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Quality of Life Assessment in the Randomized PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) Trial of Patients at Risk for Stroke With Nonvalvular Atrial Fibrillation

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Objectives This study sought to assess quality of life parameters in a subset of patients enrolled in the PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial.

Background The PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial demonstrated that in patients with nonvalvular atrial fibrillation (AF) and CHADS2 (congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism) score $\geq$1, a left atrial appendage closure device is noninferior to long-term warfarin for stroke prevention. Given this equivalency, quality of life (QOL) indicators are an important metric for evaluating these 2 different strategies.

Methods QOL using the Short-Form 12 Health Survey, version 2, measurement tool was obtained at baseline and 12 months in a subset of 547 patients in the PROTECT AF trial (361 device and 186 warfarin patients). The analysis cohort consisted of patients for whom either paired quality of life data were available after 12 months of follow-up or for patients who died.

Results With the device, the total physical score improved in 34.9% and was unchanged in 29.9% versus warfarin in whom 24.7% were improved and 31.7% were unchanged ($p = 0.01$). Mental health improvement occurred in 33.0% of the device group versus 22.6% in the warfarin group ($p = 0.06$). There was a significant improvement in QOL in patients randomized to device for total physical score, physical function, and in physical role limitation compared to control. There were significant differences in the change in total physical score among warfarin naive and not–warfarin naive subgroups in the device group compared to control, but larger gains were seen with the warfarin naive subgroup with a 12-month change of 1.3 ± 8.8 versus -3.6 ± 6.7 ($p = 0.0004$) device compared to warfarin.

Conclusions Patients with nonvalvular AF at risk for stroke treated with left atrial appendage closure have favorable QOL changes at 12 months versus patients treated with warfarin. (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation [WATCHMAN PROTECT]; NCT00129545) (J Am Coll Cardiol 2013;61:1790–8) © 2013 by the American College of Cardiology Foundation

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Stroke prevention is critical to the management of patients with nonvalvular atrial fibrillation (AF). Anticoagulation therapy with oral anticoagulants including warfarin has been the standard of care for effective stroke prevention on the basis of numerous randomized clinical trials in this arena (1–3). Despite its high efficacy, there are numerous downsides to the use of warfarin, and these have led to the development of nonpharmacological approaches to stroke prevention. The multicenter randomized PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial revealed that percutaneous left atrial appendage (LAA) closure with the WATCHMAN device (Atritech, a subsidiary of Boston Scientific, Plymouth, Minnesota) was noninferior to warfarin therapy for stroke prevention (4).

Health-related quality of life (HRQOL) measures are important clinical outcome measures of therapy in the treatment of chronic disease, and based on the equivalency of the PROTECT AF trial, quality of life (QOL) indicators are important for evaluating these strategies, particularly in elderly patient populations with multiple comorbidities. It is known that QOL improves when rate and rhythm control of AF is undertaken, irrespective of the mode of treatment (5,6–20), either pharmacologic or using ablation. In contrast, the uses of warfarin for stroke prevention in patients with AF has been shown to either have no impact on QOL or may potentially have a negative impact on QOL in these patients (7).

Currently, there are no QOL data on the patient population undergoing nonpharmacologic approaches to stroke prevention using LAA exclusion. The goal of this study was to assess the changes in QOL parameters over a 12-month period in a subset of patients enrolled in the PROTECT AF trial who underwent LAA closure with the WATCHMAN device versus medical therapy with warfarin anticoagulation therapy alone.

Methods

The prospective, randomized, controlled trial PROTECT AF was performed at 59 sites in the United States and Europe. Enrollment began in February 2005 and ended in June 2008. Patients who were age 18 years or older with paroxysmal, persistent, or permanent nonvalvular AF were eligible for enrollment if they had a CHADS2 (congestive heart failure, hypertension, age, diabetes mellitus, and prior stroke, transient ischemic attack, or thromboembolism) (21) risk score of 1 or more (i.e., at least 1 of the following: previous stroke or transient ischemic attack, congestive heart failure, diabetes mellitus, hypertension, or were 75 years of age or older). Exclusion criteria included contraindications to warfarin, comorbidities other than AF that required chronic warfarin use, LAA thrombus, a patent foramen ovale with atrial septal aneurysm and right-to-left shunt, mobile aortic atheroma, and symptomatic carotid artery disease. After baseline screening, patients were randomly assigned by a computer-generated randomization sequence to intervention group or control group in a 2:1 ratio.

Abbreviations and Acronyms

AF = atrial fibrillation
HRQOL = health-related quality of life
LAA = left atrial appendage
QOL = quality of life

A subset of 547 patients in the PROTECT trial (361 device and 186 control patients) are included in this analysis. Patients with complications and adverse events with the WATCHMAN device implant were included in the analysis. Randomized patients excluded from the analysis include the following: patients who did not provide a baseline QOL; patients who did not provide a 12-month QOL (exception made for patients who died before 12 months); and patients with an unsuccessful implant of the device as they were required by protocol to exit the study at 45 days post-implant attempt, therefore not providing a 12-month QOL. As shown in Figure 1, of the 361 patients enrolled in the device arm, 12 patients died before 12 months, and of the 186 patients enrolled in the control arm, 8 patients died before 12 months; therefore, 12-month QOL analyses were unavailable for these patients.

Procedure. Patients allocated to the intervention group received percutaneous closure of the LAA with the WATCHMAN device. This device is a self-expanding nickel titanium (nitinol) frame structure with fixation barbs and a permeable polyester fabric cover. It is implanted through a transseptal approach by use of a catheter-based delivery system to seal the ostium of the LAA. The implantation is guided by fluoroscopy and transesophageal echocardiography to verify proper positioning and stability. Patients in the device group were treated with acetylsalicylic acid and warfarin for 45 days after implant to facilitate device endothelialization. If the 45-day echocardiography documented satisfactory closure of the LAA (22,23), then the patient was switched to acetylsalicylic acid and clopidogrel for 4.5 months, after which acetylsalicylic acid alone was continued indefinitely. Patients in the control group received warfarin for the duration of the study, target international normalized ratio between 2.0 and 3.0. The patient's treating physician monitored the international normalized ratio at least every 2 weeks for 6 months and at least once a month thereafter.

Quality of life assessment. HRQOL was assessed using the generic validated questionnaire Short-Form 12 Health Survey, version 2 (SF-12v2), which offers a short, precise, statistically

tego, CSI, CVRx, EndoCross, EndoTex, Epitek, ev3, FlowCardia, Gore, Guidant, Guided Delivery Systems, InSeal Medical, Lumen Biomedical, HLT, Kensey Nash, Kyoto Medical, Lifetech, Lutonix, Maya Medical, Medinol, Medtronic, NDC, NMT, OAS, Occlutech, Osprey, Ovalis, Pathway, PendraCare, Percardia, pfm Medical, Recor, ResMed, Rox Medical, Sadra, Sorin, Spectranetics, SquareOne, Trireme, Trivascular, Velocimed, Veryan, and Vessix. Dr. Mullin is a paid consultant for NAMSA. Dr. Swarup has research relationships with Biosense Webster, St. Jude Medical, Boston Scientific, Medtronic, and Biotronik. Dr. Whisenant is a consultant to and has equity in Coherex. Dr. Alli has reported he has no relationships relevant to the contents of this paper to disclose.

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