CoreValve™ System

Transcatheter Aortic Valve

Delivery Catheter System

Compression Loading System

CAUTION: Implantation of the Medtronic CoreValve™ system should be performed only by physicians who have received Medtronic CoreValve™ training.

These devices are supplied sterile for single use only. After use, dispose of the delivery catheter system and the compression loading system in accordance with local regulations and hospital procedures. Do not resterilize.

Instructions for Use

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

Explanation of symbols on package labeling

	Use By
	Consult Instructions for Use at this Website
	Do Not Reuse
	Do Not Resterilize
	Size
SN	Serial Number
STERILE LC	Sterile LC: Device has been sterilized using Liquid Chemical Sterilants according to EN/ISO 14160.
REF	Reorder Number
	Lower Limit of Temperature
	Quantity
LOT	Lot Number
STERILE EO	Sterilized Using Ethylene Oxide
	Manufactured In
	Nonpyrogenic
	MR Conditional
	Do Not Use if Package is Damaged
	Manufacturer
	Date of Manufacture
! USA	For US Audiences Only
	Model

1.0 DEVICE DESCRIPTION

The Medtronic CoreValve™ system consists of 3 components: the transcatheter aortic valve (bioprosthesis)[1], the delivery catheter system (catheter), and the compression loading system (CLS).

1.1 Transcatheter Aortic Valve (Bioprosthesis)

Figure 1

The bioprosthesis is manufactured by suturing 3 valve leaflets and a skirt, made from a single layer of porcine pericardium, onto a self-expanding, multi-level, radiopaque frame made of Nitinol. It is designed to replace the native aortic heart valve without open heart surgery and without concomitant surgical removal of the failed native valve. The bioprosthesis is processed with alpha-amino oleic acid (AOA™), which is an antimineralization treatment derived from oleic acid, a naturally occurring long-chain fatty acid.
The bioprosthesis is available for a range of aortic annulus and ascending aorta diameters as shown in Table 1.

Table 1: Patient Anatomical Diameters

Bioprosthesis Model	Size	Aortic Annulus Diameter	Ascending Aorta Diameter
CoreValve™ Evolut™ Bioprosthesis			
MCS-P4-23-AOA	23 mm	18 mm–20 mm	≤34 mm
CoreValve™ Bioprosthesis			
MCS-P3-26-AOA	26 mm	20 mm–23 mm	≤40 mm
MCS-P3-29-AOA	29 mm	23 mm–26 mm	≤43 mm
MCS-P3-31-AOA	31 mm	26 mm–29 mm	≤43 mm

1.2 Delivery Catheter System (Catheter)

The catheter with AccuTrak™ stability layer is compatible with a 0.035-in (0.889-mm) guidewire. The distal (deployment) end of the system features an atraumatic, radiopaque tip and a capsule that covers and maintains the bioprosthesis in a crimped position. The handle is located on the proximal end of the catheter and is used to load and deploy the bioprosthesis.

[1] The terms “bioprosthesis” and “transcatheter aortic valve” are synonymous terms and are used interchangeably throughout the document to refer to the CoreValve™ device.

The handle includes a macro slider to open and close the capsule and micro knob to facilitate precise bioprosthesis placement. The micro knob is turned counterclockwise to load the bioprosthesis and clockwise to deploy the bioprosthesis.

The AccuTrak™ stability layer is fixed at the handle and extends down the outside of the catheter shaft approximately 91 cm. It provides a barrier between the retractable delivery catheter system, introducer sheath, and vessel walls, thus enabling the catheter to retract freely and providing a more stable platform for deployment. The outer diameter of the catheter is 15 Fr (AccuTrak™ stability layer) and 12 Fr, and the outer diameter of the valve capsule is 18 Fr (Figure 2). The catheter can be used for femoral, subclavian/axillary, or ascending aortic (direct aortic) access sites. The catheter is available in 2 different models (Table 2).

