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Brain Magnetic Resonance Imaging Abnormalities following Off-Pump Cardiac Surgery

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ABSTRACT

Background: Neurological and cognitive deficits are known complications after coronary artery bypass surgery (CABG) and are believed to be secondary to brain ischemia. Diffusion-weighted magnetic resonance imaging (DW-MRI) of the brain is especially sensitive and can depict ischemic areas that may not be evident clinically or with conventional MRI. Abnormalities found at brain MRI following CABG performed with cardiopulmonary bypass (ie, on pump) have been reported, but data are limited for CABG performed without use of cardiopulmonary bypass (ie, off pump). The objective of this study was to determine the rate of DW-MRI detection of brain lesions following off-pump CABG.

Methods and Results: Sixteen patients consecutively undergoing off-pump CABG underwent DW-MRI prior to and after surgery. A neuroradiologist blinded to patient data coded the location and size of lesions. Neurological function was assessed with the National Institutes of Health Stroke Scale. Five (31%) of the patients had new focal ischemic lesions found at postoperative DW-MRI. Risk factors for postoperative brain ischemic lesions were similar between patients with and those without lesions found at DW-MRI. No patient had a definite clinical stroke after surgery.

Conclusions: Ischemic lesions found at DW-MRI are seen after off-pump CABG at a rate similar to that reported for CABG with cardiopulmonary bypass. This finding suggests that these lesions are not totally due to cardiopulmonary bypass. Further prospective clinical studies would be helpful for determining which factors are causally related to brain ischemia following CABG.

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INTRODUCTION

In 1998 more than 700,000 open-heart surgical procedures were performed in the United States [American Heart Association 2000]. In as many as 80% of patients, early neuropsychological impairment may follow cardiac surgery requiring cardiopulmonary bypass [Shaw 1987a]. As many as 60% of these patients have impairment when examined 6 months or more after the procedure [Shaw 1987b]. A study in 2001 showed that although the percentage of patients with a deficit declines initially, an increase is seen at long-term follow-up evaluation 5 years after the procedure [Newman 2001]. The incidence and duration of deficits have been noted to vary in different studies. This fluctuation may be due to variation in study design, type and number of cognitive tests, timing of tests, and definition of cognitive dysfunction [Borowicz 1996].

Although there have been studies of cognitive decline following cardiac surgery, the etiology of this decline is not clear. Ischemic damage caused by microemboli during cardiopulmonary bypass is suspected to be the cause, but there is little documented evidence of ischemic damage in these patients [Brown 2000]. Other suspected causes include low mean arterial pressure and problems with pH/temperature management [Mills 1995]. Cognitive impairment may be reduced by a number of measures, including use of extra arterial line filters and replacement of bubble by membrane oxygenators. However, even with these measures there is still a high incidence of cognitive decline. Evidence that cognitive decline following cardiac surgery with cardiopulmonary bypass is directly related to bypass has been provided in results of studies that showed a higher rate of cognitive decline in cardiac surgery patients compared with other surgical patients [Shaw 1987a]. Risk factors for late cognitive decline (ie, at 5 years) were older age, lower level of education, and cognitive decline at discharge [Newman 2001]. In addition to cognitive decline, clinical stroke also may be seen after cardiac surgery with cardiopulmonary bypass. Stroke, although less frequent than cognitive decline, was reported in as many as 9% of patients in a large, multiinstitutional, prospective observational study [Almassi 1999]. The many causes of clinical stroke in these patients include atrial fibrillation, which occurs frequently after cardiac surgery and is a risk factor for stroke. In addition, increasing age, hypertension, history of prior stroke, and time spent on cardiopulmonary bypass have been found to increase the risk of postoperative stroke [Almassi 1999]. Coronary artery bypass surgery without cardiopulmonary bypass (off-pump CABG) is being performed in many cases. It is hoped that performance of off-pump CABG will avoid the cognitive deficits and stroke attributed to cardiopulmonary bypass. There are, however, few data on cognitive and neurological deficits following off-pump CABG [van Dijk 2001].

Many studies have investigated cognitive decline following cardiac surgery, but few studies have been performed with routine neuroimaging examinations to look for evidence of ischemic damage to the brain [Baker 2000]. Magnetic resonance imaging (MRI) is a very sensitive test for imaging ischemic areas of the brain [Prichard 1999]. MRI with diffusion weighting (DW-MRI) is especially sensitive to acute ischemic damage. DW-MRI depicts areas of abnormal water movement resulting in increased (bright) signal intensity. It is believed that this abnormality of water movement occurs very soon after the onset of ischemia and persists for several days to weeks after the ischemia. With DW-MRI it may be possible to detect ischemic areas that are not evident at clinical examination, on computed tomographic scans, or at conventional MRI. It is also possible to use DW-MRI to differentiate acute and chronic areas of ischemia [Provenzale 1999].

