What Makes New Ischemic Lesions Symptomatic after Aortic Valve Replacement?

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Background: Acute cerebral infarctions on diffusion-weighted magnetic resonance imaging (MRI) are common after cardiothoracic surgery. However, most are asymptomatic and we aimed to identify features associated with clinical stroke symptoms. *Methods:* Patients over 65 years of age undergoing surgical aortic valve replacement (AVR) for calcific stenosis were prospectively recruited (N = 196). All patients underwent neurological evaluation preoperatively and on postoperative days 1, 3, and 7, and MRI on planned postoperative day 5. Among those with new postoperative DWI lesions, we performed univariate and multivariable analyses to identify clinical, demographic, surgical, and imaging factors associated with clinical stroke symptoms. *Results:* Of the 129 patients who completed a postsurgical MRI, 79 (61%) had DWI lesions and 17 (21.5%) of these had new stroke symptoms concordant with the infarct distribution. In an exploratory multivariable analysis, focal neurological symptoms were associated with increased age, a longer bypass duration, and a larger pre-existing lesion burden on fluid-attenuated inversion recovery. Limiting the analysis to the 61 patients with analyzable volume and location data, logistic regression failed to identify any location-related determinant of symptomatic lesions. *Conclusions:* New DWI lesions are common after AVR, but most are asymptomatic. Patients are more likely to have symptoms with longer bypass durations, increasing age, and larger pre-existing lesion burdens. **Key Words:** Stroke—aortic valve—surgery—diffusion-weighted MRI.

Introduction

Stroke is a feared complication of cardiothoracic procedures including aortic valve replacement (AVR).[1-4] Diffusion-weighted magnetic resonance imaging (MRI) is the gold standard for the radiological diagnosis of stroke.[5] However, only a portion of new diffusion-weighted imaging (DWI) lesions identified after AVR are associated with clinical manifestations of stroke and many are silent in the acute setting.[3] What makes lesions symptomatic remains unclear. Therefore, we sought to determine the attributes of clinically evident stroke in a prospective cohort of patients who underwent surgical AVR.

Methods

Patients undergoing surgical AVR at 2 academic centers (N = 196) were enrolled in a prospective cohort study as

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previously described.[3] Patients undergoing transcatheter aortic valve implantation and patients with recent stroke or TIA were excluded. All patients underwent neurological exams preoperatively and on postoperative days 1, 3, and 7 by a neurologist. All patients were scheduled for brain MRI at postoperative day 5 as previously detailed.[3]

We compared baseline characteristics, surgery, and imaging data between symptomatic and asymptomatic patients with new DWI lesions. The symptomatic state was determined by the presence of focal neurological symptoms and signs consistent with the distribution of the DWI lesion on postoperative days 1-7 as determined by a neurologist and graded with the National Institutes of Health Stroke Scale (NIHSS). The NIHSS score was used to quantify the deficit, but was not used to determine whether or not a patient was symptomatic. Symptomatic status was based on the clinical judgment of the neurologist evaluating the patient. Furthermore, all symptomatic strokes were further reviewed and adjudicated by 2 other stroke neurologists with access to MRI images to confirm that diagnosis.

MRI studies were analyzed by experienced neuroradiologists who were blinded to the clinical state. Studies were analyzed with a standardized pipeline approach.

The T1-weighted scan of each subject was preprocessed for the correction of intensity inhomogeneities and brain extraction.[6] White matter lesions, which are typically characterized by a hyperintense fluid-attenuated inversion recovery (FLAIR) signal, were segmented by applying a supervised learning-based multimodal segmentation method on the FLAIR and T1-weighted images of each subject.[7] DWI lesions were manually segmented by 2 trained raters on the DWI images, which were linearly aligned to the T1-weighted image of each subject using FMRIB Software Library (FSL) tools.[8] A multi-atlas label fusion-based segmentation method[9] was used for partitioning the brain into 154 anatomic regions of interest (ROIs), which were organized within a hierarchical structure to allow derivation of volumetric measurements in various resolution levels. Briefly, the brain was first divided into right and left hemispheres; each hemisphere was then divided into lobes; each lobe was then divided into gyri; and each gyrus was further divided into subzones. Within each ROI, white matter lesion and DWI lesion volumes, as well as DWI lesion counts, were calculated. Finally, binary DWI lesion masks were transferred to a common template space (e.g., a single T1-weighted template image in standard Montreal Neurological Institute MNI space) through nonlinear registration of the subject T1 image to the template T1 image using deformable registration via attribute matching and mutual-saliency weighting.[10]

Statistical evaluations were performed with SPSS 22 (IBM, Armonk, New York). Continuous variables were compared with the Student *t*-test, and categorical variables were compared with the chi-square test. We next performed exploratory logistic regressions, first including all variables that yielded a P value of <.05 in the univariate analysis to identify independent factors associated with the symptomatic state. In a separate model, age and other prominent determinants of increased risk for stroke, including prior stroke or atrial fibrillation, were also added to the analysis. With the subset of 61 patients with complete data sets that allowed for adequate brain mapping, we next used a separate model for logistic regression assessing the link between the lesion location and the stroke symptoms after adjusting for lesion load on FLAIR and DWI and the number of new lesions on DWI imaging.

Results

Of the 196 patients enrolled in the study, 129 (66%) completed a postoperative MRI scan and were included in this analysis. The most common reasons for the inability to obtain an MRI were patient unwillingness or medical instability (see details in Reference 3). Compared with patients who did not have an MRI, those who underwent MRI less often had ischemic heart disease (64% versus 82%, $P = .01$) and previous strokes (9% versus 19%, $P = .04$) and also had shorter bypass durations (113 ± 44 versus 129 ± 47 minutes; $P = .01$). However, age ($75.3.0 \pm 6.0$ versus 76.7 ± 6.4), gender (women 33% versus 42%), and all other vascular risk factors and intraoperative variables did not differ between the groups.[3]

New DWI lesions were found on 79 of 129 patients (61%). Among these patients, we compared symptomatic (n = 17, 21.5%) to asymptomatic patients (n = 62, 78.5%). For those who developed symptoms, the symptoms appeared early after surgery (mean 3 ± 3 days) and were relatively mild (median NIHSS score 2, range 1-17). The most common symptoms were motor impairment (47%) followed by consciousness abnormalities (46%) and dysphasia (20%). Among those with DWI infarcts, the presence of clinical symptoms was associated with longer hospital stays (16 ± 12 versus 10 ± 4 days, $P < .001$).

Baseline demographic, clinical, and radiological data are presented in Tables 1-3, respectively. Symptomatic lesions were associated with longer times on bypass ($P = .006$) and smaller drops in arterial pressures during surgery ($P = .001$). Symptoms were more frequent in patients who underwent concomitant procedures during surgery ($P = .047$) compared with those who had AVR only. Symptomatic patients had a higher number of new DWI lesions ($P = .012$), higher DWI lesion volumes ($P = .002$), and a higher old lesion burden on FLAIR ($P = .028$).

We next sought to explore whether the lesion location was associated with symptoms. This analysis included 61 patients (16 symptomatic) who had adequate MRI data for location and volumetric assessments. The main reason for excluding patients from this analysis was inadequate T1 imaging not allowing for a full transfer of the DWI mask to the T1 space. This analysis (Fig 1) showed that symptomatic lesions more frequently involved the