Table 2: Catheter Models and System Compatibility

Catheter Model	Corresponding CLS Model	Corresponding Bioprosthesis Model(s)
DCS-C4-18FR-23	CLS-3000-18FR	MCS-P4-23-AOA
DCS-C4-18FR	CLS-3000-18FR	MCS-P3-26-AOA, MCS-P3-29-AOA, MCS-P3-31-AOA

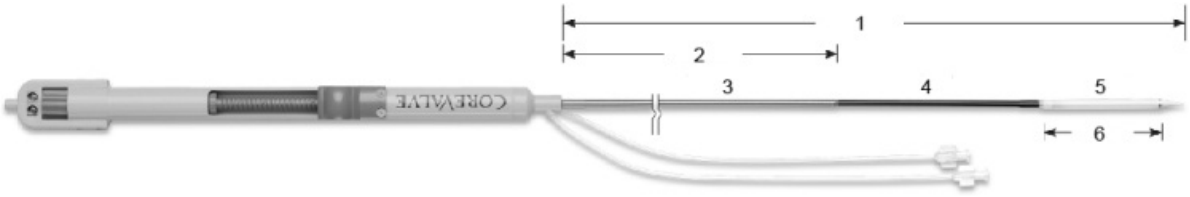

Figure 2

1. 112.5 cm
2. 90.9 cm
3. 15 Fr
4. 12 Fr
5. 18 Fr
6. 7.3 cm (Model DCS-C4-18FR); 6.9 cm (Model DCS-C4-18FR-23)

1.3 Compression Loading System (CLS)

The CLS compresses the bioprosthesis into the catheter. The CLS comprises the following:

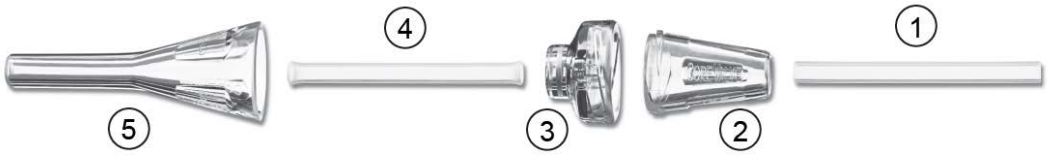

Figure 3

1. Inflow tube (straight tube)
2. Outflow cone
3. Outflow cap
4. Outflow tube (tube with flared ends)
5. Inflow cone

2.0 INDICATIONS

The Medtronic CoreValve™ system is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area ≤0.8 cm^2, a mean aortic valve gradient of >40 mm Hg, or a peak aortic-jet velocity of >4.0 m/s) and with native aortic annulus diameters between 18 and 29 mm who are judged by a heart team, including a cardiac surgeon, to be at extreme risk or inoperable for open surgical therapy (predicted risk of operative mortality and/or serious irreversible morbidity ≥50% at 30 days).

3.0 CONTRAINDICATIONS

The CoreValve™ system is contraindicated for patients presenting with any of the following conditions:

- known hypersensitivity or contraindication to aspirin, heparin (HIT/HITTS) and bivalirudin, ticlopidine, clopidogrel, Nitinol (Titanium or Nickel), or sensitivity to contrast media, which cannot be adequately premedicated
- ongoing sepsis, including active endocarditis
- preexisting mechanical heart valve in aortic position

4.0 WARNINGS AND PRECAUTIONS

4.1 Warnings

4.1.1 General

- Implantation of the Medtronic CoreValve™ system should be performed only by physicians who have received Medtronic CoreValve™ training.
- The transcatheter aortic valve is to be used only in conjunction with the delivery catheter system and the compression loading system.
- This procedure should only be performed where emergency aortic valve surgery can be performed promptly.
- DO NOT use any of the Medtronic CoreValve™ 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
- Mechanical failure of the delivery catheter system and/or accessories may result in patient complications.

4.1.2 Transcatheter Aortic Valve (Bioprosthesis)

- DO NOT use the bioprosthesis if any of the following conditions is observed:
    - there is any damage to the container (e.g., cracked jar or lid, leakage, broken or missing seals)
    - the serial number tag does not match the container label
    - the freeze indicator in the secondary package has activated
    - the storage solution does not completely cover the bioprosthesis
- Accelerated deterioration of the bioprosthesis may occur in patients presenting with an altered calcium metabolism.

4.2 Precautions

4.2.1 General

- DO NOT contact any of the Medtronic CoreValve™ system components with cotton or cotton swabs.
- DO NOT expose any of the Medtronic CoreValve™ system components to organic solvents, such as alcohol.
- DO NOT introduce air into the catheter.

