Medtronic

Harmony™

TPV 22 and TPV 25 Transcatheter Pulmonary Valves and Delivery Catheter System

Instructions for Use

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

Explanation of symbols on package labeling

	MR Conditional
	For US audiences only
	Model
	Size
	Serial number
	Consult instructions for use at this website
	Catalog number
	Lot number
	Manufacturer
	Do not resterilize
	Do not reuse
	Do not use if package is damaged
	Sterilized using ethylene oxide
	Sterile LC: Device has been sterilized using liquid chemical sterilants according to EN/ISO 14160
	Use-by date
	Quantity
	Temperature limit
	Nonpyrogenic
	Keep dry
	Do not freeze
	Fragile, handle with care
	Keep away from sunlight
	Maximum guidewire diameter

Temperature limit maintained

Temperature limit exceeded

Date of manufacture

Manufactured in

1.0 Device description

The Harmony TPV system consists of a self-expanding transcatheter pulmonary valve and a delivery catheter system.

Table 1: Model numbers

Device	Model
TPV 22	HARMONY-22
TPV 25	HARMONY-25
Delivery catheter system	HARMONY-DCS

1.1 Transcatheter pulmonary valve (TPV)

The TPV consists of a porcine pericardial valve that is preserved in buffered 0.2% glutaraldehyde and sutured within a Nitinol frame that is sewn onto a polyester knit fabric. The inflow end of the TPV features an attachment suture loop on each crown to thread onto the delivery catheter system coil during loading. The TPV is treated with an alpha amino oleic acid antimineralization process (AOA), which has been shown to mitigate leaflet calcification in animal studies. A final sterilization step is performed using a 0.2% glutaraldehyde sterilant in which the TPV is preserved and packaged until used.

1.2 Patient anatomical criteria

Caution: The Harmony TPV bioprosthesis size must be appropriate to fit the patient's anatomy measured using a perimeter base framework. Proper sizing of the device is the responsibility of the physician. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed in *Chapter 5*.

Caution: The Harmony device is not intended for patients previously treated with an RV-PA conduit or previously implanted bioprosthesis.

The Harmony TPV bioprosthesis is available in two sizes (TPV 22, model number HARMONY-22 and TPV 25, model number HARMONY-25), and each is appropriate for a range of patient main pulmonary artery (PA) sizes (measured with ECG-gated CTA at the end of the diastolic phase, i.e. 90% time point in the cardiac cycle) as shown in *Figure 1* and *Figure 2* respectively. Please also note the following points:

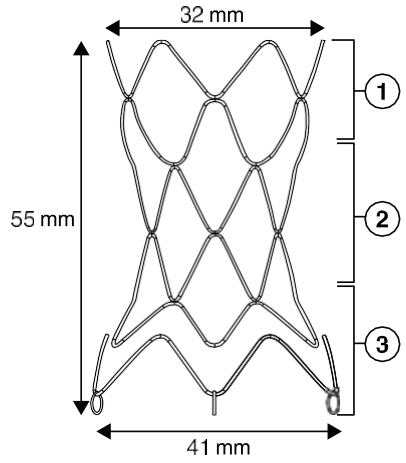
- this device is intended to be implanted in a section of the main PA (between the RVOT and main PA bifurcation) with proper distal, proximal and axial dimensions to ensure sufficient oversizing of the device with respect to the anatomy

- the perimeter values along the main PA should be compared to those of the device at all possible implant locations or in all possible implant scenarios within the implant zone (i.e., within the main PA and between the RVOT and main PA bifurcation)

- the patient's main PA should have cross-sectional perimeters described in *Figure 1* or *Figure 2* on the distal and proximal parts of the PA within the implant zone of the main PA

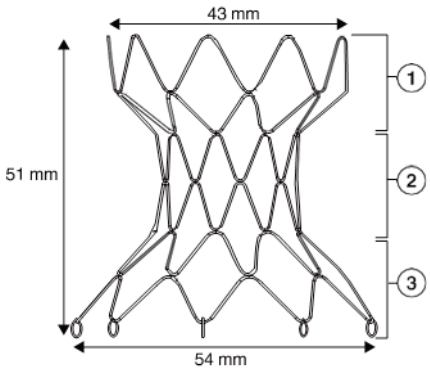
- the combined RVOT and overall PA length should be longer than or equal to the device length

- The patient's venous anatomy should accommodate an 8.33 mm (25Fr) delivery catheter system



Harmony TPV22 PA section	Anatomical Size (perimeter-derived diameter)
(1) Outflow Distal PA/Bifurcation	22 mm - 28 mm
(2) Valve Housing	>22 mm
(3) Inflow Proximal PA/RVOT	23 mm - 39 mm

Figure 1: TPV 22 (Nitinol frame profile) with dimensions and HARMONY-22 sizing matrix



Harmony TPV25 PA section	Anatomical Size (perimeter-derived diameter)
(1) Outflow Distal PA/Bifurcation	25 mm - 38 mm
(2) Valve Housing	>25 mm
(3) Inflow Proximal PA/RVOT	32 mm - 48 mm

Figure 2: TPV 25 (Nitinol frame profile) with dimensions and HARMONY-25 sizing matrix

1.3 Delivery catheter system (DCS)

The delivery catheter system (DCS) has a braided outer shaft with a polytetrafluoroethylene (PTFE) lined capsule in which the TPV is housed. The DCS has a soft, tapered distal tip. The TPV is attached to the distal end of the DCS by the DCS coil and is protected by the capsule during delivery. The deployment of the self-expanding TPV is controlled by pulling back the outer shaft, allowing the TPV to open. Rotating the proximal handle on the proximal end of the DCS rotates the DCS coil and releases the TPV for final deployment.

The DCS has a nominal outside diameter of 8.33 mm (25 Fr) and a nominal effective length of 101 cm. The DCS is compatible with an 0.889 mm (0.035 in) intravascular guidewire.

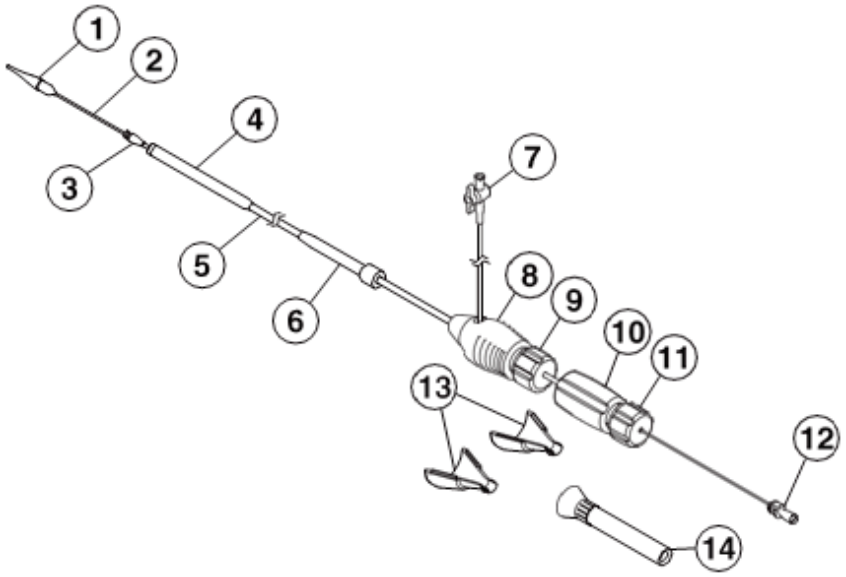


Figure 3: Delivery catheter system

1. Distal tip
2. Guidewire lumen
3. Delivery catheter system coil
4. Capsule
5. Outer shaft

6. Hemostasis sleeve
7. Stopcock
8. Hemostasis valve body
9. Hemostasis actuator
10. Proximal handle
11. Proximal handle actuator
12. Guidewire luer
13. Loading funnel halves (packaged with delivery catheter system)
14. Capsule support tube (preloaded on the delivery catheter system)

2.0 Indications

The Harmony Transcatheter Pulmonary Valve (TPV) System is indicated for use in the management of pediatric and adult patients with severe pulmonary regurgitation (i.e., severe pulmonary regurgitation as determined by echocardiography and/or pulmonary regurgitant fraction ≥ 30% as determined by cardiac magnetic resonance imaging) who have a native or surgically-repaired right ventricular outflow tract and are clinically indicated for surgical pulmonary valve replacement.

3.0 Contraindications

The following are contraindications for the use of this device:

- Active bacterial endocarditis or other active infections
- Known intolerance to Nitinol (titanium or nickel) or an anticoagulation/antiplatelet regimen

4.0 Warnings and precautions

Carefully read all warnings, precautions, and instructions for use for all components of the system before use. Failure to read and follow all instructions or failure to observe all stated warnings could cause serious injury or death to the patient.

4.1 Warnings

4.1.1 General

- Implantation of the Harmony TPV system should be performed only by physicians who have received Harmony TPV system training.

- The transcatheter pulmonary valve (TPV) is to be used only in conjunction with the Harmony delivery catheter system (DCS).

- This procedure should only be performed where emergency pulmonary valve surgery can be performed promptly.

