Left Atrial Appendage occlusion - A novel way to Reduce risk of stroke in Atrial Fibrillation

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is becoming a major concern with aging population. It is estimated to affect about 1 to 5% of the population in developed world and the incidence increases with age especially above 65 yrs. Stroke prevention is one of the main aspects in treatment of atrial fibrillation[1]. Of the overall 800,000 strokes occurring every year worldwide, one sixth are presumed to be related to AF[2]. The Swedish Stroke Registry data from 2001 to 2005 show that, patients who develop stroke and have AF have significantly higher mortality as compared to those who do not have AF. Further, the data from SPINAF (Stroke Prevention in Non-rheumatic AF)[3] shows that 15% patients with AF suffer silent cerebral infarctions.

Role of Left atrial Appendage in Emboli of Cardiac Origin

Left Atrial Appendage (LAA) thrombi are considered to be the cause of cardioembolic stroke based on studies showing pathological changes in LAA[4] and presence of spontaneous echo contrast suggestive of intracavitary blood stasis[5]. In a review of 23 studies of atrial fibrillation by Blackshear and Odel,[6] 91% of left atrial thrombi were isolated to or had originated from LAA. Although, multiple other factors (extensive atherosclerosis with aortic atheroma, disorders of coagulation and increased platelet activation) contribute to embolic stroke in patients with AF, LAA remains a major source of the cardioembolic strokes. It is quite understandable why the recent work has focused on occlusion of LAA in prevention of stroke.

Oral anticoagulants have been shown to reduce incidence of strokes by almost 65% in various randomized studies[7]. However incidence of major bleeding remains a concern. Besides maintaining INR in therapeutic range is a huge challenge especially in India. The variability in response to oral anticoagulants mandates frequent INR monitoring to adjust the dose to prevent bleeding complications, especially in AF patients (elderly population). Food and drug interactions with oral anticoagulants also pose a great challenge in adjusting the dose of these agents.

Alternative Approaches to reduce risk of Strokes in AF

Since LAA is the source of embolus in approximately 90% cases of non valvular AF, multiple approaches have been tested recently for stroke prevention. Surgical LAA obliteration is recommended by ACC/AHA guidelines for all patients undergoing mitral valve surgery and is also performed as a part of ablation surgery for AF (Maze procedure). LAA exclusion is not a routine part of coronary surgery and the strategy of LAA obliteration was tested in a small randomized study[8] of 77 patients of whom 52 underwent LAA occlusion. During surgery 9 patients developed LAA laceration and 2.6% patients developed stroke during a follow up of 13+7 months. The data on surgical LAA closure in non valvular AF patients is very sparse today and the strategy cannot be recommended as a routine.

Considerable progress has been achieved in trans-catheter closure of LAA over past decade. The procedure involves trans-septal delivery of LAA occlusion device into the opening of LAA so as to occlude the LAA. The first device developed for LAA occlusion was PLAATO, which was a self expanding nitinol cage covered with an impermeable PTFE membrane. In a non randomized study[9] of 111 patients with $CHADS_2$ score of 2.5, the device reduced annual stroke rate to 2.2% (as against the expected rate of 6.3% according to $CHADS_2$ score). Although the follow up was limited to 17 months, this study showed promising results which encouraged further development of the technology.

The next device developed was WATCHMAN device which is a self expanding nitinol frame with permeable

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polyethylene membrane and is available in various sizes to fit the varying LAA anatomy. Initial experience of WATCHMAN device was reported on 66 patients treated successfully with a mean follow-up of 740+341 days[10]. Successful sealing of LAA was achieved in 93% patients and 91.7% patients were able to discontinue warfarin. No ischemic stroke was reported during the follow up although there were two incidences of TIA. The results were comparable to PLAATO system. Following the initial results, PROTECT AF[11] study was conducted on 800 patients. Patients with non valvular AF were randomized in 2:1 ratio to either WATCHMAN device or warfarin. All patients were suitable for warfarin therapy. Patients undergoing device implantation were treated with warfarin for 45 days after which a TEE was performed to check complete sealing of LAA. 87% patients were able to discontinue warfarin based on the TEE results. The composite of efficacy events occurred in3.4% of device group and 5.0% in the control group. Device group also had fewer deaths and hemorrhagic strokes as compared to control. However more safety events occurred in the device group, majority during the peri-procedural period. The most important being pericardial effusion which occurred in 5% without any mortality related to pericardial effusion. The incidence of pericardial effusion declined over the study period indicating the learning curve for the device implantation.

The results of PROTECT AF are quite encouraging, although more work is clearly required to establish LAA occlusion as alternative therapy to oral anticoagulation for patients of non valvular AF. Safety considerations related to device implantation include air embolism due to usage of large sized sheath in the left heart, device embolization and pericardial effusion. Considerable expertise in interventional procedures is required to circumvent the safety issues. The most important observation from the existing studies is that the safety issues are only during the peri-procedural period and the risk declines dramatically during follow-up. Better operator experience, design improvements and imaging techniques will help in future to minimize the safety concerns.

A new device – Trans catheter patch - has been recently reported in a small series of patients to provide reliable LAA occlusion without risk of pericardial effusion[12]. The TP is a frameless balloon deliverable device which is held in LAA with use of surgical adhesive and released after 45 min once the adhesion of patch is confirmed on TEE. The frameless structure allows use of single size for all LAA occlusions and frameless structure eliminated incidence of pericardial effusion.

Conclusions

Stroke prevention in AF has heavily rested on the use of oral anticoagulants in absence of other reliable modalities. Advent of oral Factor Xa inhibitors is a welcome development, although cost of these agents will be an important issue in a country like ours. Trans-catheter LAA occlusion devices have been evolving and appear promising in stoke prevention without a need of continuous monitoring and risks of bleeding complications. However, data on larger number of patients and a longer follow up is needed before these devices can be recommended as alternative to oral anticoagulants.

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