# Clipping It in the Bud

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*Information about a real patient is presented in stages (boldface type) to expert clinicians (Drs Murthy and Yang), who respond to the information and share their reasoning with the reader (regular type). A discussion by the authors follows.*

**Patient presentation: Mr H is a 50-year-old male admitted in 2013 with methicillin-sensitive *Staphylococcus aureus* bacteremia and aortic valve endocarditis. Other medical history includes hypertension, paroxysmal atrial fibrillation, end stage renal disease, undergoing hemodialysis through a left upper extremity arteriovenous fistula, and stroke. He underwent intraoperative pulmonary vein isolation, epicardial left atrial appendage closure using a 50-mm AtriClip device, and bioprosthetic aortic valve replacement at an outside hospital.**

*Dr Yang:* Because 90% of thrombi in nonvalvular atrial fibrillation originate in the left atrial appendage (LAA), this structure has emerged as a therapeutic target to reduce the risk of cardioembolic stroke. Mr H has a history of labile international normalized ratios, a HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition [anemia], Labile INR, Elderly [age>65], Drugs/Alcohol concomitantly) score of 4, and prior stroke while on anticoagulation, thereby warranting consideration of alternative therapies to warfarin for stroke protection, if feasible. The 2014 American College of Cardiology/American Heart Association guideline statement on atrial fibrillation makes a class IIb recommendation for surgical occlusion of the LAA during other cardiac surgeries. Despite this guideline, surgical occlusion with a prosthetic device is not advisable in this patient because of active endocarditis and the risk for recurrent infection in the future. Moreover, patients with valvular heart surgery and those with active systemic infection were excluded in the pivotal EXCLUDE trial, which studied the safety and efficacy of the AtriClip placement.[1] A suture-based LAA occlusion strategy to minimize implanted prosthetic material would have been preferred.

The underlying rationale that exclusion of the thrombogenic LAA may reduce short- and long-term postoperative stroke is supported by a recent meta-analysis comparing stroke rates in 7 studies of surgical LAA occlusion, by either LAA resection or closure using sutures or staples. Reduced occurrence of stroke at 30 days (0.95% in LAA occlusion and 1.9% in LAA preservation) and in longer follow-up (1.4% vs 4.1%)[2] was noted. The Left Atrial Appendage Occlusion Study (LAAOS III), a large-scale randomized clinical trial, is underway to test this hypothesis prospectively. The AtriClip Device System is a dedicated LAA exclusion device with high rates of LAA occlusion but is lacking long-term efficacy data.

***Patient presentation (continued):* He was admitted 2 years later and underwent redo aortic root replacement for methicillin-sensitive *Staphylococcus aureus* prosthetic valve endocarditis (PVE) and aortic root abscess with assumption that the source of infection was the punctures of**

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**arteriovenousfistula for hemodialysis. The AtriClip was scarred down and unable to be visualized during the first redo operation; consequently, infection of AtriClip was not suspected or pursued. Over the next 6 months, he was admitted and treated with intravenous antibiotics for polymicrobial bacteremia (ampicillin-sensitive *Enterococcus faecalis*, *Citrobacter koseri*, and *Escherichia coli*) without evidence of valvular infection on** transesophageal echocardiogram **(TEE). Nine months after redo sternotomy for PVE, he presents with a 5-day history of fever, chills, headache, myalgia, and nonexertional, sharp chest pain. He is febrile to 102.5°F and has a systolic murmur in the left lower sternal border that is old, no meningeal signs, and no physical examination evidence of systemic embolization. Initial labs are significant for white blood cell count of 18 400, hemoglobin of 7.8 g/dL, platelet count of 97 000, troponin T of 0.14 ng/mL, and no significant electrolyte abnormalities. His chest x-ray is clear of pneumonia, atelectasis, and effusion but demonstrated a stable left atrial appendage occlusion device (Figure 1). Blood cultures are pending. He is placed on broad spectrum antibiotics.**

*Dr Murthy:* As a patient on hemodialysis, Mr H is at high risk for early recurrent PVE, defined as infection for <12 months after implantation. His risk factors for PVE include ongoing hemodialysis, history of multiple bouts of bacteremia, and presence of a left atrial appendage closure device that could be infected. In the literature, recurrent endocarditis of prosthetic valves is unfortunately high and without prompt surgical intervention can result in significant in-hospital mortality. Timely diagnosis enables prompt surgical treatment, which is crucial for reducing short- and long-term adverse outcomes. The traditional approach to diagnosis of PVE combines microbiological, clinical, and echocardiographic factors defined in the Modified Duke criteria, with echocardiography playing a pivotal role. I recommend TEE to better characterize the prosthetic valve and aortic root.