- The safety and effectiveness of the Medtronic CoreValve™ system have not been evaluated in the pediatric population.
- The safety and effectiveness of the bioprosthesis for aortic valve replacement have not been evaluated in the following patient populations:
    - without Aortic Stenosis (AS)
    - who are at high, moderate, or low surgical risk (predicted perioperative mortality risk of <50%)
    - with untreated, clinically significant coronary artery disease requiring revascularization
    - with a preexisting prosthetic heart valve in any position
    - with cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support
- The safety and effectiveness of a CoreValve™ bioprosthesis implanted within a failed preexisting transcatheter or surgical bioprosthesis have not been demonstrated.
- The safety and effectiveness of the bioprosthesis for aortic valve replacement have not been evaluated in patient populations presenting with the following:
    - blood dyscrasias as defined: leukopenia (WBC <1000 cells/mm^3), thrombocytopenia (platelet count <50,000 cells/mm^3), history of bleeding diathesis or coagulopathy, or hypercoagulable states
    - congenital bicuspid or unicuspid valve verified by echocardiography
    - mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation [3-4+])
    - moderate to severe (3-4+) or severe (4+) mitral or severe (4+) tricuspid regurgitation
    - hypertrophic obstructive cardiomyopathy
    - new or untreated echocardiographic evidence of intracardiac mass, thrombus, or vegetation
    - native aortic annulus size <18 mm or >29 mm per the baseline diagnostic imaging
    - transarterial access not able to accommodate an 18-Fr sheath
    - sinus of valsalva anatomy that would prevent adequate coronary perfusion
    - moderate to severe mitral stenosis
    - severe ventricular dysfunction with left ventricular ejection fraction (LVEF) <20% as measured by resting echocardiogram
    - end-stage renal disease requiring chronic dialysis or creatinine clearance <20 cc/min
    - symptomatic carotid or vertebral artery disease

    - severe basal septal hypertrophy with an outflow gradient
- DO NOT expose the bioprosthesis to solutions other than the storage and rinse solutions.
- DO NOT add antibiotics or any other substance to either the storage or rinse solutions. DO NOT apply antibiotics or any other substance to the bioprosthesis.
- DO NOT allow the bioprosthesis to dry. Maintain tissue moisture with irrigation or immersion.
- DO NOT attempt to repair a damaged bioprosthesis.
- DO NOT handle or use forceps to manipulate the bioprosthesis leaflet tissue.
- DO NOT deform the bioprosthesis in excess of what is experienced during crimping, loading, and implantation.

4.2.2 Prior to Use

- Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water (minimum of 15 minutes). In the event of eye contact, flush with water for a minimum of 15 minutes and seek medical attention immediately.
- The bioprosthesis and the glutaraldehyde storage solution are STERILE. The outside of the bioprosthesis container is NONSTERILE and must not be placed in the sterile field.
- Damage may result from forceful handling of the catheter. Prevent kinking of the catheter when removing it from the packaging.
- This device was designed for single patient use only. Do not reuse, reprocess, or resterilize this product. 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.
- The bioprosthesis size must be appropriate to fit the patient's anatomy. Proper sizing of the device is the responsibility of the physician. Refer to Table 1 for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed in Section 5.0.
- Patients must present with femoral or subclavian/axillary access vessel diameters of ≥6 mm or an ascending aortic (direct aortic) access site ≥60 mm from the basal plane.
- Implantation of the bioprosthesis should be avoided in patients with aortic root angulation (angle between plane of aortic valve annulus and horizontal plane/vertebrae) of >30° for right subclavian/axillary access or >70° for femoral and left subclavian/axillary access.
- Use caution when using the subclavian/axillary approach in patients with a patent Left Internal Mammary Artery (LIMA) graft (for left subclavian/axillary approach only) or patent Right Internal Mammary Artery (RIMA) graft (for right subclavian/axillary approach only).

4.2.3 During Use

- Adequate rinsing of the bioprosthesis with sterile saline, as described in the Instructions for Use, is mandatory before implantation. No other solutions, drugs, chemicals, or antibiotics should ever be added to the glutaraldehyde or rinse solutions as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.
- During rinsing, do not touch the leaflets or squeeze the bioprosthesis.
- With the exception of attaching the bioprosthesis frame loops to the catheter tabs, do not touch the capsule or the transition between the capsule and the catheter shaft. To protect the capsule, handle the catheter using the catheter shaft or, during loading, the loading tools.
- If a capsule becomes damaged during loading or the capsule fails to close, replace the entire system (bioprosthesis, catheter, and CLS). Do not use a catheter with a damaged capsule.
- Prevent contamination of the bioprosthesis, its storage solution, the catheter, and the CLS with glove powder.
- After a bioprosthesis has been inserted into a patient, do not attempt to reload that bioprosthesis on the same or any other catheter.
- During implantation, if resistance to deployment is encountered (e.g., the micro knob starts clicking or is tight or stuck), apply upward pressure to the macro slider while turning the micro knob. If the bioprosthesis still does not deploy, remove it from the patient and use another system.
- While the catheter is in the patient, ensure the guidewire is extending from the tip. Do not remove the guidewire from the catheter while the catheter is inserted in the patient.
- Once deployment is initiated, retrieval of the bioprosthesis from the patient (e.g., use of the catheter) is not recommended. Retrieval of a partially deployed valve using the catheter may cause mechanical failure of the delivery catheter system, aortic root damage, coronary artery damage, myocardial damage, vascular complications, prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery.
- During deployment, the bioprosthesis can be advanced or withdrawn as long as annular contact has not been made. Once annular contact is made, the bioprosthesis cannot be advanced in the retrograde direction; if necessary, and the frame has only been deployed $\leq 2/3$ of its length, the bioprosthesis can be withdrawn (repositioned) in the antegrade direction. However, use caution when moving the bioprosthesis in the antegrade direction.
- Use the handle of the delivery system to reposition the bioprosthesis. Do not use the outer catheter sheath.
- Once deployment is complete, repositioning of the bioprosthesis (e.g., use of a snare and/or forceps) is not recommended. Repositioning of a deployed valve may cause aortic root damage, coronary artery damage, myocardial damage, vascular complications,

