Original Article

Intensive Care and Anesthesia Management for HARPOON Beating Heart Mitral Valve Repair

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Abstract

Patients with severe mitral valve regurgitation secondary to degenerative disease are known to benefit from mitral valve repair surgery. Novel techniques for achieving mitral valve repair on the beating heart have been developed and are being introduced into clinical practice. The HARPOON Beating Heart Mitral Valve Repair System (MVRS) in recent studies has demonstrated efficacy and safety for the repair of degenerative mitral valve disease on the beating heart. The device uses transoesophageal echocardiographic guidance to implant artificial expanded polytetrafluoroethylene (ePTFE) cords on prolapsed mitral valve leaflets in the beating heart. It requires general anaesthesia and there are specific intensive care and anaesthesia considerations for the safe management of these cases. This article describes the general principles of intensive care and anaesthesia management employed for the initial patients treated with the HARPOON Beating Heart MVRS, the outcomes for these patients, and the potential challenges for the future management of these cases.

Keywords: *Cardiovascular anaesthesia and surgery, catheter-based coronary and valvular interventions, image guidance, mitral valve repair, transesophageal echocardiography, valvular heart disease*

Introduction

Conventional mitral valve repair operations have been performed using cardiopulmonary bypass on the arrested heart either via a median sternotomy or a small thoracotomy. Mitral valve repair for degenerative mitral valve disease utilizing expanded polytetrafluorethylene (ePTFE) cords has proven safe and effective since it was first introduced in 1986. Randomized trials[1] and retrospective series[2] have supported widespread use of chordal replacement techniques for mitral valve repair.[3] It remains a challenge for cardiac surgeons to determine how best to size the artificial cords in an arrested heart.[4]

Recently, several technologies have been developed which allow mitral valve repair on the beating heart without cardiopulmonary bypass.[5,6] The HARPOON Beating Heart MVRS is one technology designed to anchor ePTFE cords to precisely defined locations (using trans-esophageal echocardiography [TEE] guidance) on the prolapsed posterior mitral valve using a delivery system inserted via a dedicated 12Fr hemostatic introducer sited close to the left ventricular apex. Upon deployment a 21-gauge needle protrudes out of the device end-effector, through the posterior mitral leaflet, and into the left atrium, carrying with it an ePTFE cord that automatically knots on the atrial side. Multiple ePTFE cords are anchored in this fashion on the leaflet and the cords are brought out through the left ventricular wall and secured to an epicardial pledget under sufficient tension to achieve a good surface of mitral valve coaptation [Figure 1].

The early results of both an initial feasibility study[7] and a further trial toward gaining CE approval (the "Tracer Trial"),[8] have involved a total of 43 patients in six centers in Europe, with a reported procedural success rate of 95% (41 out of 43 patients), and of those patients with a HARPOON Beating Heart MVRS repair, freedom from moderate magnetic resonance (MR) or worse at 6 months of 89%. In the most recently reported "Tracer Trial,"[8] 28 out of 30 patients underwent successful intraoperative HARPOON Beating Heart MVRS repair; the remaining two cases had to be converted intra-operatively to an open repair on cardiopulmonary bypass. The

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baseline characteristics of those patients who underwent HARPOON Beating Heart MVRS repair are summarized in Table 1.

HARPOON Beating Heart MVRS insertion requires close collaboration between anesthesiologist, image guidance physician (IGP) and surgeon at all procedural phases particularly during the intraoperative guidance and location of the ventricular access site, the placement of the device onto the predetermined targets on the mitral valve, and when guiding the dynamic tensioning of the cords to optimize mitral valve coaptation surface area [Videos 1-3].

General considerations relating to procedures involving a minithoracotomy apply to this procedure including the need to consider analgesia strategies and potential fast-tracking in the postoperative period. There are also specific considerations related to the use of this technology that are outlined in this article.