***Patient presentation (continued):* One out of 4 blood culture bottles from admission grew *C. koseri*, but subsequent cultures have been clear. TEE shows a 10x5-mm nonmobile echodensity on ventricular aspect of the right cusp of the aortic prosthesis and mild aortic insufficiency. The aortic root appears thickened, with an adjacent echolucent space concerning for paravalvar abscess (Figure 2). Moderate to severe tricuspid regurgitation is present, unchanged from previous TEE. No bacterial involvement of the tricuspid or pulmonary valves is seen. Ejection fraction is within the normal range.**

*Dr Murthy:* Based on the modified Duke infective endocarditis (IE) criteria,[3] Mr H has a definite diagnosis of IE based on the presence of 1 major (evidence of endocardial involvement on TEE) and 3 minor (previous prosthetic valve, fever, and positive blood culture with an organism not typical of IE) criteria. Although no reports in the literature document bacterial colonization of an epicardial left atrial appendage closure device, this possibility is distinct given the history of multiple bouts of bacteremia and the fact that this device was placed during surgery for active endocarditis. Also notable are the nonexertional, sharp chest pain and elevated troponin, which could be related to myopericardial inflammation, infection, or compression of coronary arteries from adjacent abscess.

To further investigate this possibility, I would recommend cardiac and whole-body fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging. Growing evidence indicates that this technique improves accuracy and time to diagnosis of PVE[4] and can identify remote sites of infection, thus it has been recently incorporated into the 2015 European Society of Cardiology Update on IE.[5] In select cases, the addition of whole-body FDG PET/CT imaging in patients with PVE may identify vascular graft infection, cardiac implantable electronic device infection, and other loci of infection, such as arterial mycotic aneurysms or septic emboli, which may require therapy before or concomitant with valve replacement. Because of the presence of aortic

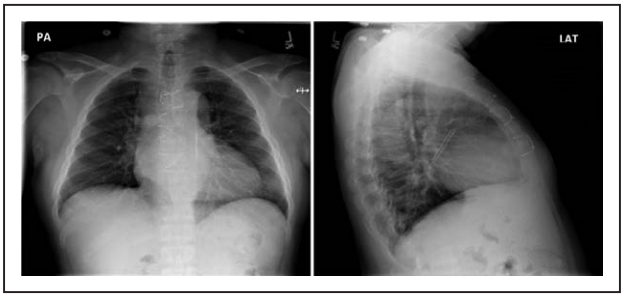


**Figure 1. Posterioanterior (PA) and lateral (LAT) chest x-ray film demonstrating no acute cardiopulmonary process, median sternotomy, and stable left atrial appendage occlusion device.**

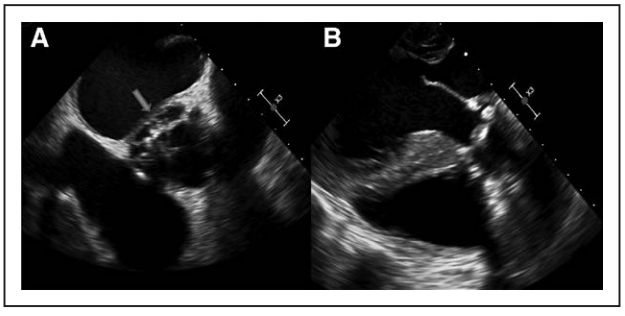


**Figure 2. Short axis (A) and long axis (B) of the bioprosthetic aortic valve with surrounding aortic root abscess (blue arrow) as seen on transesophageal echocardiographic images.**