In 2 studies with results reported in 2002, authors evaluated DW-MR images obtained after on-pump CABG. Bendszus et al [2002] found new ischemic lesions after on-pump CABG in 9 (26%) of 35 patients. Ischemic lesions were not correlated with neuropsychological impairment. However, there was a correlation between metabolic neuronal disturbance at MR spectroscopy and neuropsychological impairment. In a study at Johns Hopkins University, Restrepo et al [2002] found new ischemic lesions after on-pump CABG in 4 (31%) of 13 patients. In contrast to the findings of Bendszus et al [2002], the number of new ischemic lesions correlated with neuropsychological impairment.

There are no published data on ischemic lesions found at MRI after off-pump CABG. The purpose of this study was to use the DW technique to determine the rate of detection of MRI abnormalities in patients undergoing off-pump CABG.

MATERIALS AND METHODS

General

Patients scheduled for nonemergency off-pump CABG for symptomatic coronary artery disease were recruited from the Main Line Health Lankenau Hospital. In the previous year approximately 600 CABG operations had been performed at Lankenau. At Lankenau Hospital more than 90% of cardiac surgery with CABG is done off pump (without cardiopulmonary bypass).

We began recruiting patients in January 2003. All patients gave written informed consent, and the study was approved by the hospital Institutional Review Board. Demographic data and medical history were collected at baseline. Data on all cardiac surgery patients are routinely entered into the Society of Thoracic Surgeons National Cardiac Surgery Database. Neurological and neuropsychological evaluations were performed within 1 week prior to cardiac surgery and 1 to 4 months following surgery. MRI examination was performed within 1 week prior to and 4 to 14 days after surgery.

Operative Technique

All subjects underwent off-pump CABG with use of a vacuum system for access and stabilization of the heart. At our institution epiaortic ultrasound is routinely performed in patients undergoing aortic anastomosis to verify that are no abnormalities in the region of the anastomosis. A partial aortic clamp is used routinely for the proximal aortic anastomosis, but on occasion, when there is believed to be significant aortic disease, an anastomotic device may be used to obviate use of a partial aortic clamp.

Neurological Testing

A certified examiner obtained a score for the National Institutes of Health Stroke Scale. This standardized score, which is obtained with a neurological examination, has been shown to be sensitive and reliable. The scale was specifically designed for use in stroke research studies [Lyden 1994].

Neuropsychological Testing

In selection of the battery of neuropsychological tests to be performed, a number of considerations were taken into account as outlined previously in "Statement of Consensus on Assessment of Neurobehavioral Outcomes after Cardiac Surgery" from the Conference on Cardiopulmonary Bypass [Murkin 1995]. There is the potential that differing lesion locations would yield differing cognitive dysfunctions (eg, memory, attention and concentration, language, perception, motor performance, visual fields) such that no single test would be able to detect all of the possible deficits. It is crucial that tests be sensitive and reliable and that floor and ceiling effects be avoided. It is therefore recommended that a battery of tests be used to detect cognitive dysfunction following cardiac surgery. In view of the time constraints and the physical limitations of the patient in the context of a cardiac operation, we planned to limit testing to approximately 1 hour. Although the number of tests was limited, we covered an appropriate array of cognitive domains. When possible, we included tests with parallel forms. Because we were performing multiple tests over time, a practice effect was possible and was taken into account in the choice of tests and in the analysis. Testing was performed by a qualified and trained individual blinded to other results and in a standardized manner in a controlled environment. Because mood can influence cognitive function, mood was also assessed as part of the cognitive testing.

Neuropsychological function was tested with the Information and Digit Symbol subtest of the Wechsler Adult Intelligence Scale III, Beck Anxiety Inventory, Beck Depression Inventory, Hopkins Verbal Learning Test, Trail Making Test (parts A and B), Digit Symbol Test, New Adult Reading Test, Controlled Oral Word Association Test, Purdue Pegboard, target detection (cancellation) task, and Brief Test of Attention. For deficit definition, an SD unit for each test was computed from all preoperative scores. A deficit occurred in a test when a patient's postoperative score had dropped 0.5 SD from the preoperative score. For tests with a number of subtest scores, at least 1 subtest had to have significant deterioration for that test result to be considered in deficit. This definition has been used previously in research on cognitive decline following cardiac surgery [Restrepo 2002].