- **Do not** use any of the Harmony TPV system components if any of the following has occurred:

    - It has been dropped, damaged, or mishandled in any way

    - The Use By date has elapsed

4.1.2 Transcatheter pulmonary valve (TPV)

- This device was designed for single use only. Do not reuse, reprocess, or resterilize the TPV. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.

- **Do not resterilize the TPV by any method.** Exposure of the device and container to irradiation, steam, ethylene oxide, or other chemical sterilants renders the device unfit for use.

- The device is packaged with a temperature sensor. **Do not** freeze the device. **Do not** expose the device to extreme temperatures. **Do not** use the device if the arrow on the sensor points to the symbol that indicates that the temperature limit has been exceeded.

- **Do not** use the device if any of the following have occurred:

    - The tamper-evident seal is broken.
    - The serial number tag does not match the container label.
    - The arrow on the sensor points to the symbol that indicates that the temperature limit has been exceeded.
    - The device is not completely covered by the storage solution.

- **Do not** contact any of the Harmony TPV system components with cotton or cotton swabs.
- **Do not** expose any of the Harmony TPV system components to organic solvents, such as alcohol.
- **Do not** introduce air into the catheter.
- **Do not** expose the device to solutions other than the storage and rinse solutions.
- **Do not** add or apply antibiotics to the device, the storage solution, or the rinse solution.
- **Do not** allow the device to dry. Maintain tissue moisture with irrigation or immersion.
- **Do not** attempt to repair a damaged device.
- **Do not** handle the valve leaflet tissue or use forceps to manipulate the valve leaflet tissue.
- **Do not** attempt to recapture the device once deployment has begun.
- **Do not** attempt to retrieve the TPV if any one of the outflow TPV struts is protruding from the capsule. If any one of the outflow TPV struts has deployed from the capsule, the TPV must be released from the catheter before the catheter can be withdrawn.
- **Do not** attempt post-implant balloon dilatation (PID) of the TPV during the procedure, which may cause damage to or failure of the TPV leading to injury to the patient resulting in reintervention.

4.1.3 Delivery catheter system (DCS)

- This device was designed for single use only. Do not reuse, reprocess, or resterilize the DCS. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.

- **Do not** reuse or resterilize the DCS.

- If resistance is met, **do not** advance the guidewire, DCS, or any other component without first determining the cause and taking remedial action.

- **Do not** remove the guidewire from the DCS at any time during the procedure.

4.2 Precautions

4.2.1 General

- Clinical long-term durability has not been established for the Harmony TPV. Evaluate the TPV performance as needed during patient follow-up.

- The safety and effectiveness of Harmony TPV implantation in patients with pre-existing prosthetic heart valve or prosthetic ring in any position has not been demonstrated.

- The Harmony TPV system has not been studied in female patients of child-bearing potential with positive pregnancy.

4.2.2 Before Use

- Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the chemical vapor. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water (for a minimum of 15 minutes) and seek medical attention immediately.

- The TPV and the glutaraldehyde storage solution are **sterile**. The outside of the TPV container is **nonsterile** and must not be placed in the sterile field.

- The TPV and DCS should be used only in a sterile catheterization laboratory (cath lab) environment. Ensure that sterile technique is used at all times.

- Strictly follow the TPV rinsing procedure.

- For TPV 25: Ensure that all green sutures have been removed from the attachment suture loops on the TPV before loading onto the DCS.

- Prevent contamination of the TPV, its storage solution, and the DCS with glove powder.

- Verify the orientation of the TPV before loading it onto the DCS. The inflow end of the TPV with attachment suture loops must be loaded first.

- Do not place excessive pressure on the TPV during loading.

- Inspect the sealed DCS packaging before opening. If the seal is broken or the packaging has been damaged, sterility cannot be assured.

- Proper functioning of the DCS depends on its integrity. Use caution when handling the DCS. Damage may result from kinking, stretching, or forceful wiping of the DCS.

- This DCS is not recommended to be used for pressure measurement or delivery of fluids.

- Carefully flush the DCS and maintain tight DCS connections to avoid the introduction of air bubbles.

4.2.3 During Use

- The TPV segment is rigid and may make navigation through vessels difficult.

- Do not advance any portion of the DCS under resistance. Identify the cause of resistance using fluoroscopy and take appropriate action to remedy the problem before continuing to advance the DCS.

- Careful management of the guidewire is recommended to avoid dislodgement of the TPV during DCS removal.

- Once deployment is initiated, retrieval of the TPV from the patient is not recommended. Retrieval of a partially deployed valve may cause mechanical failure of the delivery catheter system or may cause injury to the patient. Refer to Section 5.0 for a list of potential adverse events associated with the Harmony TPV implantation.

- During deployment, the DCS can be advanced or withdrawn prior to the outflow struts protruding from the capsule. Once the TPV struts contact the anatomy during deployment, it is not recommended to reposition the device. Advancing the catheter forward once the TPV struts make contact with the anatomy may lead to an undesired deployment or may cause damage to or failure of the TPV and injury to the patient. Refer to Section 5.0 for a list of potential adverse events associated with the Harmony TPV implantation.

- Physicians should use judgment when considering repositioning of the TPV (for example, using a snare or forceps) once deployment is complete. Repositioning the bioprosthesis is not recommended, except in cases where imminent serious harm or death is possible (for example, occlusion of the main, left, or right pulmonary artery). Repositioning of a deployed valve may cause damage to or failure of the TPV and injury to the patient. Refer to Section 5.0 for a list of potential adverse events associated with the Harmony TPV implantation.

- Ensure the capsule is closed before DCS removal. If increased resistance is encountered when removing the DCS through the introducer sheath, do not force passage. Increased resistance may indicate a problem and forced passage may result in damage to the device and harm to the patient. If the cause of resistance cannot be determined or corrected, remove the DCS and introducer sheath as a single unit over the guidewire, and inspect the DCS and confirm that it is complete.

- If there is a risk of coronary artery compression, assess the risk and take the necessary precautions.

- Endocarditis is a potential adverse event associated with all bioprosthetic valves (*Chapter 5*). Patients should make their health care providers aware that they have a bioprosthetic valve before any procedure. Postprocedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis.

- Prophylactic antibiotic therapy is recommended for patients receiving a TPV before undergoing dental procedures.

- Postprocedure, administer anticoagulation and/or antiplatelet therapy per physician/clinical judgment and/or institutional protocol.

- Excessive contrast media may cause renal failure. Preprocedure, measure the patient's creatinine level. During the procedure, monitor contrast media usage.

- Conduct the procedure under fluoroscopy. Fluoroscopic procedures are associated with the risk of radiation damage to the skin, which may be painful, disfiguring, and long-term.

5.0 Potential complications/adverse events

Potential risks associated with the implantation of the Harmony TPV may include, but are not limited to, the following:

- Death
- Valve dysfunction
- Tissue deterioration
- Hematoma
- Heart failure
- Cerebrovascular incident
- Perforation
- Rupture of the RVOT
- Compression of the aortic root
- Compression of the coronary arteries
- Sepsis
- Pseudoaneurysm
- Erosion
- Stent fracture
- Arrhythmias
- Device embolization or migration
- Pulmonary embolism
- Occlusion of a pulmonary artery
- Laceration or rupture of blood vessels

- Device misorientation or misplacement
- Valve deterioration
- Regurgitation through an incompetent valve
- Physical or chemical implant deterioration
- Paravalvular leak
- Valve dysfunction leading to hemodynamic compromise
- Residual or increasing transvalvular gradients
- Progressive stenosis and obstruction of the implant
- Hemorrhage
- Endocarditis
- Thromboembolism
- Thrombosis
- Thrombus
- Intrinsic and extrinsic calcification
- Bleeding
- Bleeding diathesis due to anticoagulant use
- Fever
- Pain at the catheterization site
- Allergic reaction to contrast agents
- Infection
- Progressive pulmonary hypertension
- Progressive neointimal thickening and peeling

- Leaflet thickening
- Hemolysis

General surgical risks applicable to transcatheter pulmonary valve implantation:

- Abnormal lab values (including electrolyte imbalance and elevated creatinine)
- Allergic reaction to antiplatelet agents, contrast medium, or anesthesia
- Exposure to radiation through fluoroscopy and angiography
- Permanent disability

6.0 Patient information

6.1 Registration information

A patient registration form is included in each bioprosthesis package. After implantation, please complete all requested information. The serial number is located on both the package and the identification tag attached to the bioprosthesis. Return the original form to the Medtronic address indicated on the form and provide the temporary identification card to the patient prior to discharge.

Medtronic will provide an Implanted Device Identification Card to the patient. The card contains the name and telephone number of the patient's physician as well as information that medical personnel would require in the event of an emergency. Patients should be encouraged to carry this card with them at all times.

6.2 MRI safety information

Nonclinical testing and modeling have demonstrated that the TPV is MR Conditional. A patient with this device can be safely scanned in an MR system meeting the following conditions:

- Static magnetic field of 1.5 T or 3.0 T
- Maximum spatial field gradient of 2500 gauss/cm (25 T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4.0 W/kg (First Level Controlled Operating Mode)

Under the scan conditions defined above, the TPV is expected to produce a maximum in vivo temperature rise of less than 3°C after 15 minutes of continuous scanning.

In nonclinical testing, the image artifact caused by the device extends approximately 3 mm from the TPV when imaged with a spin echo pulse sequence and 5 mm when imaged with a gradient echo pulse sequence and a 3.0 T MRI system. The lumen of the device was clear for the spin echo images and only partially obscured for the gradient echo images.

