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# Effects of Atrial Fibrillation on Treatment of Mitral Regurgitation in the EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) Randomized Trial

Howard C. Herrmann, MD,* Zachary M. Gertz, MD,* Frank E. Silvestry, MD,* Susan E. Wiegers, MD,* Y. Joseph Woo, MD,* James Hermiller, MD,† Douglas Segar, MD,† David Heimansohn, MD,† William Gray, MD,‡ Shunichi Homma, MD,‡ Michael Argenziano, MD,‡ Andrew Wang, MD,§ James Jollis, MD,§ Mark B. Lampert, MD,‖ John Alexander, MD,‖ Laura Mauri, MD,¶ Elyse Foster, MD,# Donald Glower, MD,§ Ted Feldman, MD‖

*Philadelphia, Pennsylvania; Indianapolis, Indiana; New York, New York; Durham, North Carolina; Evanston, Illinois; Boston, Massachusetts; and San Francisco, California*

**Objectives** The purpose of this study was to characterize patients with mitral regurgitation (MR) and atrial fibrillation (AF) treated percutaneously using the MitraClip device (Abbott Vascular, Abbott Park, Illinois) and compare the results with surgery in this population.

**Background** The EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) randomized controlled trial compared a less invasive catheter-based treatment for MR with surgery, providing an opportunity to assess the impact of AF on the outcomes of both the MitraClip procedure and surgical repair.

**Methods** The study population included 264 patients with moderately severe or severe MR assessed by an independent echocardiographic core laboratory. Comparison of safety and effectiveness study endpoints at 30 days and 1 year were made using both intention-to-treat and per-protocol (cohort of patients with MR ≤2+ at discharge) analyses.

**Results** Pre-existing AF was present in 27% of patients. These patients were older, had more advanced disease, and were more likely to have a functional etiology. Similar reduction of MR to ≤2+ before discharge was achieved in patients with AF (83%) and in patients without AF (75%, p = 0.3). Freedom from death, mitral valve surgery for valve dysfunction, and MR >2+ was similar at 12 months for AF patients (64%) and for no-AF patients (61%, p = 0.3). At 12 months, MR reduction to <2+ was greater with surgery than with MitraClip, but there was no interaction between rhythm and MR reduction, and no difference in all-cause mortality between patients with and patients without AF.

**Conclusions** Atrial fibrillation is associated with more advanced valvular disease and noncardiac comorbidities. However, acute procedural success, safety, and 1-year efficacy with MitraClip therapy is similar for patients with AF and without AF. (J Am Coll Cardiol 2012;59:1312–9) © 2012 by the American College of Cardiology Foundation

From the *University of Pennsylvania Medical Center, Philadelphia, Pennsylvania; †Care Group Heart Center, Indianapolis, Indiana; ‡Columbia University Medical Center, New York, New York; §Duke University Medical Center, Durham, North Carolina; ‖Northshore University Health System, Evanston, Illinois; ¶Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts; and the #University of California San Francisco, San Francisco, California. Dr. Herrmann has received research funding from Abbott Vascular; and has equity in Micro Interventional Devices Inc. Dr. Hermiller is a consultant for Abbott Vascular. Dr. Gray has received research support and is a consultant for Abbott Vascular. Dr. Argenziano is a consultant receiving fees from Abbott Vascular. Dr. Wang has received research funding from Abbott Vascular and Gilead Sciences; and is on the clinical events committee for Edwards Lifesciences. Dr. Mauri has received grant support from Abbott Vascular, Boston Scientific, Cordis, Medtronic, Eli Lilly, Bristol-Myers Squibb, Sanofi-Aventis, and Daiichi Sankyo; is a consultant for Abbott Vascular, and Cordis; and is an expert witness for Cordis. Dr. Foster has received grant support from Abbott Vascular. Dr. Glower has received grant support from Abott Laboratories. Dr. Feldman is a consultant and receives research grants from Abbott, Boston Scientific, and Edwards. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Atrial fibrillation (AF) develops commonly in patients with mitral regurgitation (MR), with a reported rate as high as 5% per year (1). Patients with both AF and MR have increased rates of cardiac events (1,2). For this reason, the onset of AF is considered a class IIa indication for mitral valve surgery in patients with severe MR (3).

