We reviewed the records of 20 patients with late prosthetic valve endocarditis who were hospitalized at the University of Iowa between 1985 and 1988. There were 14 men and six women, aged 20–80 (mean 57.9) years. The infected valves were mechanical in 11 patients (six aortic and five mitral) and bioprosthetic in the other nine. Echocardiography in 12 patients demonstrated vegetations in one. Among the 20 patients, neurologic complications occurred in eight (40%), six of whom had mechanical valves (five mitral and one aortic). Infection with *Staphylococcus aureus* occurred in four of the eight patients (50%) with neurologic complications. Of the eight patients with neurologic complications, ischemic stroke was diagnosed in four, transient ischemic attacks in one, and intracranial hemorrhage in three. Prothrombin times at the time of the intracranial hemorrhage were 2.2, 1.5, and 1.3 times control in these three patients. Cerebral angiography done in four of the eight patients with neurologic complications failed to show mycotic aneurysms. Nine of the 20 patients (seven men and two women, mean age 66.8 years) died ≤90 days after the diagnosis of late prosthetic valve endocarditis. Half of the eight patients with neurologic complications died (three men and one woman, mean age 62.3 years), and all three patients with intracranial hemorrhage died. Our data suggest that the neurologic complications of late prosthetic valve endocarditis are more common with mechanical valves, particularly in the mitral position, and are associated with a high mortality. (Stroke 1990;21:472–475)

The incidence of prosthetic valve endocarditis ranges from 2% to 4%, with an average of 2.4%. Endocarditis occurring ≤60 days after surgery is described as early prosthetic valve endocarditis and is primarily related to bacteremia associated with indwelling vascular catheters or perioperative infection; offending organisms are most commonly *Staphylococcus aureus*, *S. epidermidis*, and diptheroids. Endocarditis occurring >60 days after valve replacement is described as late prosthetic valve endocarditis and is related to bacteremia associated with minor surgery, skin infections, dental procedures, or a variety of gastrointestinal and genitourinary tract procedures; offending organisms are most commonly *Staphylococcus* spp. and *Streptococcus* spp. We review the type and incidence of neurologic complications among patients with late prosthetic valve endocarditis, examine the influence of these neurologic complications on mortality, and seek to identify the subsets of patients at risk.

**Subjects and Methods**

We reviewed the records of patients who had a diagnosis of endocarditis and were referred to the Division of Infectious Disease at the University of Iowa Hospitals between January 1985 and June 1988. Criteria for the diagnosis of late prosthetic valve endocarditis included at least three of the following: 1) fever, 2) new regurgitant murmur, 3) evidence of peripheral emboli, 4) two or more blood cultures growing the same organism, and 5) direct evidence of valve infection at autopsy or surgery. We excluded patients diagnosed ≤60 days after surgery. We reviewed the cases to determine the incidence and type of neurologic complications defined as intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), cerebral infarction, or transient ischemic attack (TIA). Diagnosis of the types of cerebrovascular event were based on the clinical criteria developed for the Harvard Cooperative Stroke Registry, and for the diagnosis of TIA we used the definition of the Classification and Outline of Cerebrovascular Disease.
We identified 107 cases of infective endocarditis during the study period; 20 (14 men and six women) met the criteria for late prosthetic valve endocarditis. These 20 patients are the subject of this review (Table 1). Their ages ranged from 20 to 80 (average 57.9) years. All 20 patients had a single valve replacement procedure. The site of valve replacement was mitral in seven, aortic in 12, and tricuspid in one patient. Eleven valves were mechanical, and the other nine were bioprosthetic. *Staphylococcus* spp. were the infecting organism in 10 patients. One patient had culture-negative endocarditis; the diagnosis was made histopathologically at surgery. Echocardiography was performed in 12 patients; vegetations were found in one, who did not have a neurologic complication. Nine patients (45%) died.

Of the 20 patients, eight had neurologic complications (Table 2). Cerebral infarction occurred in four patients; three had an ICH. In one patient infarction was associated with SAH, and one patient had a transient episode of aphasia. Seven patients were on anticoagulants at the time of presentation, six were on warfarin and one was on heparin. Prothrombin time was not available in three of these seven patients prior to admission (cases 2, 7, and 9). Mortality was 50% (four of eight).

