# Early Operation in Patients With Mitral Valve Infective Endocarditis and Acute Stroke Is Safe

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*Background.* **To determine if preoperative embolic stroke is associated with an increased risk of postoperative stroke among patients undergoing early operation for mitral valve (MV) infective endocarditis (IE), we compared outcomes among patients presenting with and without acute stroke.**

*Methods.* **From 2003 to 2015, 243 consecutive patients underwent surgery for active MV IE. Patients were categorized into 2 groups: 72% (174 of 243 patients) with no preoperative acute stroke (clinical, radiographic or both) and 28% (69 of 243 patients) with stroke. Both preoperative and postoperative strokes were confirmed in all patients with brain computed tomography or magnetic resonance imaging and comprehensive examination by a neurologist.**

*Results.* **Among patients presenting with stroke, 33% (23 of 69 patients) were asymptomatic and had only positive imaging findings. The median time from admission to operation was 5 days. The overall rate of new postoperative stroke was 4% (10 of 243 patients). The rate of postoperative stroke was not different between the 2 groups: 4% (7 of 174 patients) among patients with no preoperative stroke and 4% (3 of 69 patients) with stroke ($p = 0.9$). One patient developed a hemorrhagic conversion of an acute infarct. Operative mortality was 7% (13 of 174 patients) among patients with no preoperative stroke and 7% (5 of 69 patients) among patients with stroke ($p = 0.9$).**

*Conclusions.* **MV surgery for IE and acute stroke can be performed early with a low risk of postoperative neurologic complications. When indicated, surgical intervention for MV IE complicated by acute stroke should not be delayed.**

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Infective endocarditis (IE) is the indication for operation in 5% of patients having mitral valve (MV) surgery in the United States [1]. The incidence of IE has remained high and despite introduction of new generation of antibiotics and aggressive surgical intervention, the in-hospital mortality rate is between 20% and 30% [2–4].

Neurologic complications in patients presenting with MV IE are the most common extracardiac complications of IE [5]. Clinical stroke is diagnosed in 25% to 30% of patients with MV IE [4]. There is evidence of acute brain embolism as many as 50% of patients presenting with MV IE undergoing preoperative computed tomography (CT) scan [6]. The presence of embolic cerebral injury in patients with MV IE makes management challenging, particularly when indications for operation are present. Current guidelines recommend delaying MV surgery for at least 4 weeks from the time of stroke (Class IIa, level of evidence C) [7]. The rationale behind delaying operation is that the blood-brain barrier is disrupted in an ischemic area, and therefore the risk of bleeding with anticoagulation or blood pressure variation is increased. Cerebral vascular autoregulation is dysfunctional and patients are predisposed to blood extravasation [8]. Furthermore, the ischemic area can expand with hypoperfusion during cardiopulmonary bypass [8–10]. Although greatly feared, hemorrhagic conversion of an ischemic embolic lesion in the setting of IE has been found to be rare [6, 11, 12], with reported rates between 0% and 2% [4, 6, 13]. Delaying operation to allow resolution of cerebral injury and decrease the risk of worsening neurologic deficit or hemorrhagic conversion may have adverse consequences including further valve destruction, lower rates of valve repair, repeat embolization, worsening of sepsis, and progressive worsening of heart failure. Our institutional approach to the treatment of patients with MV IE has been aggressive and early operative intervention, with delays warranted only for uncontrolled sepsis, brain injury with a large volume of intracerebral blood, or neurologic devastation [6]. The aim of this study was to evaluate the outcomes of early MV operation for IE among patients with preoperative

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neurologic injury compared with patients with no evidence of preoperative neurologic complications.

## Material and Methods

Between January 2003 and March 2015, 314 consecutive patients underwent operation for MV IE at the University of Maryland Medical Center. Patients who had treated IE (n = 71) were excluded, leaving 243 patients for analysis. If the patient was receiving antibiotics for IE at the time of surgery the disease was considered active. If no antibiotic medication was given at the time of operation other than prophylactic medications, then the infection was considered treated. The institutional review board of the University of Maryland Medical Center (HP-00040773) approved this retrospective study and patient consent was waived. Patient data were gathered through the local Society of Thoracic Surgeons Database and chart review.