prosthetic valve dysfunction (including device malposition), embolization, stroke, and/or emergent surgery.

- Do not attempt to retrieve a bioprosthesis if any one of the outflow struts is protruding from the capsule. If any one of the outflow struts has deployed from the capsule, the bioprosthesis must be released from the catheter before the catheter can be withdrawn.
- Ensure the capsule is closed before catheter removal. If increased resistance is encountered when removing the catheter 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/or harm to the patient. If the cause of resistance cannot be determined or corrected, remove the catheter and introducer sheath as a single unit over the guidewire, and inspect the catheter and confirm that it is complete.
- Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up.
- Postprocedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis.
- Postprocedure, administer anticoagulation and/or antiplatelet therapy per hospital 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.
- The safety and efficacy of implanting a second CoreValve™ bioprosthesis within the initial CoreValve™ bioprosthesis have not been demonstrated. However, in the event that a second CoreValve™ bioprosthesis must be implanted within the initial CoreValve™ bioprosthesis to improve valve function, valve size and patient anatomy must be considered before implantation of the second CoreValve™ bioprosthesis to ensure patient safety (e.g., to avoid coronary obstruction).
- In the event that valve function or sealing is impaired due to excessive calcification or incomplete expansion, a postimplant balloon dilatation of the bioprosthesis may be performed to improve valve function and sealing. To ensure patient safety, valve size and patient anatomy must be considered when selecting the size of the balloon used for dilatation. Postimplant balloon dilatation with balloon sizes larger than those shown in the following table are not recommended:

Table 3: Maximum Postimplant Balloon Dilatation Sizing

CoreValve™ Bioprosthesis Size	Maximum Balloon Diameter (mm)*
23 mm	22 mm
26 mm	25 mm
29 mm	28 mm
31 mm	30 mm

*CoreValve™ bioprosthesis device performance was maintained after dilatation with NuMED Z-MED II™ Balloon Aortic Valvuloplasty catheters of the listed sizes. Data on file.

Refer to the specific balloon catheter manufacturer's instructions for use for instructions on the proper use of balloon catheter devices.

4.3 Magnetic Resonance Imaging (MRI)

MRI may be used on the bioprosthesis only under specific conditions. See Section 6.2 MRI Information for more information.

5.0 POTENTIAL ADVERSE EVENTS

Potential risks associated with the implantation of the Medtronic CoreValve™ transcatheter aortic valve may include, but are not limited to, the following:

- death
- cardiac arrest
- coronary occlusion, obstruction, or vessel spasm (including acute coronary closure)
- emergent surgery (e.g., coronary artery bypass, heart valve replacement, valve explant)
- multi-organ failure
- heart failure
- myocardial infarction
- cardiogenic shock
- respiratory insufficiency or respiratory failure
- cardiovascular injury (including rupture, perforation, or dissection of vessels, ventricle, myocardium, or valvular structures that may require intervention)
- perforation of the myocardium or a vessel
- ascending aorta trauma
- cardiac tamponade
- cardiac failure or low cardiac output
- prosthetic valve dysfunction including, but not limited to, fracture; bending (out-of-round configuration) of the valve frame; under-expansion of the valve frame; calcification; pannus; leaflet wear, tear, prolapse, or retraction; poor valve coaptation; suture breaks or disruption; leaks; mal-sizing (prosthesis-patient mismatch); malposition (either too high or too low)/malplacement; regurgitation; stenosis
- thrombosis/embolus (including valve thrombosis)
- valve migration/valve embolization
- ancillary device embolization
- emergent percutaneous coronary intervention (PCI)
- emergent balloon valvuloplasty
- major or minor bleeding that may or may not require transfusion or intervention (including life-threatening or disabling bleeding)
- allergic reaction to antiplatelet agents, contrast medium, or anesthesia
- infection (including septicemia and endocarditis)
- stroke, transient ischemic attack (TIA), or other neurological deficits

