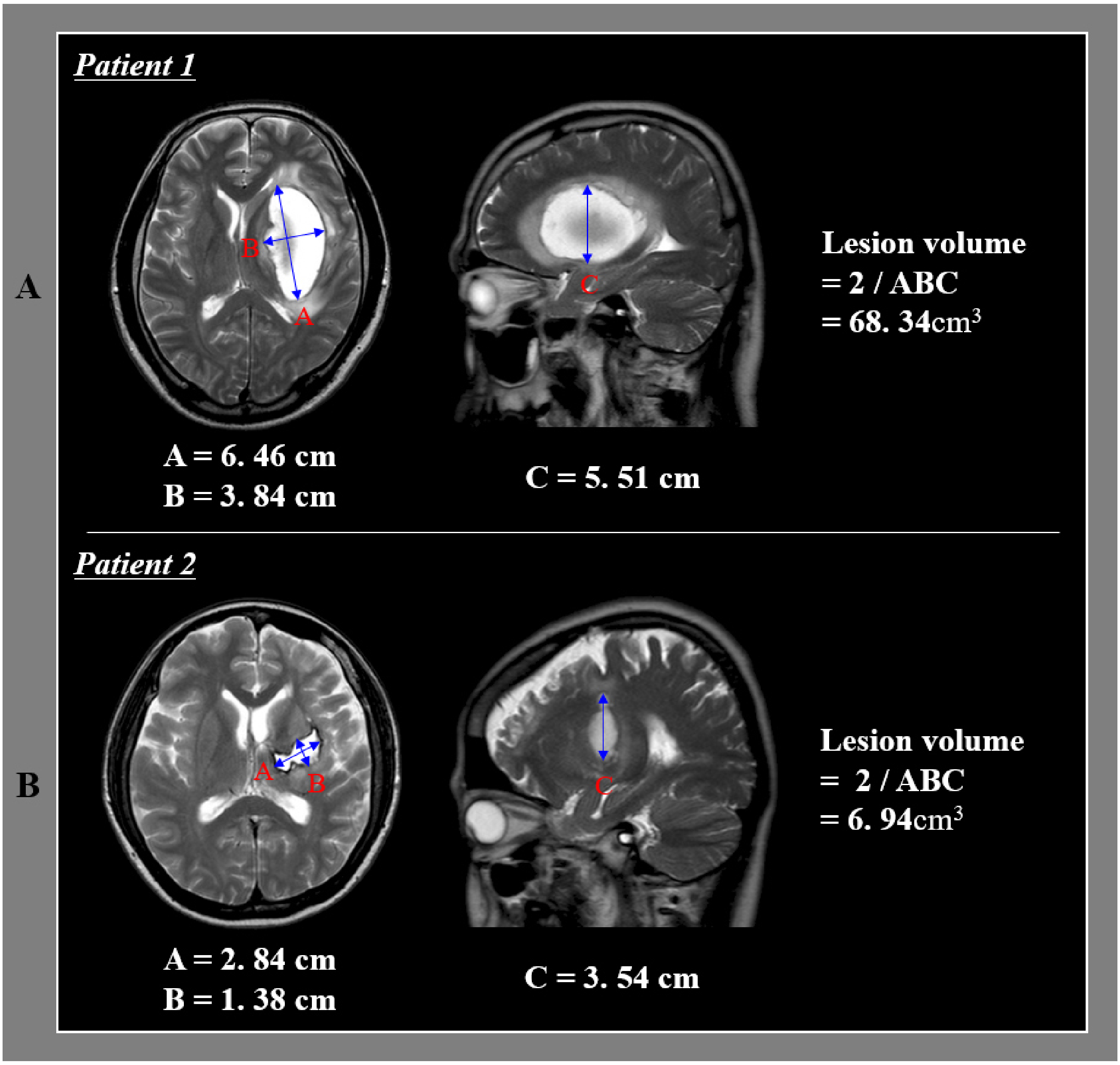

Fig. 1. Result of lesion volume measurement by applying the following formula: [A (cm) × B (cm) × C (cm)]/2 (A: lesion length; B: width at the largest cross-sectional area; C: total height from the bottom to top slices showing the hematoma). (A) Representative lesion volume measurement larger than 29.17 cm^3 (patient 1: 49-year-old male). (B) Representative lesion volume measurement smaller than 29.17 cm^3 (patient 2: 44-year-old female).