Discussion

Patients with prosthetic valves have a number of medical or neurologic complications, including prosthetic valve endocarditis. Previous reports give similar estimates of the incidence of neurologic complications for both early and late prosthetic valve endocarditis, in the range of 25–30%. When non-specific symptoms such as headache and encephalopathy are included, the incidence of neurologic complications may be as high as 40%. Patients with prosthetic valve endocarditis have a high mortality. The presence of paravalvular leak, infection with other than *Streptococcus* spp., and moderate-to-severe congestive heart failure portend a particularly poor prognosis.

Overall mortality in our series was 45%, similar to that previously reported, and mortality among our patients with neurologic complications was 50%; all three patients with ICH died. Among 13 patients with late prosthetic valve endocarditis and central nervous system complications, Karchmer et al found a mortality of 69% (nine of 13). Among 48 patients with early and late prosthetic valve endocarditis, Masur and Johnson found 15 with neurologic complications; eight of these 15 patients died, one of ICH and seven of hemiparesis followed by coma and death.

Cerebrovascular events are the most common neurologic complication in patients with late prosthetic valve endocarditis. Ischemic stroke was the most common neurologic complication in our series; it occurred in four patients and was fatal in one. The presumed mechanism of ischemic stroke in each case
was emboli arising from the infected valves. The rate of embolization from infected valves depends on the underlying coagulation status of the patient and the administration of antibiotics. Without anticoagulants, embolization rates approach 50%\(^3\); with adequate anticoagulant therapy, the incidence drops to 3–14%.\(^4\) Davenport et al\(^7\) reported a daily stroke rate ranging from 1% to 9% depending on the infecting organism, falling to almost 0% after institution of appropriate antibiotics.

ICH accounted for three fatal neurologic complications among our eight patients. Two hemorrhages were intraparenchymal and the other was subarachnoid. Characteristics of the patients with ICH included 1) prior anticoagulant use with prothrombin time ranging from 1.3–2.0 times control, 2) mechanical prostheses in the mitral position, and 3) infection with \textit{Staphylococcus aureus} (two of three patients). Previous series\(^6\),\(^13\),\(^18\) have also found that ICH carries a grave prognosis.

Because of the risk of ICH, the use of anticoagulants in the context of an infected cardiac valve remains controversial.\(^18\)–\(^20\) In a review of 17 patients with both native and prosthetic valve endocarditis, Hart et al\(^15\) postulated three mechanisms of ICH: 1) sterile embolic events causing bland infarction and subsequent hemorrhagic transformation, 2) septic emboli resulting in acute erosive arteritis, and 3) septic emboli occurring during adequate antibiotic therapy resulting in aneurysm formation. Anticoagulant therapy has been reported to decrease the frequency of thromboembolism and to significantly decrease mortality in patients with prosthetic valve endocarditis. Although we agree with Wilson et al\(^19\) who recommended that once ICH occurs anticoagulants be stopped, we believe that after 48–72 hours, anticoagulants can be cautiously restarted. No further studies in the last 10 years have answered the question of whether the risk of anticoagulation justifies the prevention of further embolic events in these patients.

SAH, which may be the initial manifestation of infective endocarditis,\(^22\) occurred in only one of our patients. Karchmer et al\(^6\) also found a case of SAH thought to be secondary to septic vasculitis.

Mycotic aneurysm is a rare complication of infective endocarditis.\(^23\) Angiography in four patients failed to show mycotic aneurysm. Although cerebral hemorrhage is often presumed to be secondary to aneurysm rupture, the incidence of angiographically demonstrated mycotic aneurysm (approximately 1.8%) is much lower than the incidence of hemorrhage.\(^24\)

Multiple microemboli may present with solely mental status changes. One patient in our series developed a presumed "toxic encephalopathy" without lateralizing signs. Computed tomograms and cerebrospinal fluid examinations were repeatedly normal. He died of ongoing sepsis. Autopsy revealed multiple sterile cerebral microemboli.

A number of conclusions can be drawn from our experience: 1) neurologic complications are a frequent cause of morbidity and mortality among patients with late prosthetic valve endocarditis, 2) mortality is higher among patients with neurologic complications, 3) patients with neurologic complications are more likely to have a mechanical valve in the mitral position, and 4) early recognition and treatment of late prosthetic valve endocarditis is needed as mortality remains high.

References


**KEY WORDS** • cerebrovascular disorders • endocarditis, bacterial
Neurologic complications of late prosthetic valve endocarditis.
D L Keyser, J Biller, T T Coffman and H P Adams, Jr

Stroke. 1990;21:472-475
doi: 10.1161/01.STR.21.3.472

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/21/3/472

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/