Utility of Fractional Anisotropy in Cerebral Peduncle for Stroke Outcome Prediction: Comparison of Hemorrhagic and Ischemic Strokes

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Background: Diffusion-tensor fractional anisotropy (FA) has been used for predicting stroke outcome. However, most previous studies focused on patients with either hemorrhagic or ischemic stroke. The aim of this study was to assess the correlation between FA and outcome for patients with hemorrhagic stroke and those with ischemic stroke, and then compare their correlation patterns. *Methods:* This study sampled 40 hemorrhagic and 40 ischemic stroke patients from our previously published reports. Diffusion-tensor images were obtained on days 14-21, and FA images were generated, after which the ratio of FA within the cerebral peduncles of the affected and unaffected hemispheres (rFA) was calculated. Outcome was assessed using Brunnstrom stage (BRS), motor component of the functional independence measure (FIM-motor), and total length of hospital stay (LOS) at discharge from our affiliated rehabilitation hospital. The data were then compared between the hemorrhage and the infarct groups. Correlation analyses between rFA and outcome assessments were performed separately for both groups and then were compared between the groups. *Results:* The hemorrhage group exhibited significantly more severe BRS, longer LOS, and lower rFA than the infarct group. The correlations between rFA and outcome measures were all statistically significant for both the hemorrhage and the infarct groups. The correlation patterns for BRS and LOS were very similar between the hemorrhage and the infarct groups. However, such similarity was not evident for FIM-motor. *Conclusions:* FA in the cerebral peduncles may be used to predict extremity functions and LOS for both types of stroke. **Key Words:** Correlation—outcome—prognosis—ischemia, hematoma.

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Introduction

Stroke is a major cause of disability worldwide,[1] and rehabilitation is often prescribed to help reduce disability.[2] To maximize the efficacy of rehabilitation programs, outcome prediction is critically important.[3] Several methods for outcome prediction have been proposed. Most previous studies focused on clinical manifestations (e.g., motor deficits) and patient characteristics (e.g., age).[4-6] Other studies have also incorporated brain imaging data such as lesion size and site.[7-9] Owing to recent progress in neuroradiologic techniques, outcome prediction using noninvasive brain imaging is now available in clinical settings. Diffusion-tensor imaging (DTI) is one of these newly developed magnetic resonance imaging techniques, enabling in vivo assessment of the neural fiber integrity of white matter.[10] DTI has been used to predict outcome after stroke.[11,12] In particular, DTI is becoming a popular method of assessing the corticospinal tracts in relation to clinical manifestations such as extremity function and activities of daily living (ADL).[11,12]

To predict outcome after stroke, DTI affords 2 major methods for interpreting recorded parameter estimates: diffusion tensor tractography (DTT) and fractional anisotropy (FA) brain mapping (DTI-FA).[13] DTT performs fiber tracking and then outlines neural fiber integrity within the brain. The advantage of this modality is that it visualizes the targeted neural fiber bundle in 3-dimensional space.[12] This is especially useful when determining the pathway of approach for surgical removal of lesions, such as hematomas, while preserving intact neural fiber bundles.[14] However, DTT is susceptible to minute differences in fiber-tracking settings (e.g., seeds and thresholding).[15,16] Because of this limitation, DTT is not always used for quantitative estimation of neural fiber integrity. In fact, most previous DTT studies of stroke outcome prediction employed neural fiber bundle classifications such as "complete disruption," "partial disruption," and "sound integrity" of corticospinal tracts.[17-23]

Of the parameters obtained from DTI, FA values are proven indices of white matter axonal degeneration.[10] Although DTI-FA does not provide 3-dimensional images of neural fiber bundles, it allows simple quantitative estimation of neural fiber integrity indexed by FA values. Neural damage is often indexed using the relative FA decrease in the region of interest (ROI), such as cerebral peduncles, and has been used as an interval scale variable for stroke outcome prediction in previous studies.[11,12]

There are 2 major types of stroke pathology: hemorrhagic and ischemic. Most previous studies investigating the relationships between FA in the corticospinal tracts and outcome were generally conducted separately according to stroke type,[11] although some studies have evaluated both types of stroke as a whole.[23-25] However, no studies have systematically compared these 2 types of stroke in terms of the relationships between outcome and decrease in FA. Accordingly, the aim of this study was to assess the differences in reduced FA values relative to outcome measures between stroke patients with hemorrhage lesions and stroke patients with infarct lesions.

Methods

Study Samples

The work presented here is an extension of our earlier studies[26,27] and is based on re-analyses of previously reported study data. The study sample consisted of 40 patients with hemorrhagic stroke[26] and 40 patients with an ischemic infarct.[27] Patient demographics (e.g., age, lesion site, severity of hemiparesis) were detailed in the previous studies.[26,27] In addition, for this study, major comorbidities among stroke patients,[28] such as hypertension, diabetes mellitus, dyslipidemia, and arrhythmia, were recorded from medical charts. The patients were typically transferred to our hospital soon after the onset of symptoms and stroke was diagnosed using computed tomography (CT) or diffusion-weighted magnetic resonance imaging. All patients subsequently underwent physical, occupational, and speech therapy for a combined daily total of up to 180 minutes, according to the standard rehabilitation methods outlined in the Japanese Guidelines for the Management of Stroke.[29] To minimize variability arising from differences in prestroke health status and lesion site, the sample population was limited to first-ever stroke patients with supratentorial lesions (hemorrhage or infarct) who had been able to walk without assistance and had been functionally independent in ADL before their stroke. To minimize variability arising from differences in the therapeutic rehabilitation regimen, this study used data from only those patients who were transferred to our affiliated long-term rehabilitation facility (Nishinomiya Kyoritsu Rehabilitation Hospital) to receive inpatient rehabilitative care for at least 1 month.

The study data were collected during the period between December 2009 and December 2014. The Ethics Committee of Hyogo College of Medicine approved the study protocol, and patients (or their designated proxies, when necessary) provided written informed consent.

DTI Acquisition

DTI was performed 14-21 days after admission using a 3.0 T magnetic resonance scanner (Trio; Siemens AG, Erlangen, Germany) with a 32-channel head coil. Details of the DTI acquisition protocol were reported in our previous study.[30] In the DTI protocol, 12 images with noncollinear diffusion gradients ($b = 1000\ s/mm^2$) and 1 non–diffusion-weighted image ($b = 0\ s/mm^2$) were acquired using a single-shot, echo-planar imaging sequence. In total, 64 axial slices were obtained per patient. The field of view was 230.4 mm × 230.4 mm, the acquisition matrix was 128 × 128, and gapless slice thickness was 3 mm. Echo time was 83 ms and repetition time was 7000 ms.

Outcome Measures

Brunnstrom stage (BRS)[31] is commonly used by Japanese rehabilitation therapists[29] and was used in this study to assess post-stroke motor impairments of the upper and lower extremities on the affected side. Recovery of the affected extremities was evaluated by associated reactions and flexion and extension synergy patterns on a 6-point scale from severe (1) to normal (6). Conventionally, BRS is used for separate functional evaluation of the proximal (shoulder, elbow, or forearm) and distal (hand or finger) upper extremity, as well as the entire lower extremity, and its reliability and validity are well established.[32]