Relationship Between Successful Extracranial-Intracranial Bypass Surgeries and Ischemic White Matter Hyperintensities

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■ BACKGROUND AND PURPOSE: **Few studies have described regression of white matter hyperintensities (WMHs); however, no studies have described their recurrence or fluctuation. Thus, we aimed to study the course of WMHs on fluid-attenuated inversion recovery (FLAIR) magnetic resonance image (MRI) after extracranial-intracranial (EC-IC) bypass surgery and its correlation with the clinical outcome.**

■ METHODS: **We enrolled perioperative FLAIR MRIs of 12 patients with WMHs who underwent EC-IC bypass surgeries because of ischemic-vascular stenosis with postoperative improvement of the cerebral blood flow confirmed by ^{123}I-iodoamphetamine single-photon emission computed tomography. Correlation between WMHs and cerebral blood flow was confirmed by perioperative single-photon emission computed tomography and diffusion-weighted imaging MRI. The WMHs were assessed visually with meticulous volumetric grading. Depending on postoperative changes among different grades, the WMHs course was determined to be improved, fluctuating, worsened, or unchanged. A statistical analysis was performed on the course of WMHs over time.**

■ RESULTS: **Imaging analysis was done with FLAIR MRI in 12 patients. The course of WMHs over time was 41.7% improvement, 33.3% fluctuation, 16.7% unchanged, and 8.3% worsening of the deep WMHs. After unilateral bypass surgery, 80% of the improved WMHs occurred bilaterally. Among patients with improved clinical outcomes, 16.7% showed improvement and 33.3% showed fluctuation, whereas in patients with unchanged clinical outcomes, 25% showed improvement of their WMHs on follow-up FLAIR MRIs.**

■ CONCLUSIONS: **This study might be considered the first step to find a relationship between successful EC-IC bypass surgeries and the course of ischemic WMHs. It could also open the door for further studies to make more solid conclusions.**

INTRODUCTION

White matter hyperintensities (WMHs) often are seen on magnetic resonance imaging (MRI) of elderly people and have been related to cognitive decline.[1] WMHs frequently are observed on fluid-attenuated inversion recovery (FLAIR) T2 MRI which is considered as a marker for ischemic lesions.[2] They are attributed mainly to degenerative small-vessel disease (SVD) and, once present, considered progressive, irreversible areas of demyelination, gliosis, and loss of axons.[2] Few reports, however, have described the regression of WMHs.[3-8] Therefore, the change of WMHs over time may be dynamic[3] and can be attenuated after ischemic stroke.[4] Successful surgical brain revascularization can restore oxygen extraction fraction to normal levels,[9] improve ischemic WMHs,[6] and reverse cerebral cortical thinning.[10] In the present study, we performed a retrospective study to investigate WMHs in patients who underwent bypass surgery for cerebral ischemia.

Key words
- Cerebral ischemia
- EC-IC bypass
- FLAIR MRI
- Fluctuation
- White matter hyperintensities

Abbreviations and Acronyms
CBF: Cerebral blood flow
EC-IC: Extracranial-intracranial
FLAIR: Fluid-attenuated inversion recovery
ICA: Internal carotid artery
IMP SPECT: ^{123}I-iodoamphetamine single-photon emission computed tomography
MRI: Magnetic resonance imaging
PAS: Period after surgery
PVH: Periventricular hyperintensity
SPECT: Single-photon emission computed tomography
SVD: Small-vessel disease
TIA: Transient ischemic attack
WMH: White matter hyperintensity

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MATERIALS AND METHODS

Ethical Statement

Approval was obtained by the institutional review board of Shinshu University School of Medicine under registration number 3208. Consents were obtained from all patients who participated in this study.

Patients

For this retrospective observational study, the aim was to study the course of WMHs on FLAIR MRIs after extracranial-intracranial (EC-IC) bypass surgery and its correlation with the clinical outcome. The Carotid Occlusion Surgery Study (COSS)[9] was reviewed carefully. Herein, the surgical indications of our patients were transient ischemic attacks (TIAs) or ischemic stokes attributed to ischemic vascular stenosis or occlusion of the internal carotid artery (ICA) or its territories in cases who were considered good candidates for EC-IC bypass.