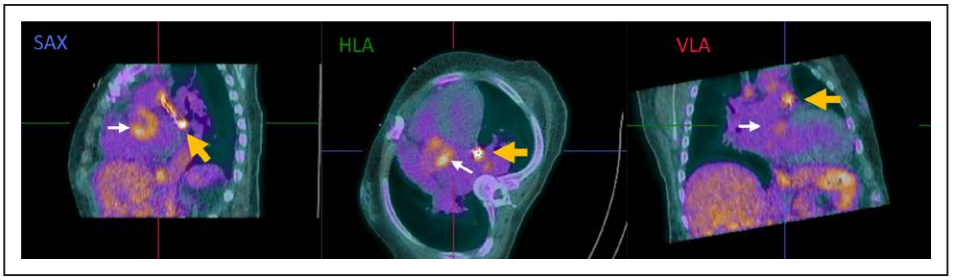


**Figure 3. Short axis (SAX, left), horizontal long axis (HLA, middle), and vertical long axis (VLA, right) hybrid $^{18}$F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) fusion images demonstrating intense FDG uptake surrounding AtriClip device (thick yellow arrows) and aortic annulus (thin white arrows).**
FDG uptake in mediastinal lymph nodes is also seen.

abscess and its proximity to the nodal conduction system, I would also recommend daily electrocardiogram to monitor for progressive arteriovenous nodal block. Given his headache and thrombocytopenia, I would recommend a head CT scan and computed tomography angiography to rule out intracranial hemorrhage or mycotic aneurysm. Although magnetic resonance imaging to assess for intracranial hemorrhage would be another choice, this patient has a bullet fragment in his psoas muscle, a relative contraindication to this diagnostic modality.

***Patient presentation (continued):*** **Cardiac and whole-body FDG PET/CT was performed to identify other loci of infection. FDG uptake was present circumferentially around the aortic annulus, with a peak standardized uptake value of 3.4 with blood pool standardized uptake value of 1.4. FDG uptake was also present surrounding the entire left atrial appendage closure device (peak standardized uptake value 3.4). Together these findings are consistent with infection of both devices (Figure 3). No other areas of significant FDG uptake concerning for infectious loci are seen in whole-body imaging. Head** computed tomography angiography **revealed a 0.7-cm saccular right anterior cerebral artery aneurysm and a subacute infarction involving the left occipital lobe. Neurosurgical evaluation to assess perioperative bleeding risk was undertaken. His** computed tomography angiography **findings were consistent with a pericallosal artery bifurcation aneurysm. Suspicion was low for this aneurysm being mycotic, but rather it was found in the sporadic type of intracranial cerebral aneurysm that does not increase the risk of perioperative bleeding.**

*Dr Yang:* The findings support infection of his aortic valve prosthesis, aortic root, and the AtriClip device. I would proceed with third redo aortic root replacement and removal of the AtriClip. We will plan to explant the AtriClip device with high risk of injury to the circumflex artery because of its close proximity to the base of LAA. He is at substantially increased risk of developing heart block because of extensive, recurrent infection of his prosthetic aortic valve, annulus, and aortic root, requiring a third round of debridement. However, prophylactic permanent epicardial pacing leads were not considered at the time of surgery because of the contaminated surgical field (aortic root abscess and infected AtriClip) with risk of reinfection of epicardial leads and mediastinitis.