7.0 How supplied

7.1 Packaging

7.1.1 TPV

The TPV is chemically sterilized and provided **sterile** and **nonpyrogenic** in a sealed glass container filled with a buffered 0.2% glutaraldehyde solution. If the jar is undamaged and unopened, the TPV is **sterile**. The outer surfaces of the jar are **nonsterile** and must not be placed in the sterile field.

7.1.2 Delivery catheter system (DCS) and loading system (LS)

The DCS and the LS are sterilized with ethylene oxide gas and packaged in a double-pouch configuration. The packaging is designed to ease placement of the DCS and the LS in the sterile field. If the pouches are undamaged and unopened, the DCS and the LS are **sterile**. The outer surfaces of the outer pouch are **nonsterile** and must not be placed in the sterile field.

7.2 Storage

Store the TPV at room temperature (5°C to 25°C [41°F to 77°F]). Store the DCS at room temperature in a dry environment and away from direct sunlight.

8.0 Instructions for use

The following is a sequential outline of the implant procedure. The type of diagnostic catheters, guidewires, and other tools needed are at the discretion of the operator.

Note: See *Figure 1*, *Figure 2*, and *Figure 3* for TPV and DCS components.

8.1 Access site preparation and preimplantation imaging

Sterilize the access site before implanting the TPV; maintain sterile techniques throughout the procedure. Obtain preimplantation imaging of the anatomy to confirm that the anatomy is suitable for successful implantation of the TPV.

Note: Periprocedural antibiotics may be administered according to institutional policy.

1. Prepare the venous access site using aseptic techniques and drape to provide a sterile field.

2. Gain venous and arterial access.

3. Administer heparin to achieve a target ACT of >250 seconds.

4. Use an end-hole catheter through the venous introducer to obtain pressure measurements in the right atrium, right ventricle (RV), and pulmonary artery.

5. Obtain right ventricular angiography in lateral and cranial projections, if necessary. A right or left anterior oblique projection (RAO or LAO) may also be required.

6. Using direct measurement of the intended implantation site, obtain dimensions to confirm that morphology is an acceptable size for implantation.

7. Place a pigtail catheter through the arterial introducer and advance to the aorta to obtain systemic pressures. Perform an aortic root angiography to show the coronary anatomy relative to the implantation site.

8. Simultaneously record the aortic and RV pressures to obtain an RV-to-systemic systolic pressure ratio.

9. Advance an end-hole catheter to the distal pulmonary artery for secure guidewire placement through the venous access site.

10. Deploy a 0.889 mm (0.035 in) ultra-stiff guidewire to the most distal position possible in the pulmonary artery through the end-hole catheter.

11. Remove the end-hole catheter; leave the guidewire in place.

8.2 Preparation of the DCS

1. Carefully inspect the package before opening.

   Caution: Do not use after the Use By date or if the integrity of the sterile package has been compromised (for example, damaged package).

2. Verify that the outer shelf carton label matches the outer pouch label.

3. Using aseptic technique, remove the product from the protective package. Discard the protective packaging.

4. Visually check that the product is free of defects and that the LS components are present. Do not use if any defects are noted.

5. Remove the loading funnel halves from the tray. Rinse in a clean saline bowl and leave in the bowl until required for loading.

6. Remove the DCS (including the capsule support tube) from the tray by gripping the DCS appropriately and overcoming the packaging snap features. Lay the DCS on the sterile bench in a straight configuration and discard the tray.

8.3 Preparation of the TPV

The TPV is packaged **sterile** in a jar with a hermetic seal and a tamper-evident seal. Before opening, carefully examine the jar and lid for damage, leakage, or broken seals. **The jar should contain enough sterilant to cover the TPV completely.**

The following steps must be followed in correct sequence to ensure adequate rinsing of the sterilant from the TPV:

1. Using aseptic technique, prepare 3 sterile bowls: 2 containing isotonic saline solution (500 mL, enough to cover the TPV completely) for rinsing and 1 remaining empty.

2. Remove the TPV from the jar, following the steps for either TPV 22 or TPV 25.

   For TPV 22: remove the TPV by grasping the fabric with atraumatic forceps and lifting the TPV from the jar.

   For TPV 25: remove the TPV by grasping the serial number tag, which is attached to the inflow end of the TPV, with atraumatic forceps and lifting the TPV from the jar. If the

serial number tag is not accessible, it is acceptable to remove the TPV by grasping the fabric with atraumatic forceps and lifting the TPV from the jar.

The outside of the jar is **nonsterile**. Do not allow the TPV to come into contact with the outside of the jar.

Note: On TPV 22, the serial number tag is sutured end-to-end around the center TPV segment. On TPV 25, the serial number tag is attached to the inflow end of the TPV.

3. Verify that the serial number on the tag matches the jar label serial number. If any difference is noted, do not use the TPV.

4. To detach the serial number tag, follow the steps for either TPV 22 or TPV 25.

   For TPV 22: Hold the TPV over the empty sterile bowl. Use scissors to clip the single suture line between the 2 ends of the tag. Do not cut the knots that secure the tag. Do not cut or clip the polyester knit fabric or Nitinol struts. Once the suture is clipped, the tag and suture fall away from the TPV. Verify that no tag-attachment suture remains on the TPV.

   For TPV 25: Hold the TPV over the empty sterile bowl. Use scissors to clip the green suture lines at one location between the attachment suture loops. Do not cut the attachment suture loops or the knots that secure the tag. Do not cut or clip the polyester knit fabric or Nitinol struts. Once the suture is clipped, manually pull the serial tag to remove the tag and green suture away from the TPV. Verify that no green suture remains on the TPV.

5. Drain the residual storage solution from the TPV into the empty discard bowl (bowl 1) by holding the TPV outflow end downward.

6. Transfer the TPV to the first rinse bowl (bowl 2). Rinse the TPV by emptying, filling, inverting, and swirling the TPV for a minimum of 1 minute. Empty the rinse solution from the TPV into the bowl.

7. Transfer the empty TPV to the second rinse bowl (bowl 3) and repeat *Step 6* for a minimum of 1 minute. Leave the TPV in the rinse bowl until needed for loading to prevent the tissue from drying.

8. Empty any rinse solution from the TPV before loading the TPV onto the DCS. Ensure that the valve is in the open position before loading the TPV onto the DCS.

8.4 DCS loading

1. Before beginning the loading sequence, flush through the hemostasis valve body to wet the internal seal.

2. Position the pre-mounted capsule support tube over the DCS capsule. Ensure the flared end is facing the distal tip of the DCS.

3. Advance the distal tip until the luer touches the proximal handle edge.

4. Retract the outer shaft to expose the holding coil by pulling the hemostasis valve body proximally, while holding the proximal handle stationary.

5. Lock the hemostasis valve body by rotating the actuator clockwise. Flush with sterile saline through the hemostasis valve body. Unlock the hemostasis valve body by rotating the actuator counter-clockwise

6. Slide the TPV over the distal tip of the DCS, with the TPV's inflow end first. Take care not to puncture the valve's leaflets with the pointed distal tip of the DCS.

7. Thread each attachment suture loop onto the DCS coil in sequence. Rotate the TPV 2 full turns onto the DCS coil so that the TPV is securely attached to the DCS. Ensure that the attachment suture loops do not become entangled at the proximal collar of the DCS coil.

   Note: During loading of the suture loops, if there is any observation of infolding, reload the attachment suture loops.

8. Assemble the 2 loading funnel halves over the inflow end of the TPV. Carefully connect the 2 halves. Do not catch the TPV or the capsule's distal edge in the process.

9. Hold the loading funnel stationary and rotate the capsule support tube clockwise until reaching a full stop to assemble the loading tools. Retract the assembled loading tool until the funnel shoulder engages with the distal end of the capsule.

10. Keep both the assembled loading tools and the outer shaft stationary. Pull the proximal handle in the proximal direction to load the TPV into the capsule. Continue to flush the DCS while loading the TPV.

    Caution: Do not place excessive pressure on the TPV or DCS during loading.

11. Adjust the position of the valve within the capsule so there is an approximately 1 cm gap between the distal end of the capsule and the distal end of the frame.

12. Once the TPV is fully enclosed in the capsule, lock the hemostasis valve body by rotating the actuator clockwise.

13. Disassemble the loading tools by rotating the capsule support tube counter-clockwise and taking the loading funnel halves apart. Slide the capsule support tube over the distal tip to remove it from the DCS.

14. Hold the DCS with its distal tip pointed upward. Flush the DCS with normal saline, taking care not to rotate the DCS coil (which would release the TPV prematurely).

15. To close the tip into the capsule, push the tip proximally until the max tip outer diameter is flush with the capsule distal edge.

    Note: Do not pull the tip into the DCS by pulling on the guidewire luer.

16. If there is a gap between the tip and the TPV in the capsule, unlock the hemostasis valve body by rotating the actuator counter-clockwise. Adjust the position of the crimped TPV to minimize the gap. Lock the hemostasis valve body by rotating the actuator clockwise.