Patient Selection

Careful preoperative screening is required to identify patients potentially suitable for the HARPOON Beating Heart MVRS. This includes detailed preoperative three-dimensional TEE. At present, this device has only been used on regurgitant mitral lesions affecting the posterior mitral valve leaflet (PMVL); it has not been evaluated for anterior mitral valve leaflet (AMVL) prolapse, bileaflet prolapse or functional mitral regurgitation lesions. A ratio of at least 1.5 to 1 for the length of the prolapsed PMVL compared to the anteroposterior distance from the base of the prolapsed PMVL to the free edge of the AMVL is also required to predict adequate coaptation [Figure 2]. There has been no experience of using this device with rheumatic valve disease; full details of the inclusion and exclusion criteria that were used in the Harpoon Beating Heart MVRS studies have been previously published.[7,8]

Table 1: Baseline characteristics of the 28 patients who had successful deployment of the HARPOON Beating Heart MVRS in the "Tracer Trial"[8]

Factor	Mean (±SD)
Age	60.2 (±12.8)
Sex (male:female)	21 (75%):7 (25%)
STS score	0.7±0.7
LVEF (%)	68.5±7.2

STS: Society of Thoracic Surgeons, LVEF: Left ventricular ejection fraction

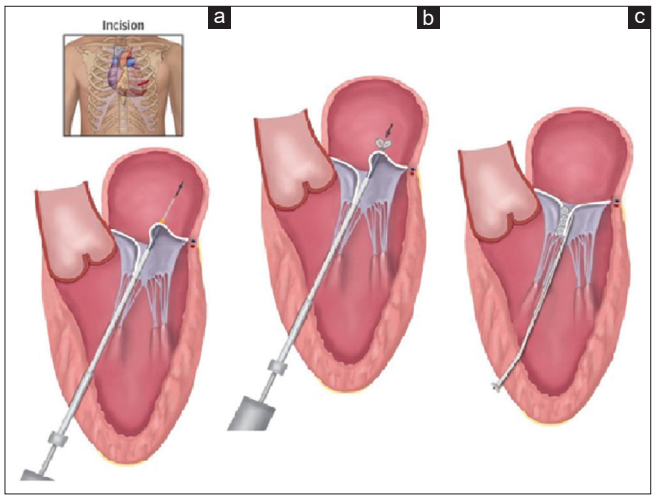

Figure 1: Diagram demonstrating deployment and tensioning of the HARPOON Beating Heart MVRS. (a) Needle fired through prolapsed mitral valve leaflet, (b) Knot deployed on atrial surface of mitral valve, (c) Harpoon cord appropriately tensioned. Reproduced with permission from: Gammie JS, Bartus K, Gackowski A *et al*., Beating-Heart Mitral Valve Repair Using a Novel ePTFE Cordal Implantation Device: Prospective Trial. *Journal of the American College of Cardiology*, 2018 Jan; 71(1): 25-36

Monitoring and Preparation

The layout of the operating room or hybrid laboratory should allow the surgeon to have easy vision of exactly the same echocardiographic images that the IGP is acquiring. This necessitates the use of a "slave screen" that can be seen by the surgeon whilst manipulating the HARPOON Beating Heart MVRS; the surgeon stands to the left side of the patient and the slave screen is positioned on the patient's right side, so it may be viewed at all times. It is critically important that there is clear communication at all times between the surgeon, anesthetist and IGP. All surgical instruments and bypass equipment that would be required for open cardiac surgery, including a clinical perfusionist, should be immediately available in case of the need for conversion to conventional open-heart surgery. Patient testing equipment for heparin management and for hematocrit, electrolyte, and arterial blood gas measurements should be available nearby.

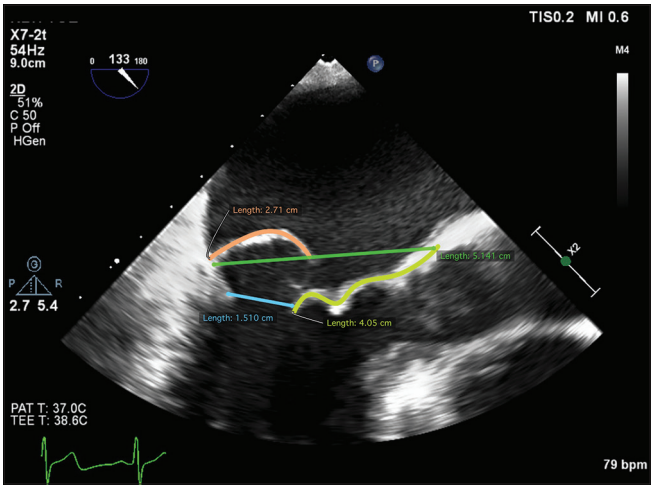

Figure 2: TEE image (mid-esophageal long-axis view), illustrating some of the measurements made when screening for suitability for HARPOON Beating Heart MVRS. Particular importance is made to the ratio between PMVL length (orange line) and the distance between the base of PMVL and the tip of the AMVL (blue line). Note that multiple measurements are made along the breadth of the prolapse, one for each target position for a HARPOON cord. These measurements are made at the peak of the T wave of the electrocardiogram to standardize for multiple measurements

If premedication is deemed necessary, then a short-acting agent is used with a view to promote a rapid emergence in the postoperative period. It is important for successful repair that the patient's underlying heart rate be well controlled; this permits finer, more controlled manipulation of the tip of the HARPOON Beating Heart MVRS to the mitral valve leaflet. The use of preoperative beta-blockade is recommended (for example, using oral bisoprolol), aiming for a resting heart rate of 50-70 beats per minute. Atrial fibrillation is not a contra-indication to the procedure, rate control, regardless of the rhythm is the most important consideration.