Stroke Diagnosis

The stroke diagnosis was made by G.F. with independent confirmation by the collaborating investigator (E.K.), both using standardized criteria [Johnson 1995]. G.F. and E.K. are board-certified neurologists with expertise in stroke diagnosis.

MRI Methods

MRI examinations were performed in the week prior to surgery and 4 to 14 days after surgery. The images were obtained with a 1.5-T MR unit (Intera; Philips Medical Systems, Andover, MA, USA) and included 2 sequences (fluid-attenuated inversion recovery [FLAIR] and DW). The FLAIR sequence was obtained with an imaging time of 2:36 minutes, 5-mm axial interleaved sections, 256 × 256 matrix, 23-cm × 23-cm field of view, 9000/140 ratio of repetition time to effective echo time (TR/TE_{eff}), 2500 inversion time, and 32-kHz bandwidth. For the DW sequence we used spin-echo multisection single-shot echoplanar imaging sequences with a pair of diffusion gradients centered on the 180-degree pulse with 5-mm axial section thickness, 1.0-mm gap, 256 × 128 matrix, 23-cm × 23-cm field of view, and 2825/95 TR/TE_{eff}. Twenty-two sections were acquired with baseline T_2 acquisition $b = 0$ and $b = 1000$ (diffusion gradient G = 22 mT/m, active during 31 milliseconds). The diffusion gradients were successively and separately set in the 3 orthogonal directions for a total DW acquisition time of 11 seconds to cover the entire brain. Trace images were generated with a dedicated software program.

By performing MRI both prior to and after surgery we were able to identify any acute ischemic lesions that might have been present before the surgery and to take these lesions into account in the analysis. Location and size of lesions were coded by a neuroradiologist (A.C.) blinded to the findings at the neuropsychological and neurological examinations.

Statistical Methods

Descriptive statistics were used to characterize demographics. Analysis of the relation between risk factors (except age) and development of new lesions found at MRI was conducted with chi-square and Fisher exact tests. Because the other 2 risk factors of interest (age and number of diseased vessels) were continuous variables (rather than nominal coded variables), point biserial correlations were conducted to determine their relation to the presence of new lesions.

RESULTS

Enrollment into the preliminary portion of the study began in January 2003, and 27 patients gave written consent for the study. Of the 27 patients, 7 withdrew consent prior to MRI (1 because of claustrophobia). One patient could not undergo MRI because of the presence of a pacemaker, and another patient because of a history of metal fragments in the eye. Two patients refused follow-up MRI (1 because of claustrophobia and another because of shortness of breath). The baseline characteristics of the 16 patients who underwent postoperative MRI are listed in the Table. The mean age of the subjects was 69 years. Twelve patients had 3-vessel coronary artery disease. All 16 patients underwent off-pump CABG. Partial aortic clamping was used in 14 patients. One patient received only an internal mammary artery graft, and in 1 patient the aortic anastomosis was performed with an anastomotic device, so partial aortic clamping was not used for these 2 patients. The number of distal anastomoses ranged from 2 to 5 (mean, 3.6), and the number of proximal anastomoses ranged from 0 to 3 (mean, 1.4).

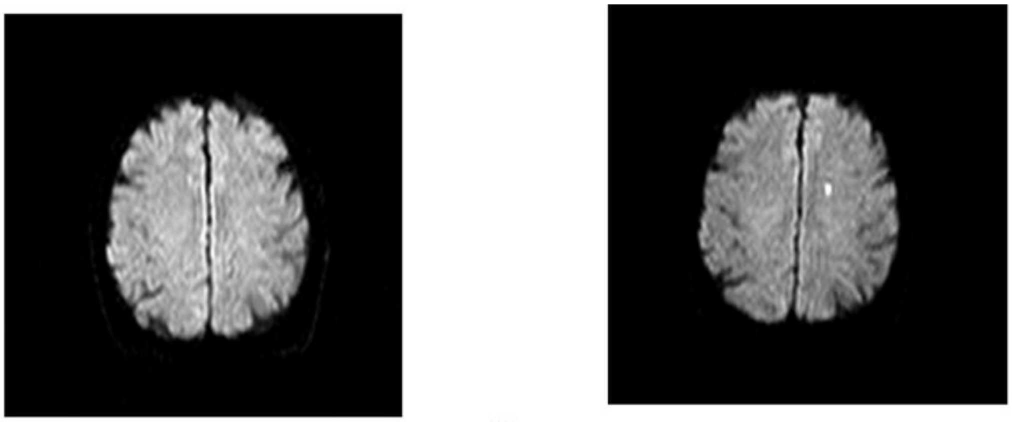
Baseline Characteristics of 16 Study Patients