Surgical series of mitral repair or replacement have demonstrated that patients with AF are older, have more comorbidities, and have more advanced disease (4–6). In some studies, the outcomes of surgery in patients with AF have been similar to those in patients without AF (4,7), whereas others have reported worse surgical outcomes (8,9). Persistent AF after surgery is associated with reduced medium- and long-term survival (4–6,8,10).

Recently, a less invasive catheter treatment for MR with the MitraClip device was compared with surgery in the EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) randomized controlled trial (11,12). In the present analysis of the EVEREST II study, we sought to determine: 1) the effects of both surgery and MitraClip device (Abbott Vascular, Abbott Park, Illinois) therapy with core laboratory assessment of MR in AF patients who are older than those in most prior series; 2) whether a less invasive therapy than surgery would have a better outcome for AF patients than for those in previous surgical series; and 3) whether AF makes it more difficult to grasp leaflets with the MitraClip device.

**Abbreviations and Acronyms**

**AF** = atrial fibrillation
**ITT** = intention to treat
**LA** = left atrial
**LV** = left ventricular
**MR** = mitral regurgitation
**NYHA** = New York Heart Association
**PP** = per protocol

## Methods

**Study population.** The study included 279 patients at 37 study centers in the United States and Canada who participated in the randomized EVEREST II study (11). A detailed description of the trial methodology, inclusion and exclusion criteria, and the results have been previously described (11,12). Briefly, all patients had moderately severe or severe mitral regurgitation (3+ or 4+) with a left ventricular (LV) ejection fraction >25%. Patients were symptomatic, or if asymptomatic, had a LV end-systolic diameter of 40 mm to 55 mm, new AF, or pulmonary hypertension. Patients were randomly allocated 2:1 to MitraClip repair or surgery and the primary composite endpoint for effectiveness was freedom from death, from surgery for mitral valve dysfunction, and from grade 3 or 4+ MR at 12 months. The primary safety endpoint was the rate of major adverse events at 30 days. All echocardiograms were assessed by an independent core laboratory, and quantitative and qualitative MR grading was performed according to the American Society of Echocardiography guidelines (11,12).

**Flow chart of AF patients.** For this post-hoc analysis of the EVEREST II randomized study, patients were classified on the basis of their baseline rhythm at the time of randomization. The rhythm data were missing in 15 patients, leaving a total of 264 subjects available for analysis. A flow chart detailing the patients available at various timepoints stratified by analysis group, rhythm, and treatment received is shown in Figure 1.

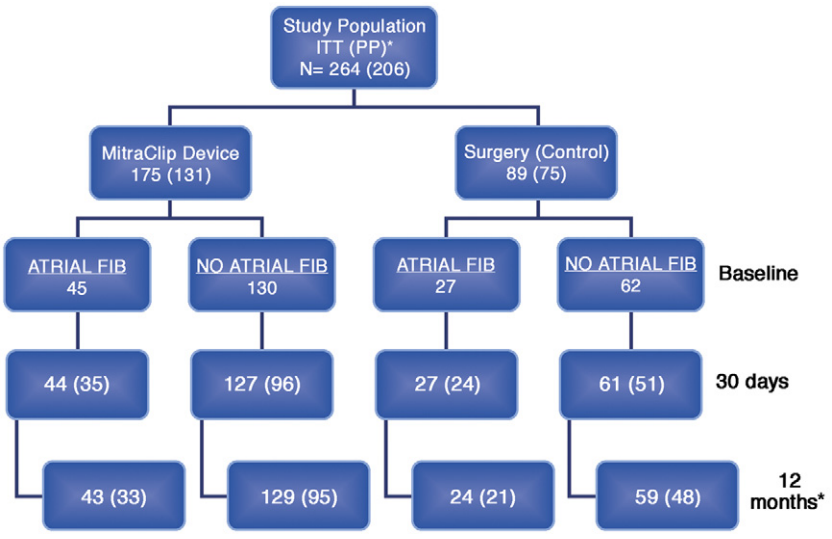


**Figure 1** Flow Chart of Study Population

The number of patients available for analysis at each time point are shown for the intention-to-treat (ITT) population and also for the per-protocol cohort (PP [in parentheses]). *At 12 months, ITT patients who did not receive treatment (MitraClip device or mitral valve surgery) were assumed to have 3+ or 4+ MR and were included in the analysis. FIB = fibrillation.