Assessment of the safety and performance of the HARPOON* Beating Heart Mitral Valve Repair System; a multi-center post-market study (The ASCEND Study).

Published: 25-05-2021
Last updated: 30-11-2024

To evaluate the long-term safety and performance of the HARPOON* MVRS for use in patients presenting with severe degenerative mitral regurgitation due to posterior leaflet prolapse in the post-market phase.

Ethical review	Approved WMO
Status	Completed
Health condition type	Cardiac valve disorders
Study type	Observational non invasive

Summary

ID

NL-OMON50870

Source
ToetsingOnline

Brief title
HARPOON ASCEND study

Condition

- Cardiac valve disorders

Synonym
mitral regurgitation or leaking

Research involving
Human

Sponsors and support

Primary sponsor: HARPOON Medical, an indirect wholly-owned subsidiary of Edwards Lifesciences Corporation
Source(s) of monetary or material Support: the industry

Intervention

Keyword: HARPOON, Mitral regurgitation, Mitral valve repair

Outcome measures

Primary outcome

Primary Safety Endpoint:

Freedom from all-cause mortality, disabling stroke and life- threatening

bleeding at 30 days post-implant.

Primary Performance Endpoint:

Procedure success at 30 days post-treatment, as measured by: Technical success

with reduction of MR to less than or equal to mild and the absence of major

device or procedure-related SAEs.

Secondary outcome

- Technical success defined as survival and exit from the operating room (OR)

with successful implantation of 3 or more expanded polytetrafluoroethylene

(ePTFE) chords.

- Freedom from major device or procedure-related serious adverse event (SAE) at

30 days, 1 year and 2 years post-implant

- Quality of Life (change from baseline to 1 and 6 months)

- 6-minute walk test (change from baseline to 1 and 6 months)

- Freedom from ePTFE chord rupture as reported by echo core lab at 1 year and 2

years post-implant

- Freedom from reoperation or re-intervention due to ePTFE chord rupture at 1

year and 2 years post-implant

- Functional improvement from baseline NYHA Functional Classification at 1 year

and 2 years post-implant

- Freedom from reoperation or reintervention on the mitral valve annually

through 5 years post-implant

- Freedom from >= moderate MR annually through 5 years post-implant

Study description

Background summary

Mitral valve disease is the second most common valvular heart disorder requiring surgery in Europe, with nearly 8 million Europeans estimated to have severe mitral valve regurgitation (MR) (AGENAS, 2015). MR results in a volume overload on the left ventricle which in turn leads to ventricular dilation, decreased ejection performance, pulmonary hypertension, symptomatic congestive heart failure, atrial fibrillation, right ventricular dysfunction and death. Successful surgical mitral valve repair restores mitral valve function, eliminates volume overload on the left ventricle, improves symptom status and prevents adverse left ventricular remodelling.

The large majority of MR results from either degenerative disease (caused by elongated or ruptured native chords that fail to support the mitral valve leaflets) or functional ischemic or idiopathic MR (the motion of the normal mitral valve leaflets is restricted by the enlarged ventricle) both of which lead to ineffective valve closure and regurgitation. Other less common causes of chronic primary MR include infective endocarditis, connective tissue disorders, rheumatic heart disease, cleft mitral valve, and radiation heart disease. If the subsequent volume overload of chronic primary MR is prolonged and severe, it causes myocardial damage, heart failure (HF), and eventual death. Correction of the MR is curative (Nishimura et al., 2014).

There is no effective medical treatment for degenerative MR (DMR). Medical treatment, e.g. diuretics, vasodilators, might relieve HF symptoms but does not alter the course of DMR and ultimately surgery will be required (Nishimura et

al., 2016). Two-thirds of all mitral valve surgical procedures in North America are performed on patients with degenerative MR and that percentage is estimated to be similar in Europe. Open cardiac surgery is a common method of treating DMR which involves replacing and/or supplementing elongated or ruptured chords with artificial chords made of ePTFE, a commercially available material which has a 20+ year history of safety in conventional mitral valve repair procedures.

Current ESC/EACTS Guidelines state that surgery is indicated in:
• asymptomatic patients with LVEF <=60% or LVESD >=45mm, new onset AF or SPAP >50mmHg and who are at low surgical risk;
• symptomatic MR patients with LVEF >30% or those who are refractory to medical treatment and in whom a durable valve repair is likely with low comorbidity.