17. Lock the proximal handle by rotating the actuator clockwise.

18. Flush the DCS through the guidewire luer.

19. Advance the hemostasis sleeve until it is flush with the proximal end of the capsule.

    Caution: Do not load or re-load the TPV onto the DCS after the TPV or the DCS has been inserted into a patient. A second attempt may be made to load an undamaged TPV onto the DCS but only if neither the TPV nor the DCS has entered the body. Do not load the TPV onto the DCS more than 2 times.

8.5 TPV implantation

1. Dilate the vein using a venous dilator, being careful not to displace the guidewire.

2. Remove the venous dilator from the vein and advance the DCS over the guidewire until the hemostasis sleeve working length is fully inserted.

3. Carefully advance the DCS through the sleeve towards the intended implant zone. This action requires manipulation of the DCS and the guidewire.

   Note: Attention must be paid to maintain adequate guidewire position at all times.

4. Once the TPV has reached the implant zone, ensure the proper TPV position using angiography.

Caution: Ensure careful consideration to position the TPV within the target implant zone. TPV implantation outside of target implant zone may lead to an undesired deployment or sub-optimal placement requiring manipulations that may cause damage to or failure of the TPV and injury to the patient.

5. Unlock the proximal handle by rotating the actuator counter-clockwise, and advance the distal tip forward.

6. Unlock the hemostasis valve body by turning the actuator counter-clockwise. While holding the proximal handle stationary with one hand to control TPV position, slowly pull back the hemostasis valve body to retract the outer shaft. Expose the first 2 Nitinol struts and ensure correct TPV expansion and position using angiography.

7. Once correct expansion is confirmed, continue to slowly pull back the hemostasis valve body while holding the proximal handle stationary to retract the outer shaft and maintain TPV position at the intended site. Continue to deploy the TPV while maintaining TPV position until the TPV frame is fully exposed in the RVOT. Ensure that the capsule is fully retracted under fluoroscopy with the aid of the capsule marker band.

8. While maintaining the TPV position, gradually rotate the proximal handle counter-clockwise, releasing the TPV crown by crown. If heart rhythm disturbance is detected, maintain the catheter position and do not release the TPV further until the disturbance resolves. Resume gradually rotating the proximal handle counter-clockwise until all the inflow sutures on the TPV are released from the DCS coil.

9. Retract the outer shaft while maintaining the position of the distal tip of the DCS in relation to the TPV.

10. Carefully retract the DCS coil into the capsule.

11. With careful manipulation of the guidewire and inner shaft, remove the distal tip of the DCS back through the TPV.

    Caution: Use careful management of the guidewire to avoid dislodgement or movement of the TPV.

12. Using fluoroscopy and guidewire manipulation, pull on the inner shaft to center the distal tip back into the DCS. Lock the proximal handle by rotating the actuator clockwise. Remove the DCS from the patient.

    Note: Take care not to overcapture the tip by using too much force on the inner shaft.

13. Valve function can be verified at this point by repeating pressure measurements. Compare the RV pressure to the systemic pressure measured through the arterial approach.

14. Inject contrast media into the main pulmonary artery to aid in demonstrating valve function and position. Ensure that the valve is not held open by the guidewire, which may give the false impression of pulmonary regurgitation.

15. Perform an RV angiogram to assess the TPV position and paravalvular leakage (if any).

16. Remove the guidewire and introducer sheath while maintaining hemostasis.

    Caution: Dispose of the DCS in accordance with applicable laws, regulations, and hospital procedures, including those regarding biohazards, microbial hazards, and infectious substances.

9.0 Return of explanted TPV

Medtronic is interested in obtaining explanted TPVs. Specific pathological studies of the explanted TPV will be conducted under the direction of a consulting pathologist. A written summary of the findings will be returned to the physician. Contact a Medtronic representative to request a product return kit to return explanted TPV for analysis and disposal. If a kit is not available, place the explanted TPV in a container filled with glutaraldehyde or 10% buffered formalin immediately after explantation. For further return instructions, contact a Medtronic representative.

10.0 Summary of clinical studies

10.1 The Medtronic Harmony Transcatheter Pulmonary Valve Clinical Study

The Harmony clinical study was a prospective, non-randomized, multi-center study and included two phases, i.e., the early feasibility study (EFS) phase and the pivotal study phase. The EFS treated (i.e., catheterized) 21 patients between May 30, 2013, and May 13, 2015, at 3 investigational sites in the U.S. and Canada. The pivotal study treated 50 patients between March 14, 2017, and November 8, 2019, at 13 investigational sites in the U.S., Canada, and Japan. Clinical data from the EFS phase and the pivotal study phase were pooled because largely similar clinical protocols were followed in the two phases.

The study utilized an independent Data Safety Monitoring Board (DSMB), a Clinical Events Committee (CEC), and MRI/echocardiography/explant pathology core laboratories.

At the time of database lock, a total of 340 patients had enrolled in the clinical study of the Harmony TPV System, 71 of which were catheterized ("Catheterized Cohort") and the remainder were not treated due to various reasons, such as screen failures and enrollment completion. Seventy (70) of the 71 catheterized patients received a Harmony TPV implant ("Implanted Cohort"), including 20 EFS patients with a Harmony TPV 22 implant, 31 pivotal study patients with a TPV 22 or TPV 25 and 19 pivotal study patients with an earlier clinical design iteration of the TPV 25 (designated as "cTPV 25" [1]) implant. One EFS patient did not receive a Harmony TPV implant after catheterization due to high pulmonary artery pressure. Of the 70 patients in the Implanted Cohort, two originally implanted with a cTPV 25 valve were explanted within 24 hours post implant due to valve migration and subsequently received a surgical valve: one on the day of the index procedure and the other the following day. The remaining 68 patients constitutes the "Implanted > 24 Hours Cohort."

Refer to **Table 2** below for additional details. The data in this IFU represents data through 6 months of follow-up for these 70 patients. Medtronic intends to commercialize the Harmony TPV 22 and the Harmony TPV 25. From the data represented on this IFU, it is inclusive of data from the earlier clinical design iteration of the Harmony TPV 25 (cTPV 25) which was later modified (TPV 25) during the study.

[1] The cTPV 25 implant was modified to become the TPV 25 implant due to it not deploying as intended in some cases with challenging anatomies.

Table 2. Studies and Valve Sizes

	Catheterized Cohort	Attempted Implant Cohort	Implanted Cohort	Implanted >24 Hours Cohort
All Patients	71	70	70	68
Feasibility Phase (TPV 22 only)	21	20	20	20
Pivotal Phase	**50**	**50**	**50**	**50**
TPV 22	21	21	21	21
cTPV 25[1]	19	19	19	17
TPV 25[2]	10	10	10	10

[1] Earlier clinical design iteration used in the Pivotal study
[2] Modified version in the Pivotal study, Commercial version

10.1.1 Patient Population

The demographics and baseline characteristics of the study population are typical for a transcatheter pulmonary valve replacement study performed in the U.S., as summarized in **Table 3**. Of the 71 catheterized patients with medical history data available, 63 included Tetralogy of Fallot as their original diagnosis while the remaining patients had other diagnoses, the most common of which was pulmonary stenosis. All patients presented with moderate or severe pulmonary regurgitation.

Table 3. Patient Demographics and Baseline Characteristics - Catheterized Cohort

Assessment	Summary Statistics* (N= 71)
Sex	
Female	40.8% (29/71)
Male	59.2% (42/71)
Age at baseline (years)	28.5 ± 12.0 (71)
<22	38.0% (27/71)
12 to <18	19.7% (14/71)
18 to <22	18.3% (13/71)
≥22	62.0% (44/71)
Original Diagnosis	

Assessment	Summary Statistics* (N= 71)
Tetralogy of Fallot	88.7% (63/71)
With pulmonary stenosis	60.6% (43/71)
With pulmonary atresia	7.0% (5/71)
Absent pulmonary valve	0.0% (0/71)
Sub-type not indicated	21.1% (15/71)
Pulmonary stenosis‡	6.0% (3/50)
Pulmonary atresia with intact ventricular septum‡	2.0% (1/50)
Transposition of the Great Arteries	0.0% (0/71)
Truncus arteriosus	0.0% (0/71)
Branch Pulmonary Artery Stenosis§	0.0% (0/21)
Other diagnosis†	8.5% (6/71)
Type of Surgical Patch Material	
None	11.3% (8/71)
Dacron	2.8% (2/71)
Gore-Tex	4.2% (3/71)
Autologous pericardium	11.3% (8/71)
Bovine pericardium	2.8% (2/71)
Unknown/not available	47.9% (34/71)
Other	19.7% (14/71)
Pacemaker or ICD Implant	9.9% (7/71)
Pulmonary regurgitation by echocardiography	
None - Mild	0.0% (0/71)
Moderate	4.2% (3/71)
Severe	95.8% (68/71)
Mean RVOT gradient (mmHg) by echocardiogram‖	9.7 ± 5.3 (56)
Number of previous open heart surgeries	1.3 ± 0.5 (71)
Previous history of endocarditis‡	2.0% (1/50)

Assessment	Summary Statistics* (N= 71)
* Continuous measures - Mean ± SD (Total no.); categorical measures - % (no./Total no.) † Patients with “Other diagnosis” as Original Diagnosis had: double outlet right ventricle (DORV), atrial septal defect, DORV with pulmonary stenosis, “absent” left pulmonary artery, Noonan syndrome and dysplastic pulmonary valve stenosis, and variant of Tetralogy of Fallot (DORV with pulmonary stenosis, secundum atrial septal defect and patent ductus arteriosus). ‡ Information only collected in the 50 patients catheterized in the pivotal study phase. § Information only collected in the 21 patients catheterized in the EFS phase. ‖ Fifty-six (56) of the 71 patients had available core laboratory echocardiography data.	