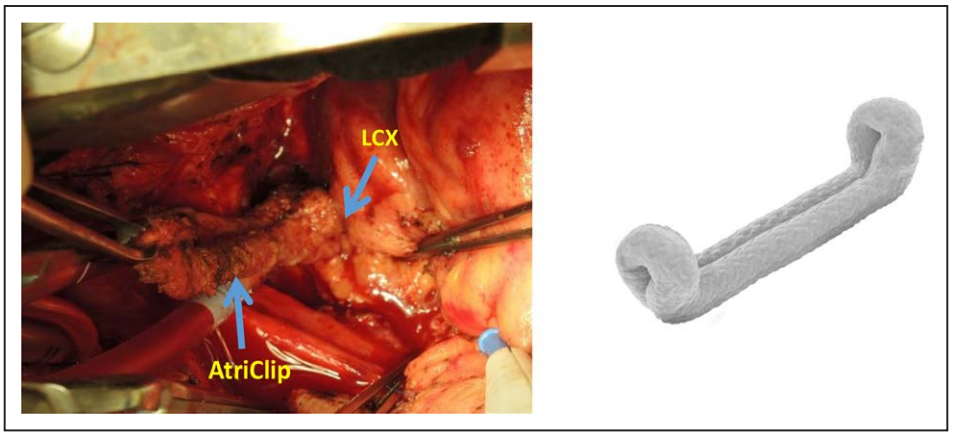


**Figure 4. Intraoperative picture (left) showing AtriClip that was scarred to the base.**
The left atrial appendage (LAA) between the limbs of the AtriClip was necrotic, appearing infected. The implanted device is seen adjacent to the circumflex artery (LCX). Manufacturer picture of the AtriClip device before implantation (courtesy from AtriCure).

***Patient presentation (continued):*** **A third-time redo total aortic root replacement was performed. A large root abscess was found as expected. The previous prosthetic valve was removed, and the aortic root was debrided and replaced with a 25-mm Freestyle porcine aortic root. The AtriClip was stuck and scarred to the base of the LAA (Figure 4), which was removed by dividing and peeling the limbs of AtriClip off the surrounding tissue, including the circumflex coronary artery. The LAA between the limbs of the AtriClip was necrotic, appearing infected. Intraoperative cultures from the AtriClip grew methicillin-sensitive coagulase-negative *Staphylococcus*. The surgery was complicated by complete heart block requiring dual-chamber pacemaker placement. Recovery was otherwise uneventful, and he completed an antibiotic course per recommendations of infectious disease consultants. No infection recurrence has occurred since then.**

*Dr Murthy:* This is the first reported case of an infected surgical LAA occlusion device and also the first reported case where recurrent PVE may have been caused by an undertreated locus in the LAA given similarity between culprit organisms. Generally, the incidence of epicardial prosthetic device infection is low possibly because of the absence of direct exposure of these prostheses to circulating blood. However, consideration of these devices as a source of infection is important given their increasing use. Also important is that surveillance echocardiography, which is the workhorse of imaging in endocarditis, has a poor sensitivity for identifying infection in this location. In this case, cardiac FDG PET/CT imaging revealed infection of his AtriClip device that would have been missed with echocardiography alone and would likely have led to further recurrent infections. Potentially, use of this modality earlier in his course could have markedly altered surgical management, prompting removal of this device during his second operation and preventing the need for third sternotomy.

## DISCUSSION

Early surgery in recurrent PVE or endocarditis with other complication (valve dysfunction, heart block, and abscess) is associated with better early and long-term outcomes especially when the culprit microorganism is *S. aureus*.[6] To prevent recurrent infection of prosthetic valves, identification of unexpected loci of infection before redo sternotomy is crucial to tailor surgical and medical strategy. In this case, FDG PET imaging revealed the first documented case of infection in an AtriClip and substantially modified the surgical approach. This testing strategy is supported by a growing body of evidence in the literature and has been incorporated into the 2015 European Society of Cardiology infectious endocarditis guidelines, which expand the modified Duke Criteria to include abnormal FDG PET/CT or radiolabeled leukocyte single-photon emission computed tomography results as major diagnostic criterion. We contend that in selected patients with definite or suspected PVE, particularly when complex surgical intervention is necessary, FDG PET/CT can be an invaluable adjunct to identify vascular graft infection, cardiac implantable electronic device infection, epicardial implant infection, and mycotic arterial aneurysms or septic emboli that would be missed by echocardiography. In applying this imaging modality, 1 important caution is that FDG may be taken up by both leukocytes and fibroblasts, and therefore normal postoperative healing can be mistaken for active infection. Consequently, caution should be used in the early postoperative period to avoid false-positive studies.

## DISCLOSURES

Dr Murthy owns minor stock in General Electric, a manufacturer of PET and ultrasound instruments, and Cardinal Health, a manufacturer of FDG.

## AFFILIATIONS

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## FOOTNOTES

*Circulation* is available at http://circ.ahajournals.org.

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