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Left atrial appendage occlusion – Closure or just the beginning?

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Patients with atrial fibrillation account for one of every six strokes, and thromboemboli originating from the left atrial appendage are the suspected culprit in the vast majority of these cases. Warfarin, a vitamin K antagonist, is the most commonly prescribed treatment for stroke prevention in patients with atrial fibrillation; yet despite warfarin's proven benefit, its effective delivery is challenged by a narrow therapeutic window and an increased risk of bleeding. Efforts have been made to develop alternative treatment strategies — including occlusion of the left atrial appendage. Interest in removing or occluding the left atrial appendage for stroke prevention dates back to the 1930s. Many centers now routinely remove it during valve or arrhythmia surgery, and removal is recommended to reduce the risk of stroke in selected patients undergoing cardiac-valve surgery. Interest in nonsurgical closure of the left atrial appendage has spawned development of percutaneous devices, but no device has been approved by the FDA for this purpose. The Watchman device is a self-expanding structure made of nitinol that is delivered percutaneously, with the use of femoral venous access and a transseptal technique, to the left atrial appendage.The pivotal clinical trial evaluating this device was the Embolic Protection in Patients with Atrial Fibrillation (PROTECT-AF) trial,a multicenter, prospective, unblinded study of patients with nonvalvular atrial fibrillation. Patients were randomly assigned to receive conventional warfarin therapy or the Watchman device plus short-term warfarin therapy (45 days). The primary effectiveness end point was a composite of the absence of ischemic and hemorrhagic stroke, cardiovascular and unexplained death, and systemic embolism.

Results:After 900 patient-years of observation, the rate of these events was 32% lower in the Watchman group than in the conventional-therapy group — a result that met the prespecified criterion for noninferiority. The interpretation of the data and the device's proper clinical role, however, are complicated by several important considerations: the compliance at warfarin was low and INR remained in the therapeutic range only 55% of the time; after 449 attempted implantations, the device was successfully placed in 408 patients (90.9%) and 12.3% of patients had serious procedural complications, including pericardial effusion requiring drainage or surgery. The protocol for the PROTECT-AF trial allowed warfarin therapy to be discontinued if transesophageal echocardiography that was performed 45 days after the implantation of the device showed complete or nearly complete occlusion of the

left atrial appendage. Patients who discontinued warfarin therapy were required to take aspirin indefinitely and clopidogrel for 6 months. Despite therapeutic heparinization at implantation, 45 days of warfarin therapy, and aggressive antiplatelet regimens, thrombus was identified on the device in 15 patients (3.7%), including 1 patient in whom it was detected 6 days after an ischemic stroke. The rate of ischemic stroke was 50% higher in the device group than in the warfarin group (3.0% vs. 2.0%), with almost half the events in the device group occurring within 30 days after implantation. Routine brain imaging was not performed, so the true incidence of subclinical cerebral infarcts is not known. The fact that fewer than 100 patients with the device were followed for 2 or more years contributes to the uncertainty regarding efficacy. *Conclusion*: The Watchman device is designed to reduce the risk of thromboembolic events and to offer an alternative to warfarin therapy. Routine implantation does not appear to be warranted, though the device is promising and may be a reasonable option for selected patients with a particularly high risk of bleeding complications. ❑

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