ship between two variables [34]. Mediation analyses were used to determine whether the TV value of the left AF mediates the relationship between the AQ value and LV. According to the Baron and Kenny [35] mediational model, the mediating role of a variable exists when the following conditions met: (1) the first step, the independent variable (LV) significantly affects the mediator variable (TV); (2) the second step, the independent variable (LV) significantly affects the dependent variable (AQ) ; (3) the third step, the independent variable (LV) and mediator variable (TV) simultaneously and significantly affect the dependent variable (AQ) and the standardized β is greater in the second step than in the third step, and R^2 indicates the coefficient of determination increases sequentially. In the third step, perfect mediation occurs when the independent variable does not significantly affect the dependent variable, on the other hand, partial mediation occurs when the standardized β of the independent variable in the third step is less than that in the second step [35]. The Sobel test was used to assess the significance of the mediation effect [35, 36]. The sensitivity, specificity and area under the curve of the AQ with subset (fluency, comprehension, repetition and naming) scores, diffusion tensor tractography parameters and LV values were used to assess discontinuations of the left AF between Wernicke's and Broca's areas and were determined by examining the receiver operating characteristic curves. This curve reveals the diagnostic ability of a binary

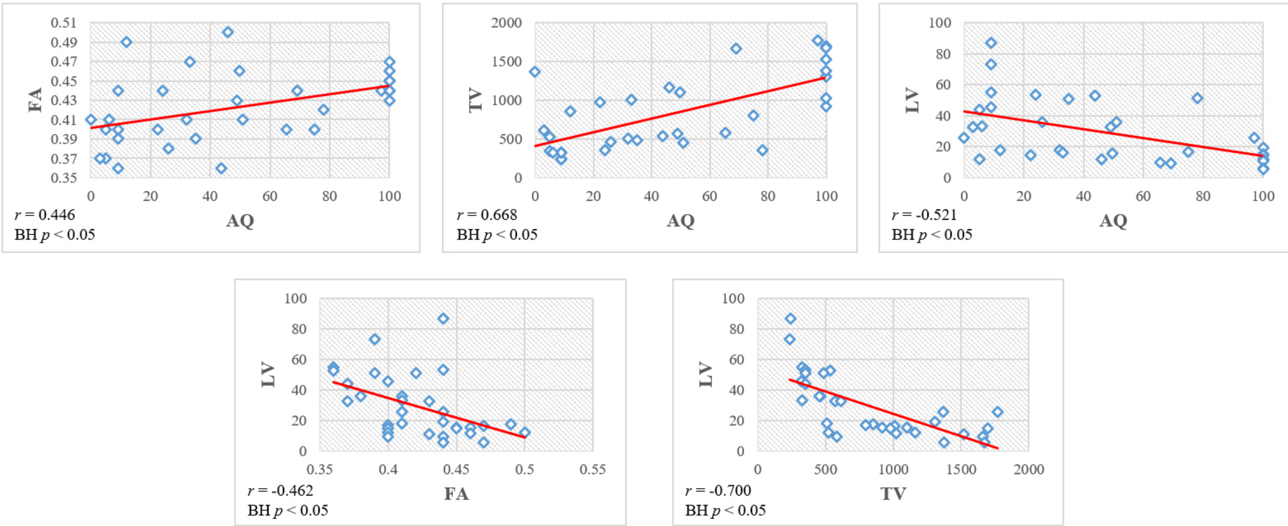

Fig. 2. Scatter plots of the correlation among the aphasia quotient (AQ) values, diffusion tensor tractography parameters (FA: fractional anisotropy; TV: tract volume) and lesion volume (LV) of subjects.

classifier system based on an identification threshold generated by displaying the true-positive rate for the false-positive rate at the threshold setting [37]. The sensitivity, known as the true-positive rate, represents the ability of a test to correctly identify patients with a disease, while the specificity, known as the 1–false-positive rate, indicates the ability of a test to correctly identify people without the disease [37, 38]. The area under the curve was used to indicate test accuracy (1.0: perfect test; 0.99–0.90: excellent test; 0.89–0.80: good test; 0.79–0.70: fair test; 0.69–0.51: poor test; 0.50 or lower: fail) [39].

