## Inter-Operative Time between Neurosurgery and Cardiac Surgery for Native Valve Endocarditis

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### ABSTRACT

**Introduction:** Infective endocarditis is well known to produce neurologic complications from septic emboli, which mandates a multidisciplinary approach including neurosurgery and cardiac surgery. However, the literature is not conclusive as to the optimal interval between neurosurgery and cardiac surgery.

**Case Report:** The first case is a 60-year-old woman with significant past medical history presenting with native valve methicillin-resistant staphylococcus aureus (MRSA) endocarditis causing cerebral vascular infarcts. The second case is a 45-year-old man with no significant past medical history presenting with infective endocarditis of the aortic and mitral valve.

**Discussion:** After neurosurgical intervention cardiac surgery was performed 27 and 17 days later for each case, respectively. All operations were successful with few complications. Guidelines suggest waiting at least one week until valvular surgery, but other reports suggest earlier surgery produces preferable outcomes. In the cases presented, both patients experienced no further significant events to date after receiving cardiac surgery >3 weeks after the initial ischemic stroke event.

**Conclusion:** Neurological deficits mandate a collaborative approach between neurosurgery and cardiac surgery. The significance of the time between neurosurgical intervention and cardiac surgery remains controversial, but waiting at least one week shows positive results.

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### Introduction

Infective endocarditis is known to produce complications during the in-hospital course of patients. In particular, septic emboli are frequently dislodged from the affected left heart valves and produce an ischemic, embolic stroke. Left-sided infective endocarditis can affect the aortic valve (44%), mitral valve (36%), or both (17%) (1). There is no difference in occurrence of stroke between aortic or mitral valve endocarditis (37% vs. 34%, p=0.54) (2). Neurological findings in patients with infective endocarditis include ischemic stroke (75.7%), meningoencephalitis (12.9%), and intra-cerebral hemorrhage (8.6%) (1). Whenever these complications arise, the risk of morbidity and mortality of cardiac surgery increases significantly.

The mainstay therapy for infective endocarditis is medical management with antibiotics. Empirical antibiotics that cover the common pathogens, including *Streptococcus*, *Staphylococcus*, and *Enterococcus* species, are highly recommended. This includes antibiotics with strong coverage of these bacteria, including vancomycin. However, if the pathogen is either *Candida* species (fungal) or part of the HACEK bacteria group, prognosis worsens with medical management. Surgery for native valve endocarditis is strongly recommended if the case is not treated effectively with antibiotics, the vegetations continue to grow, the regurgitation seen with afflicted valves is severe, the pathogen is fungal, or if there are abscesses around the valvular annulus that produce complications including heart

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blocks and need for pacemakers.

Complications that can arise from left-sided endocarditis include septic embolism to the cerebral vasculature. Septic embolization results in an ischemic stroke event. Furthermore, pathogens in the blood may cause infective, or mycotic, aneuysms within the vasculature. Mycotic aneuysms are prone to rupture and can worsen the prognosis of the patient. When compromise of the cerebral vasculature is noted with serial angiograms, that patient is treated either with a neurosurgical or endovascular approach [3].

After neurological intervention, cardiac surgery is usually indicated in order to repair the afflicted valve and remove the source of infection (4). Early surgical management of patients with infective endocarditis, even with ischemic stroke, showed more preferable outcomes than medical management (5,6). However, debate in the literature continues as to the optimal interval timing between neurosurgical intervention and cardiac surgery. Patients that had cardiac surgery prolonged more than one week after neurological impairment, had a poorer prognosis; (6) however, studies do not describe the necessary interval time after neurological correction. The following two cases present outcomes in which both neurosurgery and cardiac surgery teams collaborated.

Case Report

Case 1

A 60-year-old woman presents with altered mental status, dyspnea, and left leg pain, gangrenous necrosis of the fingers and toes, and lower extremity edema. Past medical history is significant for native valve methicillin-resistant *Staphylococcus aureus* (MRSA) endocarditis causing cerebral vascular infarcts. On presentation to our hospital, MRI scan of the head revealed decreased perfusion in the middle cerebral artery bilaterally with noticeable ischemia to the parietal and occipital lobes (Figure 1). Transesophageal echocardiogram revealed vegetations accumulating on the anterior leaflet of the mitral valve along with moderate to severe mitral valve regurgitation.