On arrival in theaters, the patient has all routine monitoring applied, a large bore venous access line inserted for induction and fluid replacement and an invasive arterial pressure monitoring line. Defibrillator patches should be placed in locations which do not interfere with the mini left thoracotomy (which will likely lie close to the 3rd or 4th intercostal space just anterior to the anterior axillary line), or a potential median sternotomy incision should it be required [Figure 3]. The potential for requirement of conversion to an open mitral repair procedure should be anticipated; to date, three patients (out of a total of 65 procedural attempts) have had intra-operative conversion to open mitral valve repair.

Initial induction, airway, and line management

Following routine induction of anesthesia with short-acting anesthetic agents (avoiding high dose long-acting opiates), a single lumen endotracheal tube is inserted. Although the procedure is performed within the left thoracic cavity, it does not require the use of double-lumen tubes, although a device to isolate the lung (for example with a bronchial blocking device) should be available just in case it is required. Careful attention must be paid to patient eye protection as well as the security of the endotracheal tube, since the TEE probe will be manipulated under the drapes throughout the operation.

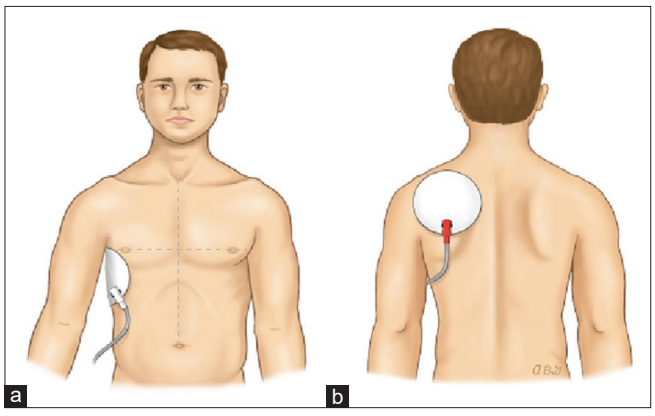

Figure 3: Suggested placement of external defibrillator pads to avoid both the areas of planned incision for the HARPOON Beating Heart MVRS (usually the 3rd or 4th left intercostal space), and a median sternotomy (should it be required). (a) Anterior chest wall, (b) Posterior chest wall. Reproduced with permission from: Cheung AT. Anesthesia for aortic surgery requiring deep hypothermia. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA (accessed on 3rd February 2018) Copyright © 2018 UpToDate, Inc. For more information visit www.uptodate.com

A multi-lumen central venous catheter (CVC) is inserted to permit measurement of right-sided filling pressures and the administration of potent vasoactive agents and heparin. There is a potential benefit to the insertion of the CVC line in the left side of the neck in order to contain any potential intrathoracic complications (such as pneumothorax), to the same side as the thoracotomy; a pulmonary artery catheter is usually not required. Core temperature monitoring and an effective active warming device are very important to maintain patient normothermia. Prophylactic antibiotics according the local hospital protocol should be administered prior to skin incision.

It is prudent to avoid excessive fluid-loading in these patients who have a high circulating fluid volume. Instead vasoactive agents may be used to temporize episodes of low blood pressure. All patients treated so far with the HARPOON Beating Heart MVRS tolerated induction of anesthesia and the procedure itself very well. No inotropic infusions were required for any patient.

Patient Positioning

The patient is positioned on the operating table supine with a padded bolster (500 ml bag of intravenous fluid, or similar) placed behind the left scapula and the arms (with appropriate padding) placed alongside the torso. Once positioned and prior to sterile draping the IGP, together with the operating surgeon, will perform a trans-thoracic echo to determine an optimal site for the skin incision.