3. Results

In diffusion tensor tractography findings, 13 subjects showed a discontinuation of the left AF, while 20 subjects exhibited an intact left AF. Correlations among the AQ values with subset scores, diffusion tensor tractography parameters and the LV of subjects are summarized in Table 2. Moderate positive correlations were detected between the AQ value ($r = 0.446$) with subset (naming: $r = 0.489$) score and the FA value of the left AF ($p < 0.05$, BH $p < 0.05$). The AQ subset (repetition) score showed a strong positive correlation with the FA value of the left AF ($r = 0.520$, $p < 0.05$, BH $p < 0.05$). After BH correction, the AQ subset (fluency and comprehension) scores showed no significant correlations with the FA value of the left AF (fluency: $r = 0.388$, comprehension: $r = 0.370$, $p < 0.05$, BH). On the other hand, the AQ value ($r = 0.668$) with subset (fluency: $r = 0.736$, comprehension: $r = 0.739$, repetition: $r = 0.649$, naming: $r = 0.766$) scores showed strong positive correlations with the TV of the left AF and strong negative correlations with LV ($r = –0.521$, fluency: $r = –0.520$, comprehension: $r = –0.513$, repetition: $r = –0.518$, naming: $r = –0.562$, $p < 0.05$, BH $p < 0.05$). A moderate negative correlation was detected between the FA value of the left AF and the LV ($r = –0.462$, $p < 0.05$, BH $p < 0.05$). By contrast, the TV of the left AF showed a strong negative correlation with the LV ($r = –0.700$, $p < 0.05$, BH $p < 0.05$). The scatter plots of the correlation among the AQ values, diffusion tensor tractography parameters and LV of the subjects are presented in Fig. 2. The results of analysis of the role of the TV as a mediator of the relationship between the AQ and LV are summarized in Table 3. In the first step, the LV showed a significant association with TV ($t = –5.455$, $p < 0.05$). In the second step, LV showed a significant association with the AQ ($t = –3.401$, $p < 0.05$). In the third step, the LV showed no significant association with the AQ ($t = –0.559$), while the TV showed a significant association with the AQ ($t = 3.135$, $p < 0.05$). In summary, the TV fully mediated the relationship between the AQ and LV (Fig. 3). Moreover, the Sobel test for this mediation analysis showed the TV to have a significant mediation effect between the AQ and LV ($z = –2.796$, $p < 0.05$). The results of the receiver operating characteristic analyses of the AQ value with subset scores, diffusion tensor tractography parameters and the LV of the patients are summarized in Table 4. The cut-off value (area under the curve) was 34.05 (0.14) for AQ, 36.00 (0.09) for AQ subset (naming) score, 41.75 (0.13) for AQ subset (comprehension) score, 50.15 (0.05) for AQ subset (repetition) score, 29.30 (0.06) for AQ subset (naming) score, 0.42 (0.10) for FA, 575.50 (0.14) for TV and 29.17 cm^3 (0.74) for LV. The sensitivity of the LV cut-off value (0.77) was higher than for AQ (0.23), AQ subset scores (fluency: 0.23, comprehension: 0.15, repetition: 0.15, naming: 0.23), FA (0.15) and TV (0.23). The specificity of the LV cut-off value (0.80) was higher than for AQ (0.25) and AQ subset scores (fluency: 0.25, comprehension: 0.20, repetition: 0.20, naming: 0.25), FA (0.25) and TV (0.25). Representative regions of interest and diffusion tensor tractography images showing AF status in patients with different LV are presented in Fig. 4.

Table 2. Correlations between the aphasia quotient value with subset scores and diffusion tensor tractography parameters and lesion volume of the patients.