The diagnosis of IE in all patients was determined based on the established criteria [14]. Preoperative transesophageal echocardiography was performed in all patients to determine characteristics of the vegetation, the degree of mitral regurgitation (MR), the involvement of other valves or the presence of an abscess. As part of the workup, patients routinely underwent head, chest, and abdominal CT scan before operation. We defined stroke based on the Stroke Council of the American Heart Association/American Stroke Association as any brain, spinal cord, or retinal cell death attributed to ischemia, based on neurological exam, neuroimaging, or evidence of primary injury [15]. Patients with neurologic signs or symptoms or any evidence of stroke on imaging were fully examined by a neurologist. Acute stroke was defined as radiographic evidence of stroke or clinical neurologic dysfunction [15]. Patients were categorized into 2 groups based on the presence or absence of stroke. Indication for operation included the presence of any of the following: severe MR, mobile vegetation, or vegetation size greater than 10 mm [16]. Operation was scheduled electively as soon as possible after preoperative workup was complete. Operation was delayed or not pursued if the patient had coma or uncontrolled sepsis, or if a large volume (>1 to 2 $cm^2$) of intracerebral blood was present on neuroimaging. Postoperative outcomes including the rate of permanent stroke and operative mortality were compared between the 2 groups. Long-term mortality data were collected from the Social Security Death Index and supplemented by direct contact with patient's physicians and directly with patients and families.

### *Statistical Analyses*

Analyses were conducted using statistical software (JMP 8.0, SAS Institute, Cary, NC). Values are presented as mean ± SD or median with first and third quartiles. Median values were used when the data had skewed distributions. We used *t* tests and chi-square tests to compare the perioperative outcomes between the 2 groups. Kaplan-Meier survival estimates were calculated for each group and compared using the log-rank test. For all analysis, a *p* value less than 0.05 in a 2-sided test was considered statistically significant.

## Results

### *Patient Characteristics*

Of 314 patients who underwent MV surgery for IE, 243 (77%) patients had active IE and were included in the study. Seventy-two percent (174 of 243 patients) had no clinical or radiographic evidence of stroke whereas 28% (69 of 243 patients) were diagnosed with preoperative acute stroke. Among patients diagnosed with stroke, 67% (46 of 69 patients) had findings on clinical examination consistent with stroke, whereas the remaining 23% (23 of 69 patients) had imaging evidence of brain infarction or hemorrhage with no clinical findings. Overall, preoperative brain imaging was performed in 91% (221 of 243 patients).

The mean age of patients was 50 ± 14 years (range, 18 to 83 years) and 65% (157 of 243 patients) were men (Table 1). Thirty percent (72 of 243 patients) had a history of intravenous drug abuse. The possible identified underlying causes of IE among nonintravenous drug abusers were hemodialysis catheter infection (n = 42), cellulitis or osteomyelitis (n = 11), infected port catheter or total parenteral nutrition line (n = 9), gastrointestinal or urinary tract infection (n = 11), immunosuppression (n = 7), recent Lyme disease (n = 3), dental abscess or infection or intervention (n = 6), and history of MV prolapse (n = 15). The possible underlying cause of IE was not identified in 67 patients.

Concomitant tricuspid valve IE was present in 14% (34 of 243 patients) and aortic valve IE was present in 30% (74 of 243 patients). There were no significant differences in the rates of preoperative comorbidities between the 2 groups. A history of prior stroke was present in 12% (28 of 243 patients) and 24% (58 of 243 patients) had dialysis-dependent renal failure. Atrial fibrillation was present in 15% (38 of 243 patients). Eighteen percent (44 of 243 patients) had prior cardiac operations. Prosthetic MV IE was present in 16% (38 of 243 patients).

The most common organism was *Staphylococcus aureus* in 42% (101 of 243 patients) (Table 2). The causative organism was not significantly different between the 2 groups.

Preoperative neurologic symptoms among the 46 patients with preoperative clinical stroke included unilateral extremity weakness (n = 19), altered mental status (n = 14), aphasia (n = 9), headache (n = 1), hemineglect (n = 1), seizure (n = 1), or visual disturbances (n = 1). Thirty-three percent (23 of 69 patients) of patients had no neurologic symptoms. Among patients with preoperative acute stroke, preoperative head CT or magnetic resonance imaging scan showed positive findings in 98% (67 of 69 patients). The most common findings included acute embolic stroke in 64%, embolic stroke with hemorrhage in 20%, hemorrhage in 5%, abscess with infarct in 2%, abscess with hemorrhage in 2%, mycotic aneurysm with infarct and hemorrhage in 2%, and mycotic aneurysm alone in 2% (Table 3). The 2 patients with negative