Anticoagulation Management

Once the surgeon has exposed the surface of the heart and purse-string sutures have been placed (typically 2-3 cm basal to the apex, between the left anterior and diagonal coronary arteries), the patient is anticoagulated prior to inserting the dedicated introducer into the left ventricle. The anticoagulation management strategy involves heparinization (with an initial dose of 300 units per kilogram) aiming for an activated clotting time (ACT) of >350 sec. Throughout the time that the introducer lies within the left ventricle, a heparinized saline infusion is run under pressure through its side-arm (2,000 units of heparin in 1 L of 0.9% saline delivered at a rate of approximately 1 ml/minute).

Following successful cordal tensioning and adequate surgical hemostasis, protamine is administered (1 mg per 100 units of the initial heparin bolus used), to return the ACT to baseline. Because HARPOON Beating Heart MVRS procedures do not involve the anticoagulant after-effects of cardiopulmonary bypass, there does not appear to be a need for the use of anti-thrombolytic therapy. In the 28 Tracer study patients who received

Harpoon system, there have not been any problems with bleeding and the need for transfusion has been minimal in the as treated cohort, with one patient requiring transfusion during their care.

Physiologic management

Throughout the procedure, maintaining a controlled heart rate of 50-70 beats per minute is crucial to allow accurate placement of the HARPOON Beating Heart MVRS on the prolapsed leaflets. If this has not been accomplished with preoperative oral beta blockade, the anesthetist should use pharmacologic agents to achieve this. This may include altering the depth of anesthesia, using anesthesia agents that can promote a bradycardia (such as dexmedetomidine) or the intravenous administration of beta-blockers, such as esmolol or metoprolol.

During placement of HARPOON Beating Heart MVRS knots in the posterior mitral leaflet, TEE is used to measure the distance from the posterior left atrial wall to the surface of the mitral leaflet as it is draped over the tip of the device. Since the needle throw during device deployment is 22 mm, the anesthesiologist should be prepared to provide a Valsalva maneuver (promoting an increase in left atrial volume) to increase the clearance distance to >25 mm during device deployment. It is prudent for the anesthesiologist to determine in advance if this maneuver will be required by discussing with the surgeon and the physician performing the TEE image guidance. If the need for a Valsalva maneuver is anticipated, the anesthesiologist should determine in advance how much airway pressure is required to provide adequate left atrial (LA) enlargement to accommodate device deployment and whether cautious fluid loading may also be required. It is important to maintain adequate levels of muscle relaxation at this phase since coughing or patient movement would risk damage to the myocardium, mitral valve, or adjacent structures.

The HARPOON Beating Heart MVRS procedure allows the surgeon to suddenly reverse severe mitral regurgitation in a beating heart when the ePTFE cords are tensioned and tied on the epicardial surface. In standard mitral valve repair operations, myocardial depression secondary to ischemic myocardial protection strategies masks the acute hemodynamic changes that are seen with the HARPOON Beating Heart MVRS. In the working, beating heart, sudden MR reversal is associated with a decrease in LA and left ventricle (LV) volume and immediate LV remodeling. This may manifest as an increase in systolic blood pressure secondary to increased forward stroke volume. For this reason, excessive volume infusion before the cords are tensioned is discouraged. Rather, blood pressure is maintained with vasoactive agents, taking care to reduce or terminate these agents prior to final tensioning. Temporary tensioning will be performed and there should be close communication with the surgeon in terms of timing of termination of vasoactive support if it has been required. Following the initial tensioning, it is important to maintain the systolic blood pressure to levels close to that which the patient had pre-operatively. This will permit fine tuning of the tension of the ePTFE cords and will assure that MR has been eliminated at physiologic levels of afterload.

Transfusion

There should be the facility for intraoperative cell salvage and rapid transfusion since there is a requirement for direct access to the left ventricle. The HARPOON Beating Heart MVRS utilizes a small, hemostatic introducer for LV access, and the experience from the "Tracer Trial" demonstrated an average intraoperative blood loss of under 300 ml [Table 2].

Postoperative Pathway

The entire surgical procedure takes approximately 2 h from skin to skin. Depending on individual hospital logistics and intensive care unit (ICU) nursing procedures for "fast track" cardiac surgical patients, extubation can either be performed in the operating room or in the ICU, usually within four hours of arrival, provided the patient is hemodynamically stable, normothermic, and not bleeding.

As in all "fast track" pathways, attention maintaining core temperature throughout the procedure close to normothermia is important. This operation ends quickly after the tensioning of the new e-PTFE cords, with only a small thoracotomy incision to close, so there may not be much time to rewarm the patient at the end of the case. Sedative infusions (propofol or dexmedetomidine) are continued on transfer to the ICU for sedation in the intubated patient.