		AQ (total)	FA	TV	LV
	r-value		0.446	0.668	–0.521
AQ (total)	*p*-value	-	0.009*	0.000*	0.002*
	BH *p*-value		0.017**	0.003**	0.008**
	r-value		0.388	0.736	–0.520
AQ (fluency)	*p*-value	-	0.026*	0.000*	0.002*
	BH *p*-value		0.019	0.003**	0.008**
	r-value		0.370	0.739	–0.513
AQ (comprehension)	*p*-value	-	0.034*	0.000*	0.002*
	BH *p*-value		0.022	0.003**	0.008**
	r-value		0.520	0.649	–0.518
AQ (repetition)	*p*-value	-	0.002*	0.000*	0.002*
	BH *p*-value		0.008**	0.003**	0.008**
	r-value		0.489	0.766	–0.562
AQ (naming)	*p*-value	-	0.004*	0.000*	0.001*
	BH *p*-value		0.011**	0.003**	0.006**
	r-value	–0.521	–0.462	–0.700	
LV	*p*-value	0.002*	0.007*	0.000*	-
	BH *p*-value	0.008**	0.014**	0.003**	

AQ, aphasia quotient; FA, fractional anisotropy; TV, tract volume; LV, lesion volume; *: correlation is significant at $p < 0.05$, **: correlation is significant using a Benjamini–Hochberg (BH) correction.

Table 3. Mediation analysis of the role of the tract volume as a mediator of the relationship between the aphasia quotient and lesion volume.

Step	Dependent variable	Independent variable	B	SE	β	t	p	R^2
1	TV	LV	–0.017	0.003	–0.700	–5.455	0.000*	0.490
2	AQ	LV	–0.001	0	–0.521	–3.401	0.002*	0.272
3	AQ	LV	0.000	0.000	–0.106	–0.559	0.580	0.451
		TV	0.045	0.014	0.593	3.135	0.004*	
Sobel test				–2.796 < –1.96*				

TV, tract volume; LV, lesion volume; AQ, aphasia quotient, *: $p < 0.05$.

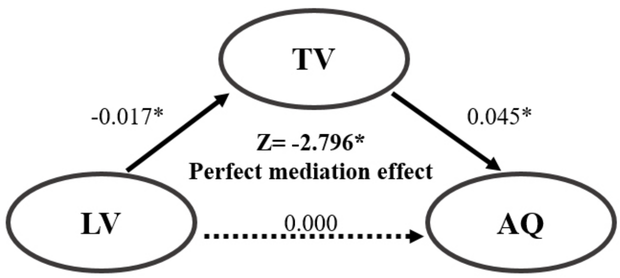

Fig. 3. Mediation analysis of the role of the tract volume (TV) as a mediator of the relationship between the aphasia quotient (AQ) and lesion volume (LV). * $p < 0.05$.

4. Discussion

This study investigated the relationships among language ability, the AF state in the dominant hemisphere, and LV in patients with putaminal hemorrhage. Results can be summarized as follows. First, the AQ value with subset (naming) score had moderate positive correlations with the FA value of the left AF. The AQ subset (repetition) score had a strong positive correlation with the FA value of the left AF, the AQ subset (fluency and comprehension) score had no significant correlations with the FA value of the left AF. By contrast, the AQ value with subset (fluency, comprehension, repetition, and naming) scores had a strong positive correlation with the TV value of the left AF, and a strong negative correlation with the LV. The FA value of the left AF had a moderate negative correlation with the LV, whereas the TV value of the left AF had a strong negative correlation with the LV. Second, the TV value of the left AF fully mediated the effect of the LV on the AQ value. Third, the LV cut-off value was 29.17 cm^3 and its area under the curve, sensitivity and specificity were higher than those of the FA, TV, and AQ cut-off values.

Regarding the assessed diffusion tensor tractography parameters, the FA value is indicative of the integrity of white matter microstructures, such as axons, myelin and microtubules and represents the degree of directionality of water diffusion [18]. Therefore, the FA value reflects the fiber den-