Serial CT head scans showed evidence of abscess formation within the parietal lobes most likely due to septic emboli. Neurosurgery proceeded to perform a bilateral craniotomy to remove the abscesses. The patient was positioned in a prone position exposing the parietal regions of the head. Two burr holes and flaps were made on the parietal bone, first the left followed by the right. The contents of the abscess oozed with pressure when discovered in both sides. Heavy irrigation was performed prior to closure of the operating field.

Delay of cardiac intervention occurred due to bilateral multifocal pneumonia and acute on chronic kidney injury. Twenty-four days post-craniotomy, a heparin challenge was performed to check for intracranial hemorrhage. With negative results, cardiothoracic surgery continued with the mitral valve replacement operation 27 days postoperative from the craniotomy.

After initiation of cardiopulmonary bypass and aortic cross-clamping, an incision was made near the interatrial septum. The mitral valve was replaced with a 29 mm Medtronic Mosaic Tissue Valve (Medtronic, Minneapolis, Minnesota, United States). Attention diverted to the aortic valve, which was congenital bicuspid, but with no evidence of regurgitation or vegetations. The operating field was then closed and the patient was taken to the intensive care unit. On the first post-operative day, the patient was returned back to the operating room due to suspicion of cardiac tamponade from excessive hemorrhage. After managing the two possible areas of hemorrhage, the patient did not experience any further post-operative complications.

Case 2

A 45-year-old man presented to our institution as a transfer from an outside facility with infective endocarditis of the aortic and mitral valve. After 5 months of continuous fever, the day prior to admission the patient developed headaches, dizziness, and left-sided weakness plus facial droop. At hospital admission, an echocardiogram was performed showing vegetations on the anterior leaflet of the mitral valve and on the bicuspid aortic valve. Blood cultures were positive for *Streptococcus parasanguinis*. After transfer from another hospital, the patient presented with slight weakness on the left hand and left facial droop. An MRI of the head was performed showing microhemorrhage in the right frontoparietal region of the brain (Figure 2).

Cardiac surgery was postponed due to this
evidence of microhemorrhage seen on head MRI due to the significant risk for conversion to hemorrhagic stroke if placed on anticoagulation. Neurosurgery was contacted in order to remove the suspected septic emboli in the cerebral vasculature.

A left craniotomy was performed to remove the small abscess detected on MRI. Two burr holes were created: one on the anterior temporal region and another on the posterior temporal region near the parietal area. Miniscule amounts of pus were discovered during exposure. After extensive irrigation, the operating field was closed and the patient was sent to the intensive care unit. The patient experienced a mild transient ischemic attack lasting 30 minutes on the eighth postoperative day caused by a small cerebral effusion.

Fifteen days post-craniotomy, and 7 days after the transient ischemic attack, a heparin challenge was performed. Cardiac surgery was performed 17 days post-craniotomy.

After initiation of cardiopulmonary bypass and aortic cross-clamping, the aortic valve was exposed. After measuring the aortic annulus, attention was directed toward the mitral valve. The mitral valve was replaced with a 33 mm St. Jude Epic Tissue Valve (St. Jude Medical, St. Paul, Minnesota, United States). Attention was then directed back to the aortic valve. An aortic pseudoaneurysm was noted beneath the right coronary ostium, but it did not prove significant, so it was closed with CorMatrix extracellular matrix (CorMatrix Cardiovascular, Inc., Roswell, Georgia, United States). The aortic valve was replaced with a 29 mm Magna Ease Tissue Valve (Edwards Lifesciences, Irvine, California, United States). After closure of the operation field, the patient was taken to the intensive care unit without further complications.

Discussion
Case Analyses
The previous two cases present different time points at which cardiac surgery was conducted. The first case had the cardiac surgery performed 27 days after the craniotomy. However, the patient had many comorbidities that required attention in order to optimize surgical outcomes. The second case presents a patient that had cardiac surgery 17 days after the craniotomy. Of note, both patients had cardiac intervention >3 weeks after their initial ischemic stroke event.

Both operations were successful with few complications during the operation and no postoperative sequelae. Neurologic complications improved after cardiac intervention with both patients. No further significant events are noted 30 days after the operation.