10.1.2 Procedure Data

Seventy-one patients were catheterized and 70 were implanted with the Harmony TPV. One Native EFS patient was catheterized with the intent to implant; however, upon further assessment, the investigator elected not to proceed with implant due to high pulmonary artery (PA) pressures. The Harmony TPV 22 implant was not attempted in this patient.

General anesthesia was utilized for all patients and venous access was achieved by the femoral vein in 67 patients and jugular vein for 4 patients. Mean total procedure time was 142.5 ± 62.9 minutes and mean fluoroscopic time was 37.5 ± 20.1 minutes, as shown in **Table 4**.

Table 4. Procedural Data - Catheterized Cohort

Assessment	Summary Statistics* (N= 71)
Anesthesia	
General	100.0% (71/71)
Local	0.0% (0/71)
Venous access site for valve delivery	
Femoral vein	94.4% (67/71)
Jugular vein	5.6% (4/71)
Total fluoroscopic time (min)	37.5 ± 20.1 (69)
Total procedural time (min)	142.5 ± 62.9 (70)
Total intubation time (min)	213.6 ± 129.0 (50)
* Continuous measures - Mean ± SD (Total no.); categorical measures - % (no./Total no.)	

10.1.3 Safety and Effectiveness Results

10.1.3.1 Primary Safety Endpoint

The primary safety endpoint is freedom from procedure or device-related mortality at 30 days post implant, for patients in the catheterized cohort.

There were no procedure- or device-related deaths reported at 30 days post implant, as summarized in **Table 5.**

Table 5. Summary of Procedure or Device-related Mortality at 30 Days Post Implant - Catheterized Cohort

Mortality	Summary Statistics* (N= 71)
	% (n)
Procedure or Device-related	0.0% (0)
Procedure-related	0.0% (0)
Device-related	0.0% (0)
* Event Rate (number of patients)	

10.1.3.2 Primary Effectiveness Endpoint

- The primary effectiveness endpoint was percentage of patients with no Harmony valve reinterventions and acceptable hemodynamic function at 6 months as defined by: Mean RVOT gradient as measured by continuous-wave Doppler ≤40 mmHg
    - If a catheterization was performed for clinical purposes, the catheterization peak gradient measurement superseded the continuous-wave Doppler measurement and was used to support the primary effectiveness endpoint. A peak gradient of ≤40 mmHg as measured by catheterization was considered acceptable hemodynamic function

-AND-

- Pulmonary regurgitant fraction <20% as measured by MRI
    - If MRI was contraindicated, a continuous-wave Doppler measurement was used to support the primary effectiveness endpoint. Less than moderate pulmonary regurgitation as measured by continuous-wave Doppler was considered acceptable hemodynamic function.

Of the 68 patients in the Implanted > 24 Hours Cohort, three patients had missing echocardiography data due to COVID-19 impact or non-evaluable echocardiography per the imaging core laboratory. A summary of patients with acceptable TPV hemodynamic function at 6 months without reintervention on the Harmony TPV within the Implanted > 24 Hours Cohort is provided in **Table 6**, which showed that 58 (89.2%) of the 65 patients with evaluable echocardiography data achieved the primary effectiveness endpoint.

Table 6: Patients with Acceptable TPV Hemodynamic Function at 6 Months without Reintervention on the Harmony TPV – Implanted > 24 Hours Cohort

Primary Effectiveness Endpoint Analysis	Summary Statistics (N=68)
Number of evaluable patients*	65
Number of patients with reintervention	5
Number of patients with mean gradient > 40 mmHg	0
Number of patients with pulmonary regurgitation ≥ moderate	2
Number and percentage of patients with acceptable TPV hemodynamic function without reintervention	58 (89.2%)
Standard error for percentage	3.8%
Two-sided 95% confidence interval†	79.1% - 95.6%
*Three patients implanted with a TPV 25 whose echocardiography data were either missing due to COVID-19 impact or not evaluable per the imaging core laboratory were excluded. †Two-sided Clopper-Pearson interval	

10.1.3.3 Additional Outcome Measures

Technical Success at Exit from Catheterization Laboratory/Operating Room

The technical success rate at exit from the catheterization laboratory/operating room is summarized in **Table 7** for the Implanted Cohort. Technical success was achieved in 92.9% of the patients.

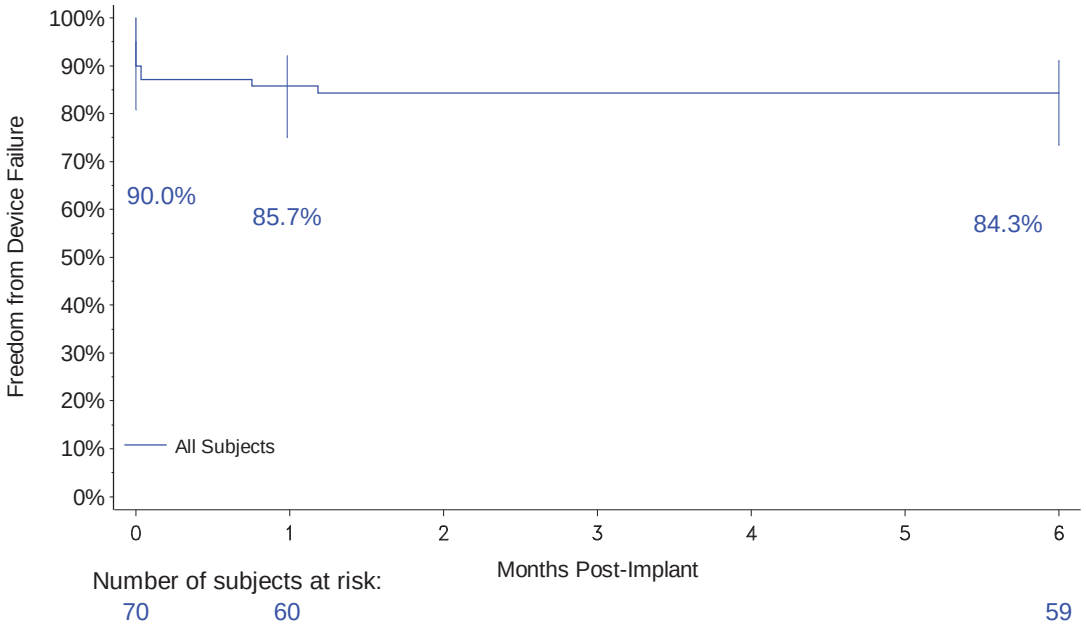
Table 7: Technical Success Rate at Exit from Catheterization Laboratory/ Operating Room - Implanted Cohort

Technical Success	Summary Statistics* (N=70)
Overall technical success	92.9% (65/70)
No device- or procedural-related mortality	100.0% (70/70)
Successful access, delivery, and retrieval of the delivery system	100.0% (70/70)
Deployment and correct positioning (including minor repositioning if needed) of the single intended device	95.7% (67/70)
No unplanned or emergency surgery or reintervention related to the device or access procedure	95.7% (67/70)
*Event rate (no./Total no.)	

Device Success (or Freedom from Device Failure)

The Kaplan-Meier rate of freedom from device failure through 6 months for the Implanted Cohort is summarized in **Figure 4**. At 6 months post implant, 84.3% of the patients were free from device failure.

Figure 4: Freedom from Device Failure through 6 Months - Implanted Cohort



Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

Eleven (11) patients in the Implanted Cohort met the device failure criteria, as summarized in **Table 8**.

Table 8: Device Failure - Implanted Cohort

Reasons for Device Failure	Summary Statistics (N= 70)
Device failure*	11/70
Device- or procedural-related mortality	0
Original intended device not in place	6
Mean RVOT gradient > 40 mmHg	1
Pulmonary regurgitation ≥ moderate	4
Surgical reoperation or catheter reintervention	7
Structural performance (migration, embolization, detachment, major stent fracture, hemolysis, thrombosis, endocarditis)	6
Erosion or RVOT/PA rupture	1

Reasons for Device Failure	Summary Statistics (N= 70)
Paravalvular leak ≥ moderate	4
*Eleven patients included 3 patients from the EFS phase and 8 from the pivotal study phase. The reasons listed for device failure are not mutually exclusive (a given patient could have more than one device failure reasons).	

Procedural Success

Procedural success was evaluated for the pivotal phase only because not all components per definition of the endpoint were captured in the feasibility phase of the study. The pivotal phase included 50 patients in the Implanted Cohort. The rate of procedural success at 30 days is summarized in **Table 9** for the Implanted Cohort of the pivotal phase, which showed an overall procedural success rate of 84.0%.