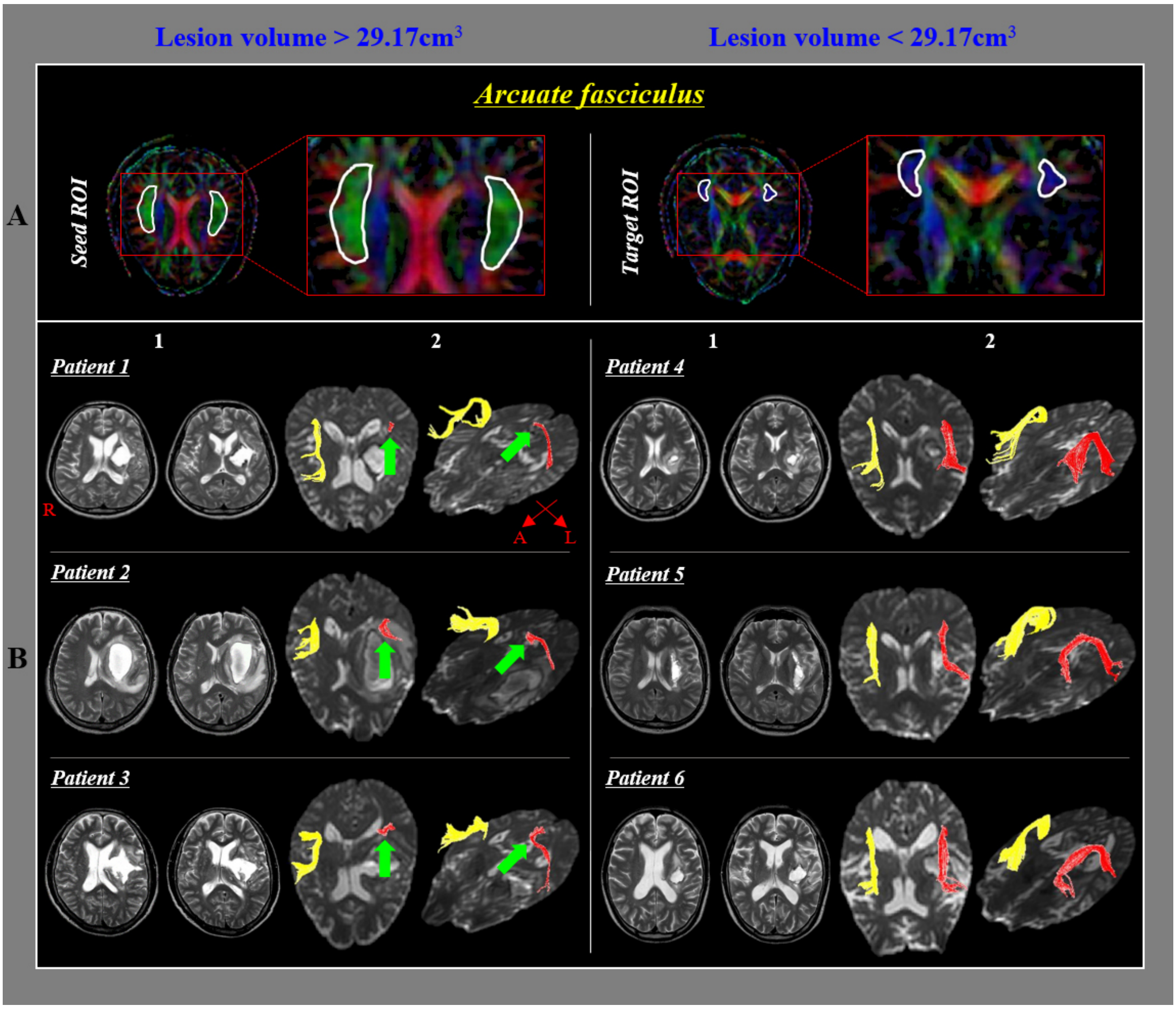

Fig. 4. Regions of interest and diffusion tensor tractography for the arcuate fasciculus (AF). (A) The seed and target regions of interest are applied to the posterior parietal area of the superior longitudinal fascicle where the longitudinal aspect of the AF and the posterior temporal lobe are expected. (B) (1) T2-weighted brain magnetic resonance images at the time of diffusion tensor imaging scanning in representative patients with a lesion volume (LV) larger than 29.17 cm^3 (patient 1: 43-year-old male, patient 2: 46-year-old male, patient 3: 59-year-old male) and with an LV smaller than 29.17 cm^3 (patient 4: 56-year-old male, patient 5: 33-year-old male, patient 6: 63-year-old male). (2) Results of diffusion tensor tractography for the left AF. The left AF in patients with an LV larger than 29.17 cm^3 shows discontinuation (green arrow) between Wernicke's and Broca's areas in the dominant hemisphere, whereas the left AF in patients with an LV smaller than 29.17cm^3shows preservation of AF integrity.