Data findings
The timing of cardiac surgery after neurological symptoms from infective endocarditis is crucial in determining the prognosis. Unfortunately, there is no official protocol for proper operation time in these scenarios. Habib et al. attempted to formulate an algorithm for endocarditis patients with neurological complications (7). For patients with neurological complications, a cerebral CT scan is required to ascertain the state of the cerebrum. Furthermore, other comorbidities and presentations should be investigated, including heart failure, uncontrolled infection, abscess formation, and high embolic risk. If any of these morbidity factors exist, then imaging of the head should be assessed for intracranial hemorrhage and damage from stroke events. If the patient presents without any of these complications and is alert, oriented, and without severe comorbidities; then surgery is indicated. If complications exist, then medical therapy with antibiotic regimens is preferred. After performing of neurosurgery or endovascular intervention, it is recommended to postpone cardiac surgery for 1-2 week late (3,7). If no post-operative neurological sequelae exist after neurovascular intervention, then the outcome of cardiac surgery becomes more favorable.

Chapot et al. describe a retrospective study with 18 patients that acquired infective endocarditis complicated with mycotic aneurysms. Endovascular treatment was performed in all patients, and all angiograms obtained 6 months to 2 years later showed stable occlusions. Five patients underwent cardiac surgery 1 week after endovascular treatment and presented post-operatively with no neurologic complications (8).

The presented cases underwent cardiac surgery from 2 to 4 weeks after neurosurgical intervention. The first case had extensive comorbidities; according to the guidelines proposed by Habib et al,
patients with extensive comorbidities should be managed medically (7). Cardiac intervention was withheld from the patient until the comorbidities were managed and optimized. The second case lacked significant comorbidities. Cardiac intervention was delayed >1 week after neurosurgical intervention. No complications occurred postoperatively.

Cardiovascular intervention and results after ischemic strokes are described extensively throughout reports. Ruttmann et al. describe an 81.9% survival rate from surgery in patients with infective endocarditis with stroke (9). In comparison with non-stroke patients, the perioperative mortality risk was 1.70-fold higher and long-term mortality risk was 1.23-fold higher in stroke patients. Hospital mortality ranges from 17.2-21.4% and long-term survival ranges from 45-68% in 5 years (1,2). Patients that presented with complicated stroke (meningitis, hemorrhage, or brain abscess) have an even higher perioperative mortality rate (38.9%), but did not have any additional neurologic sequelae or complications compared to those with ischemic strokes. Neurological recovery was up to 75% in patients with ischemic stroke after surgery unless it involved the middle cerebral artery, in which case it was limited to only 50% recovery (9).

Intracranial hemorrhage, or hemorrhagic stroke, is noted to be a contraindication to early cardiac surgery. This is due to the complications brought about from the use of cardiopulmonary bypass. The machine requires mandatory anticoagulation, which can exacerbate the hemorrhagic foci within the cranium. In addition, the period of hypotension from using the heart-lung machine could potentiate cerebral edema in areas where the blood brain barrier is less strengthened (9). Therefore, it is recommended to postpone cardiac surgical intervention 2 to 3 weeks after the onset of intracranial hemorrhage (10,11).

However, in a small study with 30 patients, the mean interval between intracranial hemorrhage onset and surgery was 22.5 days. Five cases (16%) were operated within 7 days and 6 cases (20%) within 8-14 days between onset of intracranial hemorrhage and surgery. There was no deterioration or exacerbation of the hemorrhagic foci postoperatively with any of the patients regardless of timing of surgery (12).

Conclusion

Infective endocarditis is a complex disease both in surgical and medical management. The case becomes more complicated when neurological symptoms present. Neurological deficits mandate a collaborative approach between neurosurgery and cardiac surgery. In the cases presented, both patients acquired abscess formation within the cerebrum. A craniotomy for debridement was performed by neurosurgery. Both patients then underwent cardiac surgery; 27 and 17 days later. Theorized guidelines suggest waiting at least 1 week until valvular surgery, but other reports suggest earlier surgery results in preferable outcomes. While the first case presented with significant comorbidities, the second case had few. Both cases did not experience post-operative or long-term complications 30 days after the procedure.

Conflict of Interest

The authors declare no conflict of interest.

References

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