Table 9: Procedural Success at 30 Days - Implanted Cohort (Pivotal Phase)

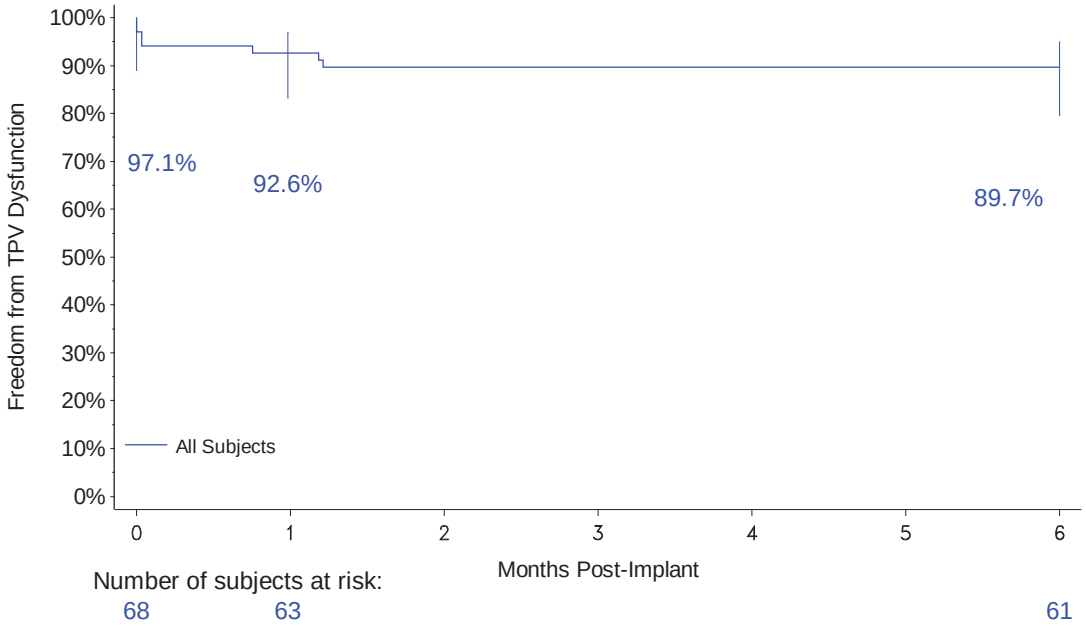
Procedural Success	Summary Statistics* (N= 50)
Overall procedure success	84.0% (42/50)
No device failure	84.0% (42/50)
No life-threatening major bleed†	100.0% (48/48)
No major vascular or cardiac structural complications required unplanned reintervention or surgery†	97.9% (47/48)
No stage 2 or 3 acute kidney injury (including new dialysis) †	100.0% (48/48)
No pulmonary embolism†	100.0% (48/48)
No severe heart failure or hypotension requiring intravenous inotrope, ultrafiltration, or mechanical circulatory support†	100.0% (48/48)
Prolonged intubation ≤ 48 hours	100.0% (50/50)
*Event rate (no./Total no.) †Information not available for 2 of the 50 patients.	

Freedom from TPV Dysfunction

The Kaplan-Meier rate of freedom from TPV dysfunction through 6 months for the Implanted > 24 Hours Cohort is shown in **Figure 5**. At 6 months post implant, 89.7% of the patients were

free from TPV dysfunction.

Figure 5: Freedom from TPV Dysfunction through 6 Months – Implanted >24 Hours Cohort

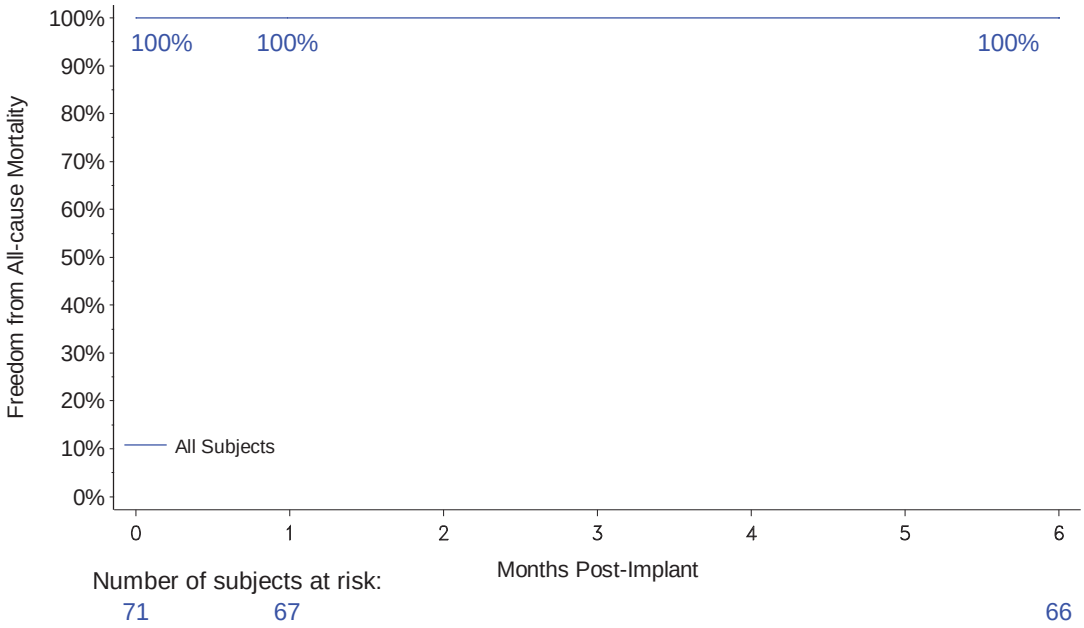


Note: The confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

All-cause Mortality

The Kaplan-Meier rate of freedom from all-cause mortality through 6 months for the Catheterized Cohort is shown in **Figure 6**. There was no death reported in the catheterized patients at 6 months.

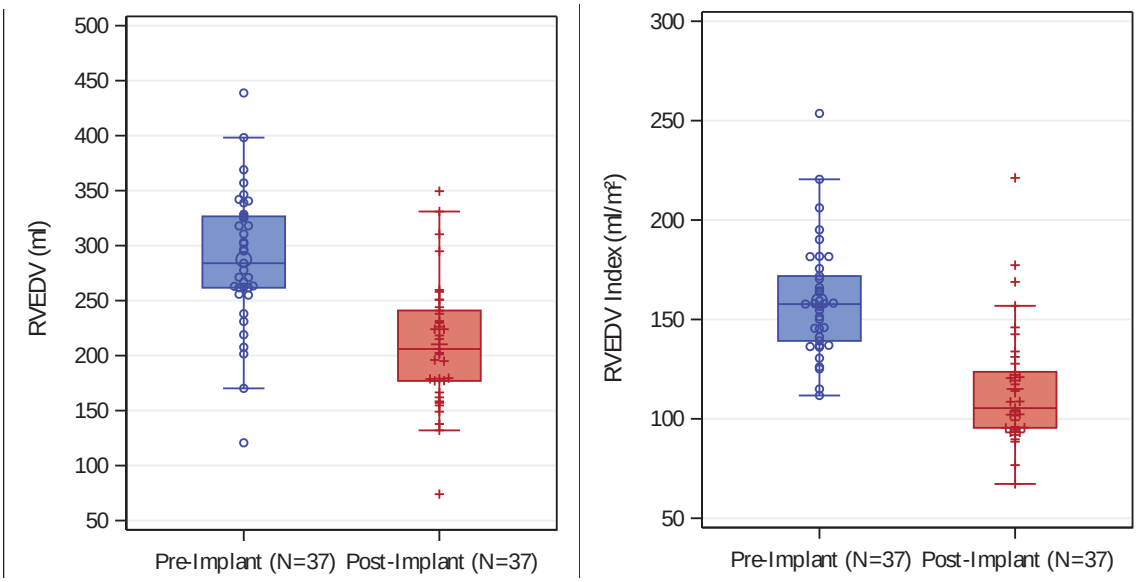
Figure 6: Freedom from All-Cause Mortality – Catheterized Cohort



Characterization of Right Ventricle Remodeling

Right ventricular remodeling post Harmony TPV implant was characterized via cardiovascular magnetic resonance (CMR) imaging, where not contraindicated. There were a significant number of patients with CMR contraindication, such as pacemaker implantation. The paired right ventricular end diastolic volume (RVEDV) and RVEDV index, pulmonary regurgitation fraction (PRF), and net right ventricular stroke volume pre- and post-implant are shown in **Figure 7** through **Figure 9**, respectively. The post-implant timepoint was 6 months for patients implanted in the pivotal stage and 12 months for patients implanted in the feasibility stage (CMR was not performed at 6 months in the feasibility stage). The RVEDV decreased from 287.5 ± 61.9 to 210.3 ± 56.7 ml, with the corresponding RVEDV index decreasing from 159.4 ± 28.9 to 115.0 ± 29.9 ml/m^2; the net right ventricular stroke volume increased from 79.5 ± 26.2 to 91.0 ± 24.2 ml/beat); and the pulmonary regurgitant fraction decreased from 40.5 ± 11.6% to 2.4 ± 3.3%.

