Left Atrial Appendage Occlusion: Data Update

Matthew J. Price, MD

KEYWORDS

• Left atrial appendage • Atrial fibrillation • Thromboembolism • WATCHMAN
• Oral anticoagulation • Amulet

KEY POINTS

- Meta-analysis of the long-term follow-up of the PROTECT-AF and PREVAIL trials demonstrate that, compared with long-term warfarin, WATCHMAN LAA closure significantly reduces the composite endpoint of cardiovascular death, stroke, or systemic embolism, and reduces hemorrhagic stroke and all cause mortality.
- Pooled analyses of the WATCHMAN trials shows a significant reduction in major bleeding compared with warfarin once the post-implant pharmacologic regimen is completed.
- Observational data confirms improved procedural safety for WATCHMAN LAA closure since the early research experience.
- The AMULET randomized trial will evaluate whether the efficacy of Amulet LAA occluder is non-inferior to the WATCHMAN device.
- Further studies are required to define the optimal post-implant medical regimen to minimize device thrombus and bleeding, to clarify the relative efficacy of LAA closure compared with non-vitamin K oral anticoagulation, and to robustly demonstrate, in a randomized fashion, the safety and efficacy of LAA closure in patients who are ineligible for oral anticoagulation.

INTRODUCTION

Resection of the left atrial appendage (LAA) to prevent recurrent arterial emboli in patients with atrial fibrillation (AF) was first suggested more than 60 years ago,[1] and concomitant exclusion or removal of the LAA during cardiac surgery in high-risk patients with AF is now commonplace. More than a decade and a half has passed since small observational experiences reported the feasibility of transcatheter LAA occlusion.[2] However, longer-term follow-up from randomized studies of the safety and efficacy of LAA occlusion have only recently been completed; data from large, observational cohorts are now being reported. These recent data provide further insights into procedural safety with current techniques and the ability of LAA closure to reduce the risk of thromboembolic stroke compared with warfarin anticoagulation. This review summarizes the latest data regarding transcatheter LAA occlusion, focusing on larger prospective studies and further analyses of seminal clinical trials.

DATA FOR THE WATCHMAN LEFT ATRIAL APPENDAGE OCCLUDER

The WATCHMAN device (Boston Scientific, Natick, Massachusetts) is a parachute-shaped self-expanding device consisting of a nitinol frame and a polyethylene terephthalate fabric membrane cap that faces the body of the left atrium. Small tines that project back toward the left atrium line the circumference of the distal portion of the device that, in combination with radial force, anchor the device within the LAA.[3] The device was approved by the US Food and Drug Administration (FDA) because of the results from 2 randomized clinical trials, the PROTECT-AF

Division of Cardiovascular Diseases, Scripps Clinic, 9898 Genesee Avenue, AMP-200, La Jolla, CA 92037, USA
E-mail address: price.matthew@scrippshealth.org

Intervent Cardiol Clin 7 (2018) 159–168
https://doi.org/10.1016/j.iccl.2017.12.002

(WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) study[4] and the smaller PREVAIL (Prospective Randomized Evaluation of the WATCHMAN Left Atrial Appendage Closure Device In Patients with Atrial Fibrillation vs Long-term Warfarin Therapy)[5] study, as well as the respective trials' continuing access registries. All of these studies enrolled patients with AF at higher risk of thromboembolism who were eligible for long-term oral anticoagulant therapy. More recent data regarding the WATCHMAN device include the final, 4-year follow-up from PROTECT-AF,[6] pooled patient-level meta-analyses of the two randomized trials,[7,8] and large prospective observational cohorts of WATCHMAN LAA closure in clinical practice.[9,10] These studies provide additional information regarding device safety and long-term bleeding, longer-term efficacy, the use of alternative post-implant pharmacologic regimens, procedural event rates in the commercial setting, and the feasibility of WATCHMAN LAA occlusion in patients who are ineligible for short- or long-term oral anticoagulant therapy.

Late Outcomes of the PROTECT-AF Trial

The PROTECT-AF trial randomly assigned 707 patients with AF with a $CHADS_2$ (congestive heart failure, hypertension, age $\geq$75 years, diabetes mellitus, and stroke/transient ischemic attack) score of 1 or greater who were eligible for long-term oral anticoagulant to either WATCHMAN LAA closure or warfarin in a 2:1 ratio.[4] The primary end point was a composite of cardiovascular or unexplained death, stroke, or systemic embolism. Patients who received the WATCHMAN device were continued on warfarin therapy for 6 weeks after the procedure, at which time they were transitioned to dual antiplatelet therapy with aspirin and clopidogrel for 5 months followed by indefinite aspirin maintenance therapy if LAA sealing was confirmed by transesophageal echocardiography (TEE) (Fig. 1). This

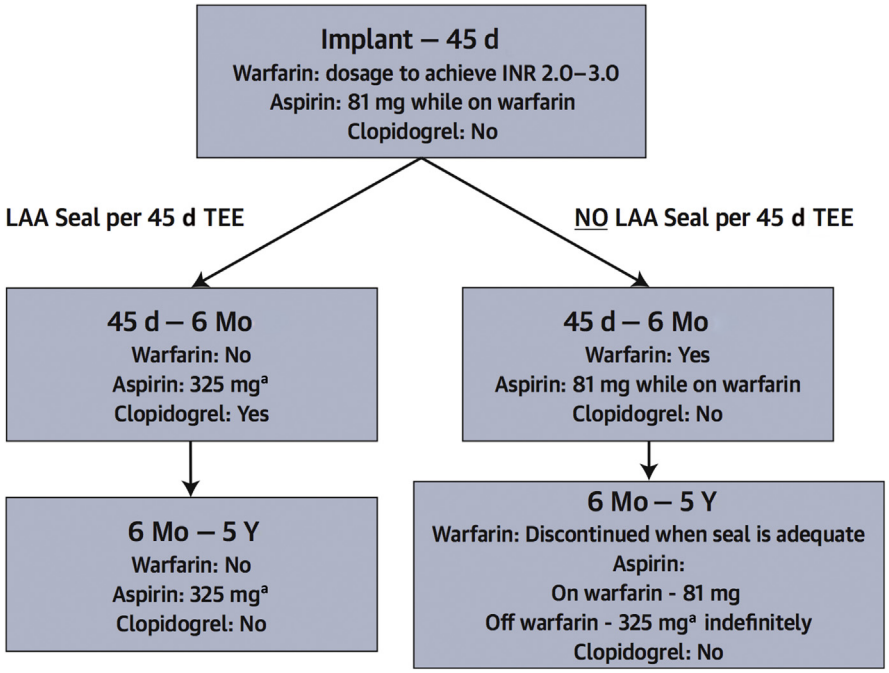

Fig. 1. Anticoagulant and antiplatelet management strategy in patients receiving device therapy in the PROTECT-AF and PREVAIL randomized clinical trials of the WATCHMAN LAA occluder. After device implantation, patients were treated with a combination of warfarin and aspirin for approximately 6 weeks, at which time TEE was performed. If the LAA was sealed (defined as a residual leak <5 mm in width without evidence of thrombus), warfarin was discontinued and the patients were treated with aspirin and clopidogrel until 6 months after the procedure, at which time the clopidogrel was discontinued and patients were continued on aspirin monotherapy. In the PROTECT-AF trial, patients could also receive clopidogrel at study entry if clinically indicated. [a]Recommended dosage. INR, international normalized ratio. (*Adapted from* Holmes DR, Jr, Kar S, Price MJ et al. Prospective randomized evaluation of the WATCHMAN left atrial appendage closure device in patients with atrial fibrillation vs long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol 2014;64:3; with permission.)