sity, axonal diameter and white matter myelination [40]. The TV value indicates the average volume of a neural tract including the total number and thickness of neural fiber and white matter microstructures such as myelin, oligodendrocytes and dendrites obtained by probabilistic tractography segmentation [40, 41]. Therefore, low FA and TV values for a neural structure represent low structure density, diameter, axonal myelination and low fiber numbers and thickness of the neural tract, respectively [18, 40]. Consequently, the result showing a moderate positive correlation between the AQ value with subset (naming) score and the FA value of the left AF indicates that language ability (especially, the naming ability) is closely related to the fiber density, axonal diameter and myelination of the left AF. By contrast, the strong positive correlations between the AQ subset (repetition) score and the FA value of the left AF and between the AQ value with subset (fluency, comprehension, repetition, and naming) scores and the TV value of the left AF suggest that repetition ability is more closely associated with fiber density, axonal diameter and myelination of the left AF than the other language (fluency, comprehension, and naming) abilities, and comprehensive language ability is more closely associated with the remaining number and thickness of neural fibers within the left AF than with the fiber density, axonal diameter and myeli-

Table 4. Receiver operating characteristic curve results of the aphasia quotient value with subset scores, diffusion tensor tractography parameters and lesion volume for discriminating discontinuation of the left arcuate fasciculus.

	Cut-off value	AUC	Sensitivity	Specificity
AQ (total)	34.05	0.14	0.23	0.25
AQ (fluency)	36.00	0.09	0.23	0.25
AQ (comprehension)	41.75	0.13	0.15	0.20
AQ (repetition)	50.15	0.05	0.15	0.20
AQ (naming)	29.30	0.06	0.23	0.25
FA	0.42	0.10	0.15	0.25
TV	575.50	0.14	0.23	0.25
LV	29.17	0.74	0.77	0.80

AUC, area under the curve; AQ, aphasia quotient; FA, fractional anisotropy; TV, tract volume; LV, lesion volume.

nation of the left AF. Consequently, this suggests that the level of language disability is closely related to injury severity of the left AF. On the other hand, the correlations of the LV with the AQ value with subset (fluency, comprehension, repetition, and naming) scores (strong negative), FA value (moderate negative) of the left AF and TV value of the left AF (strong negative) suggest that the size of the lesion negatively affects comprehensive language ability and the density, diameter, axonal myelination, number and thickness of the remaining neural fibers of the left AF. Considering the significance of these correlations, language ability and the remaining neural fibers and thickness of the left AF are more affected by LV than by AF density, diameter and myelination. Thus, LV is closely related to language disability and severity of AF injury.

Mediation analysis showed that the TV value of the left AF fully mediated the relationship between the AQ value and LV. This indicates that the effect of the LV on the language ability operates through the TV value of the left AF. It suggests that surgical intervention to remove a relevant hematoma considering the TV value of the left AF is necessary to maximize the recovery of language ability in the early stage of putaminal hemorrhage.

The receiver operator analysis suggest that an LV cut-off value of 29.17 cm^3 with a sensitivity of 77% and specificity of 80% can be used to identify AF discontinuation between Wernicke's and Broca's areas in the dominant hemisphere with good predictive accuracy. By contrast, the AQ with subset (fluency, comprehension, repetition, and naming) scores, FA and TV cut-off values have no discriminatory ability to predict discontinuation of the left AF. Further, it seems that the LV has a direct effect on AF discontinuation in the dominant hemisphere when compared to the comprehensive language ability, integrity, and fiber numbers of the AF.

