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Extended Use of Percutaneous Edge-to-Edge Mitral Valve Repair Beyond EVEREST (Endovascular Valve Edge-to-Edge Repair) Criteria

30-Day and 12-Month Clinical and Echocardiographic Outcomes From the GRASP (Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation) Registry

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ABSTRACT

OBJECTIVES This study sought to compare, in high-risk patients with 3+ to 4+ mitral regurgitation (MR) dichotomized by baseline echocardiographic features, acute, 30-day, and 12-month outcomes following percutaneous mitral valve repair using the MitraClip.

BACKGROUND The feasibility and mid-term outcomes after MitraClip implantation in patients with echocardiographic features different from the EVEREST (Endovascular Valve Edge-to-Edge Repair) I and II trials have been scarcely studied.

METHODS Clinical and echocardiographic outcomes through 12-month follow-up of consecutive patients who underwent MitraClip implantation were obtained from an ongoing prospective registry. Two different groups, divided according to baseline echocardiographic criteria (investigational group [$EVEREST_{OFF}$] and control group [$EVEREST_{ON}$]), were compared.

RESULTS Seventy-eight patients were included in $EVEREST_{OFF}$ and 93 patients in $EVEREST_{ON}$ groups. Important and comparable acute reductions in MR and no clip-related complications were revealed. The primary safety endpoint at 30 days was comparable between groups (2.6% vs. 6.5%, respectively, $p = 0.204$); in addition, MR reduction was mostly sustained, whereas equivalent improvement in New York Heart Association functional class were demonstrated. Kaplan-Meier freedom from death, surgery for mitral valve dysfunction, or grade ≥3+ MR at 12 months was demonstrated in 71.4% and 76.2%, respectively, in the $EVEREST_{OFF}$ and $EVEREST_{ON}$ groups (log rank $p = 0.378$). Significant improvements in ejection fraction and reduction in left ventricle volumes were demonstrated in both groups over time, but the baseline between-group differences were sustained.

CONCLUSIONS MitraClip implantation in patients with expanded baseline echocardiographic features, compared with the control group, was associated with similar rates of safety and efficacy through 12-month follow-up. Further validation of our findings is warranted. (J Am Coll Cardiol Intv 2015;8:74–82) © 2015 by the American College of Cardiology Foundation.

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Severe mitral regurgitation (MR) leads to incremental left ventricle (LV) dysfunction and increasing rates of hospitalization for heart failure (1). Although mitral valve surgery is the gold standard therapy in patients with moderate-to-severe (3+) or severe (4+) MR associated with symptoms or evidence of LV dysfunction (2), its benefits are controversial in functional MR, where lack of survival benefit and high rates of recurrence have been demonstrated (3). In addition, morbidity and mortality among high-risk patients that undergo mitral valve surgery are relevant in this setting (4,5), which explains why a substantial proportion of patients is referred to isolated medical management rather than surgery in daily clinical practice. Notably, although medical therapy mitigates symptoms, it does not modify the progression of the disease (6).

Percutaneous edge-to-edge mitral valve repair with the MitraClip system (Abbott Vascular, Abbott Park, Illinois) recently emerged as a viable, less invasive, therapeutic option in patients with 3+ or 4+ MR associated with high surgical risk (7). Patients from the initial experience, as well as the ones included in the only randomized controlled trial conducted so far, however, had to fulfill strict echocardiographic criteria to be considered suitable for MitraClip therapy, which largely limited its indications (7,8). Conversely, real-world registries broadened the indications for MitraClip implantation and a significant amount of included patients did not meet the previously established echocardiographic criteria (9,10), but data regarding early and mid-term outcomes in this subset are lacking. On this background, we aimed at assessing the 30-day and 12-month clinical and echocardiographic outcomes after MitraClip implantation in real-world patients who did not meet the key echocardiographic eligibility criteria determined by the EVEREST (Endovascular Valve Edge-to-Edge Repair) I and II studies (7,8).

ABBREVIATIONS AND ACRONYMS

EF = ejection fraction

LV = left ventricle

MR = mitral regurgitation

NYHA = New York Heart Association

METHODS

PATIENTS AND PROCEDURES. Patients with symptoms or signs of LV deterioration and 3+ or 4+ MR determined by combined transthoracic and transesophageal echocardiogram (11) considered to be at high surgical risk by an interdisciplinary team of cardiologists, interventional cardiologists, cardiac surgeons, and anesthesiologists underwent percutaneous edge-to-edge mitral valve repair with MitraClip at Ferrarotto Hospital, University of Catania, Catania, Italy, from August 1, 2008 to December 31, 2013 as part of the ongoing GRASP (Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation) registry; the results of which have been partly published elsewhere (9). After receiving a complete oral and written explanation of the issues surrounding the procedure, all patients included in the study provided written consent. The study was approved by the local ethics committee. Qualifying inclusion and exclusion criteria for MitraClip therapy (clinical and echocardiographic), as well as details of the procedure have been previously reported (12). Data were obtained from the MitraClip electronic database of Ferrarotto Hospital. Echocardiographic data were separately analyzed by a team of 2 expert echocardiographists and reviewed by a third reader for consensus when there was disagreement. The study groups were defined based on previously published echocardiographic criteria from the EVEREST I and II trials (7,8) as follows: 1) valve geometry features: coaptation length ≥2 mm, coaptation depth <11 mm, flail gap <10 mm, flail width <15 mm; and 2) ventricle function/geometry: ejection fraction [EF] >25%, and LV end-systolic diameter ≤55 mm. Patients that did not fulfill these criteria represented the investigational group (i.e., $EVEREST_{OFF}$ group), whereas patients that fulfilled these criteria represented the control group (i.e., $EVEREST_{ON}$ group). Clinical and echocardiographic outcomes, which were prospectively collected at 30-day and 12-month follow-ups, were then compared between the 2 groups.

ENDPOINTS. Acute device success was defined as residual MR ≤2+ after clip implantation. The primary safety endpoint was the incidence of major adverse events at 30 days, defined as the composite of death, myocardial infarction, reoperation for failed MitraClip implantation, nonelective cardiovascular surgery for adverse events, stroke, renal failure, deep wound infection, mechanical ventilation for >48 h, gastrointestinal complication requiring surgery, new-onset of permanent atrial fibrillation, septicemia, and transfusion of 2 U of blood. The primary efficacy

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