Inclusion Criteria. Perioperative FLAIR MRIs (Table 1) of patients who underwent successful EC-IC bypass surgeries as the result of ischemic-vascular stenosis or occlusion with postoperative improvement of the cerebral blood flow (CBF) confirmed by ^{123}I-iodoamphetamine single-photon emission computed tomography (IMP SPECT) at Shinshu University Hospital were studied. Correlation between WMHs and CBF was confirmed by perioperative IMP SPECT, diffusion-weighted imaging MRI, and cerebral catheter angiography. All patients except the last 3 cases (Table 1) were followed for more than 2 years. Those recently 3 treated patients were followed up 1.5, 1.4, and 1.3 years, respectively.

Exclusion Criteria. Patients without preoperative documented WMHs or patients without postoperative FLAIR MRIs were excluded from this study. As the aim of our study was to assess the relationship between successful EC-IC bypass surgeries and ischemic WMHs; therefore, other revascularization procedures (such as carotid endarterectomy) were not eligible.

MRI Protocol and Volume Measurement

With a Siemens MAGNETOM Trio 3.0 Tesla MRI Scanner (Siemens Healthcare Headquarters, Erlangen, Germany), FLAIR images were obtained via a fast-spin echo sequence having a repetition time/echo time of 10,000/126 msec, inversion time of 2601.4 msec, echo-train length of 16, provided pixel 1.3×1.3, a field-of-view of 240×168 mm, flip angle of 180°, a 320×240 matrix, 21 slice (5 mm) with 1-mm gap with voxel size $= 1.0 \times 1.0 \times 5$ mm, and study time of 3 minutes and 30 seconds.

As usual,[6] based on FLAIR MRI with DICOM (i.e., Digital Imaging and COmmunication in Medicine) viewer format, WMHs was assessed visually (modified Fazekas grading)[11] to study their course, which might have improved (defined as disappearance and/or changed from a higher to a lower grade), worsened (defined as changed from a lower to a higher grade), fluctuating (defined as fluctuation between different grades, recurrence or new lesions), or unchanged. To avoid subjective errors during WMHs grading, the volumetric threshold for each grade was determined and hyperintensities or changes less than 0.25 mL were excluded.

A scaling evaluation table was designed to be fulfilled by raters. Regions of interest were selected, and definite visible changes and the course of the WMHs were determined by 3 experienced independent raters (neurosurgeons), one of whom was blinded to the patients' clinical data. The WMHs were defined on a slice-by-slice basis. The WMH volumes were calculated by multiplying the (slice thickness + gap) term by the total lesion area. A change of WMHs was interpreted as 1) improvement, 2) worsening, 3) fluctuation, and 4) unchanged. Detailed course of both types of WMHs (deep WMHs and periventricular hyperintensities [PVHs]), including all grades, were analyzed separately to detect which was more vulnerable to show changes. There was a considerable difference in the WMH volume when we compared the preoperative, postoperative, and the follow-up FLAIR MRI.

Evaluation of Regional CBF on IMP SPECT

First, regions of interest were set to the markedly hypoperfused regions (defined as marked decrease in radioactive uptake) on the preoperative and to the same regions on the postoperative IMP SPECT studies, respectively. Then, the adequate postoperative restoration of the regional CBF (defined as improvement in radioactive uptake) and perfusion levels were examined visually by experienced raters independently, according to the standardized color scale (see Figures 2 and 3).

Data Analysis

When the IBM SPSS statistics database was used (IBM Corp., Armonk, New York, USA), the interobserver agreement (kappa value) was 0.886 between the first and second raters, 0.774 between the first and third raters, and 0.888 between the second and third raters. The reliability (interclass correlation coefficient) was 0.929 among all raters, 0.986 between the first and second raters, 0.832 between the first and third raters, and 0.860 between the second and third raters.

Clinical Data

Preoperative clinical presentations and the postoperative clinical outcome were obtained by the review of medical records.

RESULTS

Baseline Characteristics

Between January 2008 and January 2015, a total of 12 patients who fulfilled our inclusion criteria were enrolled. Their age ranged from 43 to 75 years, and the mean was 66.9 years; 9 patients were men. The most common clinical presentation was TIAs (46%), followed by speech disorder (15%) and equal presentation for monoparesis (8%), hemiplegia (8%), memory disorder (8%), cognitive disorder (8%), and asymptomatic (7%). The vascular stenosis or occlusion was mainly on the left side in 7 cases (58%), and its location was cervical ICA in 8 cases (67%), ICA in 3 cases (25%), and middle cerebral artery in 1 case (8%) (Chart 1). Postoperatively, imaging time-interval was divided into 3 periods after surgery (PAS): PAS-1 (from postoperative day 1 up to 3 months), PAS-2 (from postoperative fourth month up to the end of the first year), and PAS-3 (from postoperative second year up to