Characteristic	n (%)
Sex	
Female	2 (13)
Male	14 (88)
Hypertension	12 (75)
Hyperlipidemia	8 (50)
Diabetes	8 (50)
Cerebrovascular disease	2 (13)
Smoking	
Current	2 (13)
Former	8 (50)
Prior myocardial infarction	9 (56)
Canadian Cardiovascular Society class III/IV	9 (56)
New York Heart Association class III/IV	11 (69)

Five (31%) of the 16 patients enrolled for follow-up MRI had acute ischemic lesions found at MRI after CABG. No patient had had a clinically evident stroke. These lesions were small, the size ranging from 2 to 8 mm (Figure). The lesions were multiple in 3 patients and single in 2 patients. Lesions were found in both the anterior and the posterior cerebral circulation. None of the baseline characteristics were associated with risk of postoperative development of ischemic lesions. However, there did appear to be a trend in favor of greater likelihood of ischemic brain lesions in patients with multiple proximal anastomoses performed during surgery. Four of the 5 patients with ischemic brain lesions received multiple proximal anastomoses, and only 3 of 11 patients without ischemic brain lesions received multiple proximal anastomoses.

Eight of the 16 patients had atrial fibrillation following CABG (1 patient had preexisting atrial flutter). In 2 of those 8 patients, an acute ischemic lesion was found at postoperative MRI.

In 2 of 15 patients who underwent MRI prior to CABG, an acute ischemic lesion was found on pre-CABG images. One of these patients underwent cardiac catheterization 2 weeks and the other 1 day prior to pre-CABG MRI. Neither patient had a clinical stroke as a result of the cardiac



Diffusion-weighted magnetic resonance image of the brain before (left image) and after (right image) coronary artery bypass grafting in a representative subject. A new ischemic lesion (right image, small area of increased signal intensity, white spot) was found on the left side of the brain at follow-up imaging.

catheterization. In the patient who underwent cardiac catheterization 2 weeks before CABG, the finding that the restricted diffusion lesion subsequently was found with the use of FLAIR sequences for postoperative MRI suggests that the cardiac catheterization was not acutely responsible for this lesion.

Twelve subjects underwent neuropsychological testing both before and after CABG. All but 1 subject had a decline of 0.5 SD in at least 1 test result at follow-up evaluation 1 to 4 months after surgery.

DISCUSSION

Our preliminary results with detection of acute ischemic lesions at DW-MRI following off-pump CABG are similar to those of 2 studies of on-pump CABG [Bendszus 2002, Restrepo 2002]. Our results suggest that ischemic lesions are not solely related to the use of cardiopulmonary bypass but can be related to other factors related to surgery, possibly manipulation of the aorta during the procedure, which can lead to embolism. Lund et al [2003] randomized patients to off-pump or on-pump CABG and performed transcranial Doppler ultrasonography. The investigators found the number of microemboli detected in off-pump CABG (16.3 microemboli [range, 0-131]) was significantly lower than the number detected in on-pump CABG (90.0 microemboli [range, 15-274]). With off-pump surgery, emboli were infrequent except in association with release of the partial aortic clamp. In 2 of the 3 off-pump patients who underwent only internal mammary artery grafting, in which aortic clamping was not performed, no emboli were detected during surgery. These findings support a relation between aortic clamping and cerebral embolism, which can lead to cerebral ischemia.

The relation between cerebral ischemic lesions found at MRI and neuropsychological outcome is less clear. The sample sizes in our study and the prior 2 studies of on-pump CABG were small, and the follow-up period was short. Therefore it is not clear whether there is a significant correlation between the presence of ischemic lesions at MRI and long-term neurocognitive outcome. This area is undoubtedly important for further study.

A limitation of our study was the small sample size, but we were able to demonstrate that a significant number of patients undergoing off-pump CABG will develop ischemic lesions that are found at MRI. Because there was a delay of several days from the time of surgery to MRI, the cerebral ischemia could have occurred after rather than during surgery. At least for atrial fibrillation, which is a risk factor for stroke following surgery, this did not appear to account for most of the ischemic lesions we saw. In addition, our theory that manipulation of the aorta can cause these ischemic lesions does not require that cerebral ischemia occur during the surgery, because intimal tears resulting from aortic manipulation can lead to thrombus formation and subsequent embolism even several days after the operation. There are limits in the resolution of the DW-MRI, causing us to miss ischemic areas less than 2 mm. This limitation may lead to underestimation of total ischemic brain damage.

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