Figure 7: Right Ventricular End Diastolic Volume (RVEDV) and RVEDV Index Pre- and Post-Implant – Implanted Cohort



(a) RVEDV

(b) RVEDV Index

Figure 8: Pulmonary Regurgitation Fraction (PRF) Pre- and Post-Implant – Implanted Cohort

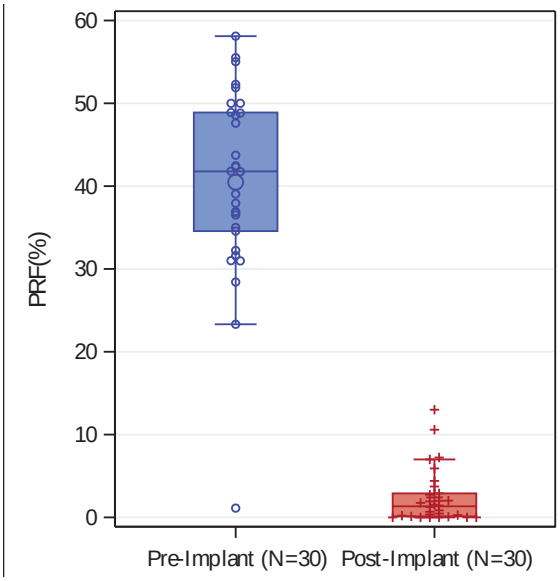
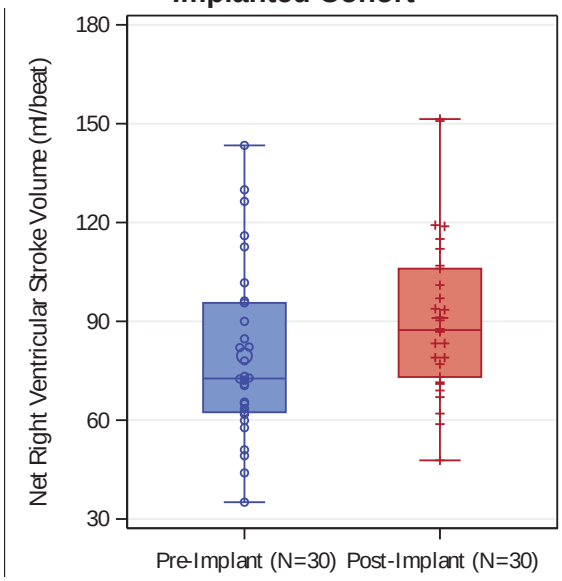


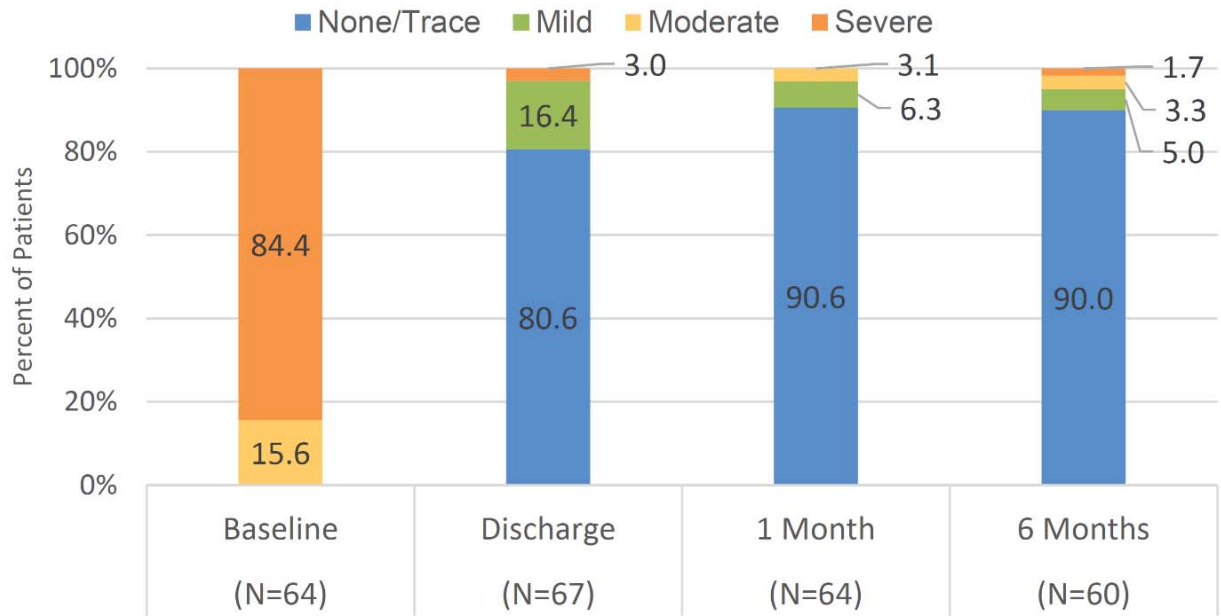
Figure 9: Net Right Ventricular Stroke Volume Pre- and Post-Implant – Implanted Cohort



Pulmonary Regurgitation

Pulmonary regurgitation through 6 months assessed by echocardiography is shown in **Figure 10**. The proportion of patients with severe pulmonary regurgitation was 1.7% at 6 months compared to 84.4% at baseline.

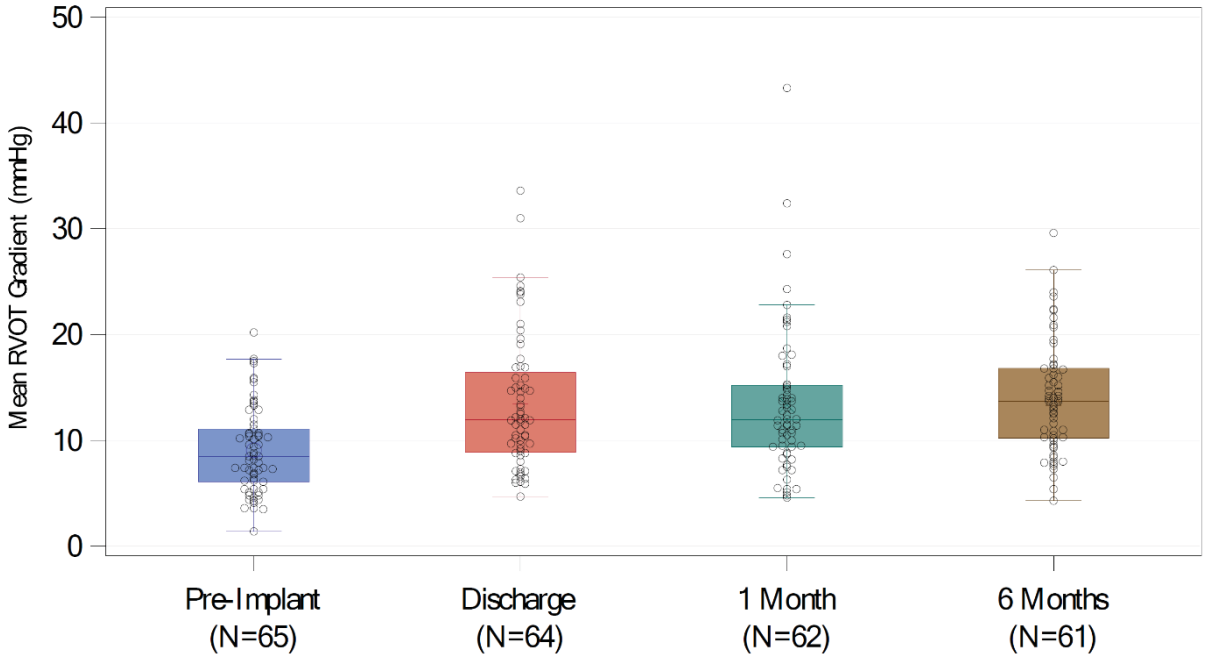
Figure 10: Pulmonary Regurgitation by Visit – Implanted Cohort



RVOT Gradient

The RVOT gradient over time post implant is shown in **Figure 11**. At discharge the mean RVOT gradient was 13.5 ± 6.3 mmHg and remained stable through 6 months (14.0 ± 5.3 mmHg).

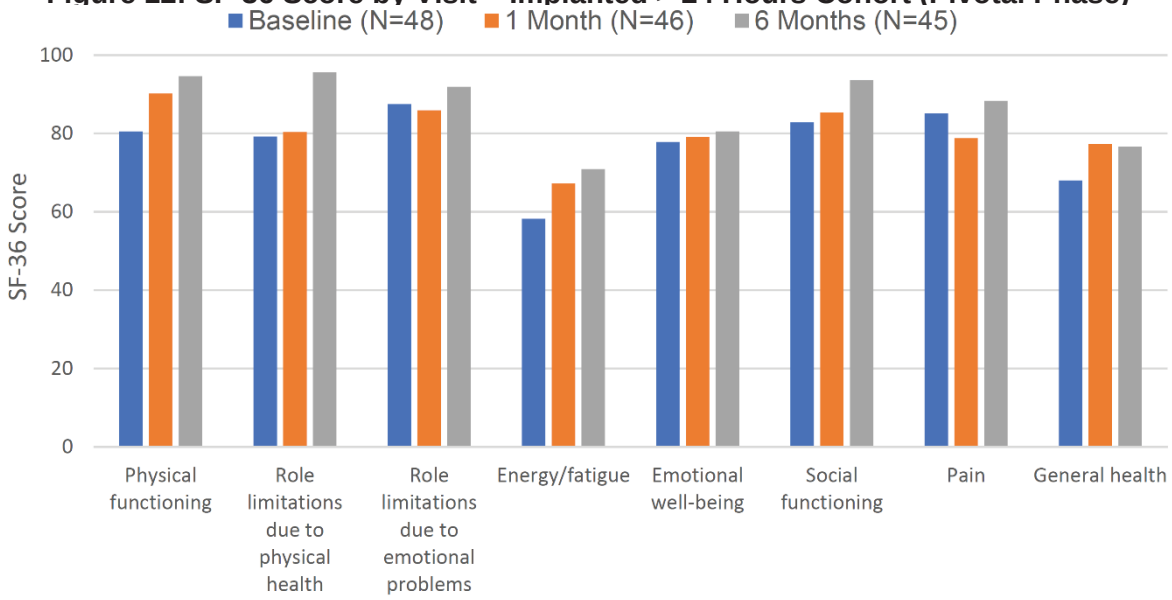
Figure 11: Mean RVOT Gradient by Visit – Implanted Cohort