Previous studies using brain mapping techniques, have reported that a patient's language ability, such as speech rate, informativeness, efficiency, fluency and naming ability, could be predicted at the chronic stage by the lesion load (a variable combining LV and lesion site) of the AF in the dominant hemisphere [42–45]. Moreover, several diffusion tensor tractography-based studies have demonstrated that language ability is related to the injury severity of the AF in the dominant hemisphere in stroke patients [20–24]. Breier *et al.* [20] have reported that speech-repetition ability was associated with the FA value of the AF in the dominant hemisphere in stroke (hemorrhage and ischemia) patients at the chronic stage. Kim *et al.* [21] observed that AQ values were higher in stroke (hemorrhage and ischemia) patients with preserved integrity of the AF in the dominant hemisphere than in those patients with a non-reconstructed or disrupted AF at the early stage after onset. Tak *et al.* [22] demonstrated that the AQ value was positively correlated with the TV value of the AF in the dominant hemisphere in chronic stroke patients and was higher if the integrity of the AF in the dominant hemisphere was preserved. Wang *et al.* [23] reported that speech-repetition disability within six months of onset was related to a low FA value for the AF in the dominant hemisphere in stroke (hemorrhage and ischemia) patients. Subsequently, Noh *et al.* [2021] reported that the AQ value and an AQ subset score (naming) were positively correlated with the FA value of the AF in the dominant hemisphere and the AQ subset scores for fluency, repetition and naming were negatively correlated with LV in stroke (hemorrhage and ischemia) patients at the early stage (within two months of onset) [24]. However, to the best of the author's knowledge, the present study is the first to demonstrate a relationship between language ability and LV and report a quantitative LV value helpful in discriminating discontinuation of the left AF. A relationship is also described between language ability and diffusion tensor tractography parameters of the AF in the dominant hemisphere in the early stage of putaminal hemorrhage.

4.1 Limitation and further research directions

Some limitations of this study should be considered. First, diffusion tensor tractography analysis is operator-dependent and thus can elicit false-positive and false-negative results, mainly due to areas of crossing fibers or the partial volume effect [46]. Second, although the language dominant hemisphere is assumed to be the left hemisphere, the functional localization of individual language dominance was not confirmed. Third, only a small number of subjects were enrolled in this study. Fourth, diffusion tensor imaging scanning was performed during the early stage of putaminal hemorrhage. If diffusion tensor imaging scanning was performed during the acute or subacute stages, those results might be useful when deciding on the necessity of surgical intervention to preserve the AF in the dominant hemisphere. Fifth, because the AF might consist of anterior, posterior and long segments, the location of regions of interest of the AF may be controversial [47]. Sixth, although the AF is related to language ability, there are other neural tracts such as the superior longitudinal fasciculus, uncinate fasciculus and extreme capsule related to language function that are affected by putaminal hemorrhage. Hence, further prospective studies that include assessment of the functional localization of the language dominance, large numbers of subjects, acute or subacute stage diffusion tensor imaging scanning, precise placement of region of interests of the AF, and additional neural tracts related to language ability are encouraged.

5. Conclusions

The use of diffusion tensor tractography allowed the conclusion that language disability was closely related to LV and to the severity of the AF injury in the dominant hemisphere in subjects with putaminal hemorrhage. In particular, the TV value of the AF in the dominant hemisphere fully mediated the effect of the LV on language ability. Additionally, following putaminal hemorrhage, an LV of approximately 30 cm^3 can differentiate a discontinuation of the AF in the dominant hemisphere. Results suggest that an LV cut-off value of 29.17 cm^3 may be clinically helpful in predicting AF discontinuation in the dominant hemisphere and when considering surgical intervention to remove a relevant hematoma. This suggestion is consistent with management guidelines for putaminal hemorrhage considering surgical intervention when the LV of putaminal hemorrhage is larger than 30 cm^3. Specifically, when the LV of putaminal hemorrhage is larger than 29.17 cm^3, the prognosis is for language disability.

Abbreviations

AF, arcuate fasciculus; LV, lesion volume; AQ, aphasia quotient; FA, fractional anisotropy; TV, tract volume; BH, Benjamini–Hochberg.

Author contributions

MJC and SHJ designed the research study. MJC performed the research. SHJ provided help and advice on the study. MJC analyzed the data. MJC and SHJ wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All participants signed a written informed consent beforehand, which abided by the Helsinki Declaration.

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Conflict of interest

The authors declare no conflict of interest.

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