In all patients, valve repair rather than valve replacement is advocated whenever possible and is now the standard of care (Vahanian et al. 2012). A systematic review found that mortality is particularly high in patients >80 years old: 10% for MV replacement (N=3,105) compared with 7% for MV repair (N=2,642), with 5-year survival rates of 23% for MV replacement (N=335) and 29% for MV repair (N=250). It was concluded that many patients are unfit for major heart surgery (Andalib et al. 2014).

Although open-heart surgery is the gold-standard approach for the treatment of severe MR, it is not performed in up to 50% of patients due to the increased risk associated with co-morbidities. Excellent outcomes can be achieved in most patients with minimally invasive approaches and transcatheter mitral interventions might be an alternative therapeutic option (Maisano et al. 2015; Lam et al. 2011).

Mitral valve repair technologies, including the HARPOON* Beating Heart MVRS (Chordal repair), can be used in cases of DMR. The other available treatments to replace ruptured or elongated chordae tendinae can reduce MR. However, other than the HARPOON* Beating Heart Mitral Valve Repair System, there is no currently effective medical therapy that treats or cures MR.

Study objective

To evaluate the long-term safety and performance of the HARPOON* MVRS for use in patients presenting with severe degenerative mitral regurgitation due to posterior leaflet prolapse in the post-market phase.

Study design

A single arm, prospective, multicentre, non-randomised and open-label post-market study.

Study burden and risks

The following is not Standard of Care:
- Study Consent form to be signed.
- STS-risk score prior to the surgery.
- 2 Quality of life questionnaires (SF-36 & KCCQ) to be filled in at 30 days and 6 month follow-up visits.
- 6 minute walk test at 6 month follow-up visits.
- Follow-up visits at 6, 12, 18, 36, 48 and 60 month including all per protocol required assessments.

Risks associated; Participation in the ASCEND study carries additional assessments and imaging above the standard-ofcare. Specifically, study subjects will be assessed via transthoracic echocardiogram (TTE) more often than they would outside of a clinical study. The risk of TTE, however, as it is based on ultrasound technology, is minimal.
Other than the TTE, all other study-specific assessments are simply clinic and physical assessments that would be within the range of standard follow-up of patients with a MR history.
An additional risk of participating in a clinical study is the risk of a lapse of confidentiality or exposure of personal identifying information.

Risk-benefit analysis; The risk involved in the clinical study is minimised due to the fact the device being used is CE-marked and the study design falls within the intended use population. The risk of participating in the study is only minimally increased as compared to receiving the device outside the study, as there is a higher degree of imaging (TTE) and clinical assessment than would be present otherwise. Additionally, there are the risks involved in data collection. These risks, though, have been mitigated by the benefit of additional clinical follow-up and closer care, as well as procedures which have been put in place to protect subjects* personal information.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Each subject is required to meet all of the following inclusion criteria:
1. Subject is > 18 years old
2. Presence of severe MR as read on a transthoracic echocardiographic study
3. Mitral leaflet coaptation surface is sufficient to reduce mitral regurgitation without undue leaflet tension (approximate leaflet to gap ratio of 2:1) based on the judgment of the patient eligibility committee and the operating surgeon
4. Degenerative mitral valve disease with mid-segment P2 prolapse
5. Patient is able to sign informed consent and able to return for follow-up and is capable of participating in all testing associated with this clinical investigation

Exclusion criteria

A subject meeting any of the following criteria shall be excluded:
1. Patient is of the age where further growth is expected
2. Active endocarditis
3. Left ventricular or left atrial appendage thrombus
4. Severe mitral annular and/or leaflet calcification
5. Cannot tolerate procedural anticoagulation or post-procedure antiplatelet regimen
6. Mitral stenosis
7. Functional Mitral Valve disease
8. Previous mitral valve replacement surgery

9. Fragile or thinning apex
10. Contraindications to transoesophageal echocardiography (atlantoaxial disease, severe generalized cervical arthritis, upper gastrointestinal bleeding, significant dysphagia and odynophagia, has received extensive radiation to the mediastinum)
11. Patient is pregnant or lactating

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-09-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	HARPOON Beating Heart Mitral Valve Repair System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	25-05-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04382612
CCMO	NL75980.100.20

Study results

Date completed: 01-12-2022

Summary results
Trial ended prematurely