Quality of Life

Quality of life over time was assessed in the Implanted > 24 Hours Cohort using the 36-Item Short Form Survey (SF-36). The SF-36 scores through 6 months for patients implanted in the pivotal stage are shown in **Figure 12**. Gains were observed across the mean scores of all eight scales at 6 months post-implant, with the most gain in the areas of physical functioning (80.5 ± 25.6 at baseline vs. 94.6 ± 8.8 at 6 months) and role limitations due to physical health (79.2 ± 33.9 at baseline vs. 95.6 ± 18.7 at 6 months). The assessment was not performed in patients implanted in the feasibility stage.

Figure 12: SF-36 Score by Visit – Implanted > 24 Hours Cohort (Pivotal Phase)



Adverse Events

The CEC-adjudicated adverse events at 6 months are summarized in **Table 10** for the for Catheterized Cohort, stratified by the study phase and implant model.

Table 10: CEC-Adjudicated Adverse Events at 6 Months – Catheterized Cohort

Adverse Events	Summary Statistics*			
	All Patients (N=71)	Feasibility Phase	Pivotal Phase	
		TPV 22 (N=21)	TPV 22 & TPV 25 (N=31)	cTPV 25 (N=19)
All-cause mortality	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Embolization of the TPV	2.8% (2)	0.0% (0)	0.0% (0)	10.5% (2)
Migration of the TPV	4.2% (3)	9.5% (2)	3.2% (1)	0.0% (0)
Misorientation of the TPV	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Misplacement of the TPV	1.4% (1)	0.0% (0)	0.0% (0)	5.3% (1)

Adverse Events	Summary Statistics*			
	All Patients (N=71)	Feasibility Phase	Pivotal Phase	
		TPV 22 (N=21)	TPV 22 & TPV 25 (N=31)	cTPV 25 (N=19)
Other device related AE†	7.0% (5)	4.8% (1)	0.0% (0)	21.1% (4)
Collapse of valve frame	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Endocarditis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Erosion	1.4% (1)	4.8% (1)	0.0% (0)	0.0% (0)
Stent fracture: major	1.4% (1)	4.8% (1)	0.0% (0)	0.0% (0)
Thrombosis of the TPV	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Structural deterioration	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Valve dysfunction	4.2% (3)	14.3% (3)	0.0% (0)	0.0% (0)
Stenosis	4.2% (3)	14.3% (3)	0.0% (0)	0.0% (0)
Regurgitation	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Stenosis & regurgitation	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Paravalvular leak	8.5% (6)‡	4.8% (1)‡	3.2% (1)	21.1% (4)
Major	1.4% (1)	4.8% (1)	0.0% (0)	0.0% (0)
Minor	7.0% (5)	0.0% (0)	3.2% (1)	21.1% (4)
Coronary compression causing myocardial ischemia	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Perforation of the heart	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Perforation of the vessel	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
RVOT rupture or dissection	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Congestive heart failure	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Cardiac arrest	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Myocardial infarction	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

Adverse Events	Summary Statistics*			
	All Patients (N=71)	Feasibility Phase	Pivotal Phase	
		TPV 22 (N=21)	TPV 22 & TPV 25 (N=31)	cTPV 25 (N=19)
Hemorrhage	7.0% (5)	0.0% (0)	9.7% (3)	10.5% (2)
Major or life threatening	0/0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Minor	7.0% (5)	0.0% (0)	9.7% (3)	10.5% (2)
Pulmonary thromboembolism	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Pseudoaneurysm	1.4% (1)	0.0% (0)	3.2% (1)	0.0% (0)
Brachial plexus injury	1.4% (1)	0.0% (0)	3.2% (1)	0.0% (0)
Arrhythmia	23.9% (17)	4.8% (1)	25.8% (8)	42.1% (8)
Heart block, 3rd degree	1.4% (1)	0.0% (0)	0.0% (0)	5.3% (1)
Supraventricular tachycardia	2.8% (2)	0.0% (0)	6.5% (2)	0.0% (0)
Ventricular premature beats	5.6% (4)	0.0% (0)	6.5% (2)	10.5% (2)
Ventricular tachycardia	14.1% (10)	4.8% (1)	12.9% (4)	26.3% (5)

*Event rate (number of patients)

†Other device-related adverse events included four TPV maldeployments with the cTPV 25 implant and one frame collapse.

‡One patient had a minor paravalvular leak reported followed by a major paravalvular leak reported, which resulted in the Harmony valve being explanted. This is reported as one major paravalvular leak event.

Surgical Reintervention

The results of surgical reinterventions at 6 months post implant are summarized in **Table 12**, stratified by the study phase and implant model. Four patients had their Harmony TPV explanted and a surgical valve placed by 6 months.

Table 11: Surgical Reinterventions at 6 Months – Implanted Cohort

Surgical Reintervention	Summary Statistics*			
	All Patients (N= 70)	Feasibility Phase	Pivotal Phase	
		TPV 22 (N=20)	TPV 22 & TPV 25 (N=31)	cTPV 25 (N=19)
Explant of the TPV	5.7% (4)	10.0% (2)	0.0% (0)	10.0% (2)
Repair or alteration of RVOT, TPV conserved	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
*Event rate (number of patients)				

Catheter Reintervention

The results of catheter reinterventions at 6 months post implant are summarized in Table 12, stratified by the study phase and implant model. Three patients had 6 total catheter reinterventions performed through 6-month follow-up, with some patients having more than one type of catheter reintervention.

Table 12: Catheter Reinterventions at 6 Months – Implanted Cohort

Catheter Reintervention	Summary Statistics*			
	All Patients (N= 70)	Feasibility Phase	Pivotal Phase	
		TPV 22 (N=20)	TPV 22 & TPV 25 (N=31)	cTPV 25 (N=20)
Implantation of another TPV	2.9% (2)	0.0% (0)	0.0% (0)	10.5% (2)

Catheter Reintervention	Summary Statistics*			
	All Patients (N= 70)	Feasibility Phase	Pivotal Phase	
		TPV 22 (N=20)	TPV 22 & TPV 25 (N=31)	cTPV 25 (N=20)
Stent placement, Branch PA	2.9% (2)	0.0% (0)	0.0% (0)	10.5% (2)
Stent placement, other	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Balloon angioplasty of the TPV	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Other†	2.9% (2)	0.0% (0)	0.0% (0)	10.5% (2)

*Event rate (number of patients)

†Reinterventions classified by sites as “other” included balloon angioplasty and balloon inflation.

10.1.3.4 Subgroup Analyses

Acceptable Hemodynamic Performance Stratified by Age

The number of patients in the Implanted >24 Hours Cohort with acceptable TPV hemodynamic function at 6 months without reintervention post implant stratified by age ("< 22 years" vs. "≥ 22 years") is shown in **Table 13**. The results are comparable between the "< 22 years" subgroup and the "≥ 22 years" subgroup.

Table 13. Patients with Acceptable TPV Hemodynamic Function at 6 Stratified By Age – Implanted > 24 Hours Cohort

Patients with Acceptable TPV Hemodynamic Function at 6 Months	Summary Statistics (N=68)	
	< 22 years (N=27)	**≥ 22 years (N=41)**
Number of evaluable patients	27	38
Number and percentage of patients with acceptable TPV hemodynamic function without reintervention	24 (88.9%)	34 (89.5%)
Standard error for percentage	6.0%	5.0%
Two-sided 95% confidence interval*	70.8% - 97.6%	75.2% - 97.1%
*Two-sided Clopper-Pearson interval		

Acceptable Hemodynamic Performance Stratified by Gender

The number of patients in the Implanted >24 Hours Cohort with acceptable TPV hemodynamic function at 6 months without reintervention post implant stratified by gender is shown in **Table 13.** The results are comparable between the female and male subgroups.

Table 14. Patients with Acceptable TPV Hemodynamic Function at 6 Months Stratified By Gender – Implanted > 24 Hours Cohort

Patients with Acceptable TPV Hemodynamic Function at 6 Months	Summary Statistics (N=68)	
	Female (N=28)	Male (N=40)
Number of evaluable patients	26	39
Number and percentage of patients with acceptable TPV hemodynamic function without reintervention	23 (88.5%)	35 (89.7%)
Standard error for percentage	6.3%	4.9%
Two-sided 95% confidence interval*	69.8% - 97.6%	75.8% - 97.1%
*Two-sided Clopper-Pearson interval.		

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