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Beating-Heart Mitral Valve Repair Using a Novel ePTFE Cordal Implantation Device

A Prospective Trial

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ABSTRACT

BACKGROUND Conventional mitral valve (MV) operations allow direct anatomic assessment and repair on an arrested heart, but require cardiopulmonary bypass, aortic cross-clamping, sternotomy or thoracotomy, and cardioplegic cardiac arrest, and are associated with significant perioperative disability, and risks of morbidity and mortality.

OBJECTIVES This study evaluated safety and performance of a transesophageal echocardiographic-guided device designed to implant artificial expanded polytetrafluoroethylene (ePTFE) cords on mitral leaflets in the beating heart.

METHODS In a prospective multicenter study, 30 consecutive patients with severe degenerative mitral regurgitation (MR) were treated with a mitral valve repair system (MVRS) via small left thoracotomy. The primary (30-day) endpoint was successful implantation of cords with MR reduction to moderate or less.

RESULTS The primary endpoint was met in 27 of 30 patients (90%). Three patients required conversion to open mitral surgery. There were no deaths, strokes, or permanent pacemaker implantations. At 1 month, MR was mild or less in 89% (24 of 27) and was moderate in 11% (3 of 27). At 6 months, MR was mild or less in 85 % (22 of 26), moderate in 8% (2 of 26), and severe in 8% (2 of 26). Favorable cardiac remodeling at 6 months included decreases in end-diastolic (161 ± 36 ml to 122 ± 30 ml; $p < 0.001$) and left atrial volumes (106 ± 36 ml to 69 ± 24 ml; $p < 0.001$). The anterior-posterior mitral annular dimension decreased from 34.7 ± 5.8 mm to 28.2 ± 5.1 mm; $p < 0.001$ as did the mitral annular area (10.0 ± 2.7 cm^2 vs. 6.9 ± 2.0 cm^2; $p < 0.0001$).

CONCLUSIONS MVRS ePTFE cordal implantation can reduce the invasiveness and morbidity of conventional MV surgery. The device's safety profile is promising and prospective trials comparing the outcomes of the MVRS to conventional MV repair surgery are warranted. (CE Mark Study for the Harpoon Medical Device [TRACER]; NCT02768870)
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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

ePTFE = expanded polytetrafluoroethylene

H-MVRS = Harpoon mitral valve repair system

IQR = interquartile range

LA = left atrial

LV = left ventricular

MAC = mitral annular calcification

MR = mitral regurgitation

MSSA = methicillin-sensitive *Staphylococcus aureus*

MV = mitral valve

MVRS = mitral valve repair system

SAE = serious adverse event

SAM = systolic anterior motion

TEE = transesophageal echocardiography

Mitral valve (MV) operations are performed most commonly for degenerative mitral regurgitation (MR) (1) and are indicated for patients with symptoms of left ventricular dysfunction, atrial arrhythmias, severe MR, and/or pulmonary hypertension (2). Short- and long-term outcomes after mitral valve repair are superior to outcomes after MV replacements for patients with degenerative disease (3), and successful MV repair alleviates symptoms, prevents and reverses unfavorable ventricular remodeling, and improves survival. Although conventional MV operations allow for complete direct visual anatomic assessment and repair, using a variety of techniques in an arrested heart, they require cardiopulmonary bypass, aortic cross-clamping, sternotomy or thoracotomy, and cardioplegic cardiac arrest and are therefore associated with significant perioperative disability as well as risks of morbidity and mortality (4). MV repair rates are highly variable, with lower successful repair rates observed in low-volume centers (5). The Harpoon MV repair system (H-MVRS) (Harpoon Medical Inc., Baltimore, Maryland) may provide an alternative treatment for patients with degenerative MR. In this procedure, access to the anterior wall of the LV is secured through a small left thoracotomy, and the delivery system is used to anchor artificial expanded polytetrafluoroethylene (ePTFE) cords on the prolapsed segment of the MV on the beating heart by using transesophageal echocardiographic (TEE) guidance. The lengths of the ePTFE cords are then adjusted to optimize leaflet coaptation and minimize MR, and are then secured on the anterior wall of the heart on an ePTFE pledget. The feasibility of this concept has been demonstrated in a pilot study that included the first 11 patients treated with the device (6). We conducted a prospective multicenter observational study to evaluate the safety and performance of this device.

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METHODS

STUDY DESIGN AND OVERSIGHT. The TRACER (Mitral TransApical NeoCordal Echo-Guided Repair; NCT02768870) trial is a prospective, nonrandomized, multicenter clinical study designed to test the safety and performance of the Harpoon MVRS (Harpoon Medical Inc., Baltimore, Maryland) for MV repair. This planned interim analysis includes protocol-specified clinical and echocardiographic follow-up conducted during the 30-day and 6-month visits from 30 consecutive patients enrolled in the study to support Conformité Européene (CE) Marking for the device. The trial was conducted at 6 clinical centers in Europe and was sponsored by the manufacturer of the MVRS. The 30 patients enrolled in this study were distinct and subsequent to the 11 enrolled in the early feasibility study. The study protocol was approved by the relevant national authorities in each country and the ethics committee at each institution. All patients provided written informed consent prior to enrollment. Serious adverse events (SAEs) were reported by site and adjudicated by an independent data safety and monitoring committee consisting of independent physicians. Monitoring and collection of data and initial data analyses were performed by the sponsor.

PARTICIPANT SELECTION. Patients 18 years of age or older with severe degenerative MR resulting from isolated posterior leaflet prolapse were enrolled. Class I indications for MV operation were present in 17 patients (57%) and Class IIa indications in 13 (43%) (2). Patients underwent protocol-directed pre-operative TEE that included 2-dimensional (2D) and 3D analyses of MV morphology to assess anatomic feasibility. A patient selection committee determined whether the predicted post-repair coaptation surface would be adequate to result in effective MR reduction. Generally, 3D imaging and analysis software (Tomtec imaging systems, Tomtec, Chicago, Illinois) and 2D pan-through TEE imaging (both 4-chamber and long-axis) were used to assess the MV anatomy, with a particular focus on the maximal distance between the free edge of the anterior leaflet and the base of the posterior leaflet (the anteroposterior dimension of the regurgitant orifice). Although a number of anatomical characteristics were evaluated, primary assessment of suitability was based on the ratio of the posterior prolapse segment length (measured with linear polygonal assessment tools (Osirix, Pixmeo SARL, Bernex, Switzerland) to the corresponding anteroposterior distance between the free edge of the anterior leaflet and the base of the prolapsed posterior leaflet segment. A minimum 1.5:1 ratio or higher indicated suitability. This ratio was measured multiple times in succession during a "pan-through" of the valve in both 4-chamber and long-axis views, and the smallest measured ratio was used. Key exclusion criteria included the presence of anterior or bileaflet prolapse, functional MR, severe calcification of the