To minimize the requirement for systemic analgesics, the surgeon should use a non-rib-spreading technique if possible. Surgical site infiltration or intercostal/paravertebral blocks with a long acting local anesthetic agent, such as bupivacaine should be considered based on local practice. Rectal acetaminophen (paracetamol) as well as the intravenous preparation can also be considered as an adjunct to analgesia management as can nonsteroidal inflammatory agents provided there are no contraindications. Minimizing the dose of the intermediate acting opioid agent (for example, with the use of tramadol)

Table 2: Selected outcome measures of the 28 patients who had successful deployment of the HARPOON Beating Heart MVRS in the "Tracer Trial"[8]

Factor	Mean (±SD)
Operative procedure time (hours)	2.1±0.5
Intraoperative blood loss (ml)	268.3±159
Intraoperative blood product transfusion (% of patients)	0%
Inotrope administration (% of patients)	25%
Postoperative reintubation (% of patients)	0%
Readmission to intensive care (% of patients)	0%

to allow for early extubation, while providing adequate analgesia, is always patient specific and depends on the judgment of the anesthesiologist/intensivist. In general, data support improved pulmonary outcomes associated with earlier rather than later extubation in cardiac patients.[9,10]

Intensive care management

Patients require at least overnight hemodynamic monitoring, just like any other patient who has had cardiac surgery. Most will have a left pleural drain on suction that should be removed as soon as there are no concerns with bleeding. The ideal pathway involves extubation either in the operating room or within 4 h of arrival to the ICU or recovery room, and the removal of CVC, drains, and arterial and urinary catheters within 24 h. Early mobilization is a priority and a nursing assessment of the return of baseline neurologic and mental status should be conducted as soon as reasonable after extubation.

Although not required in the clinical experience so far, it is important that there are the usual facilities on the ICU to perform an immediate median sternotomy (through a "virgin" chest), if required in an emergency.

Aspirin (325 mg orally) is administered on postoperative day one (provided there are no concerns regarding bleeding) and then continued through the post-operative period.

Future considerations

Up to the present time the HARPOON Beating Heart MVRS clinical trial protocols have excluded patients with significant comorbidities, such as severe pulmonary hypertension, severe right and/or left ventricular dysfunction, and significant aortic insufficiency or stenosis. Because the procedure is minimally invasive and does not require cardiopulmonary bypass or cardiac arrest, it can be anticipated that physicians may wish to apply it to patients with these and other comorbidities as further experience is gained. The challenges to anesthetic management will increase significantly in these patient groups.

Summary

The anesthetic management of HARPOON beating heart MVRS procedures involves close coordination between anesthetist, surgeon, and IGP. In many hospitals, the imaging physician will be the anesthetist, and in others there will be a cardiologist and an anesthetist at the head of the table. If the cardiac anesthetist is acting as the IGP, it is very important for another anesthesia care provider to be present in the operating room during the critical times of device placement and cord tensioning. This is because these periods of time require intense concentration on the part of the IGP and someone else must be delegated to monitor and manage the patient's physiologic status.

The anesthesia management of patients undergoing beating heart mitral valve repair using an alternative system has been previously reported.[11] In contrast to the current experience with HARPOON Beating Heart MVRS, they described the requirement for one-lung ventilation, the use of pulmonary artery catheterization and a higher blood loss and transfusion requirement.

In early studies, the HARPOON Beating Heart MVRS appears to be both safe and effective at treating degenerative mitral valve disease. Outcome data up to 6 months following the procedure has been reported and follow-up continues. The "Tracer trial" reported freedom from moderate or severe MR in 85% of patients at 6 month follow-up. Two patients (out of 28 patients who left theater with a HARPOON beating heart MVRS repair), required reoperation due to progressive MR, one at postoperative day 27 and one at 8 months after the procedure.[8] Further follow-up of all patients is underway and will be published in due course.

The lack of requirement for cardiopulmonary bypass and the minimally invasive nature of the technique are likely to make it attractive to both patients and clinicians. The ability to perform real-time image-guided titration of ePTFE cordal length on the beating, loaded heart has the potential to improve the quality of mitral valve repair. In the future, the application of this technology to patients with significant comorbidities will add new challenges to the anesthetic management of these cases both within the operating room and in the ICU. We also anticipate that experience will lead to procedure times routinely less than 1 h and care pathways that may bypass the ICU entirely.

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Conflicts of interest

PD, JSG, and MDA are consultants to Edwards Lifesciences.

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