- permanent disability
- renal insufficiency or renal failure (including acute kidney injury)
- mitral valve regurgitation or injury
- tissue erosion
- vascular access related complications (e.g., dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, stenosis)
- conduction system disturbances (e.g., atrioventricular node block, left-bundle branch block, asystole), which may require a permanent pacemaker
- cardiac arrhythmias
- encephalopathy
- pulmonary edema
- pericardial effusion
- pleural effusion
- myocardial ischemia
- peripheral ischemia
- bowel ischemia
- heart murmur
- hemolysis
- cerebral infarction-asymptomatic
- non-emergent reoperation
- inflammation
- fever
- hypotension or hypertension
- syncope
- dyspnea
- anemia
- angina
- abnormal lab values (including electrolyte imbalance)

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 Information

Nonclinical testing and modeling has demonstrated that the bioprosthesis is magnetic resonance (MR) Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 tesla and 3 tesla
- Spatial gradient field of ≤2500 gauss/cm
- Normal operating mode only with a maximum whole body specific absorption rate (SAR) of 2.0 W/kg for 15 minutes as read from equipment monitor

6.2.1 1.5 tesla[2]

Based on nonclinical testing and modeling, a 26 mm bioprosthesis was calculated to produce a temperature rise of less than 3.5°C at a maximum whole body averaged SAR of 2.0 W/kg for 15 minutes of MR scanning in a 64 MHz whole body transmit coil, which corresponds to a static field of 1.5 tesla[3].

6.2.2 3 tesla[4]

Based on nonclinical testing and modeling, a 26 mm bioprosthesis was calculated to produce a temperature rise of less than 3.6°C at a maximum whole body averaged SAR of 2.0 W/kg for 15 minutes of MR scanning in a 128 MHz whole body transmit coil, which corresponds to a static field of 3 tesla[3].

[2] Testing conducted at 1.5 tesla (64 MHz) employed a 1.5 tesla General Electric Signa RF coil with model number 46-258170G1.

[3] These calculations do not take into consideration the cooling effects of perfusion and blood flow. The maximum whole body averaged specific absorption rate (SAR) was derived by calculation and verified by calorimetry.

[4] Testing conducted at 3 tesla (128 MHz) employed a 3.0 tesla General Electric Signa HDx 3.0 MR system with Software Version 15\LX\MR Software release.15.0.M4.0910.a.

6.2.3 1.5 tesla and 3 tesla

The bioprosthesis should not move or migrate when exposed to MR scanning immediately after implantation. MRI at 3 tesla and 1.5 tesla may be performed immediately following the implantation of the bioprosthesis. The magnetic force on the bioprosthesis—determined at a location where the magnitude of the magnetic field strength was about 1.5 tesla and the magnitude of the spatial gradient of the magnetic field was about 400 gauss/cm—was determined to be less than 5% of its weight. Nonclinical testing at field strengths other than 1.5 tesla and 3 tesla has not been performed to evaluate bioprosthesis heating.

MR image quality may be compromised if the area of interest is in the same area, or relatively close to the position of the device. It may be necessary to optimize MR imaging parameters for the presence of this implant. When tested at 3 tesla[5], the image artifact extended less than 3 mm beyond the bioprosthesis for the spin echo sequence with TR = 500 ms and TE = 20 ms and less than 7 mm beyond the bioprosthesis for the gradient echo sequence with TR = 100 ms, TE = 14.4 ms and flip angle = 30°. The mid region of the device lumen was obscured.

[5] Testing conducted at 3 tesla (128 MHz) employed a 3.0 tesla General Electric Signa HDx 3.0 MR system with Software Version 15\LX\MR Software release.15.0.M4.0910.a.

7.0 HOW SUPPLIED

7.1 Packaging

The bioprosthesis is supplied STERILE and NONPYROGENIC in a sealed container made of glass and a screw cap with a liner. The outside of the container is NONSTERILE and must not be placed in the sterile field. A freeze indicator is placed inside the labeled carton. If the freeze indicator has been activated, do not use the bioprosthesis.

The catheter is packaged in a double-pouch configuration and sterilized with ethylene oxide gas. The catheter is sterile if the pouches are undamaged and unopened. The outer surfaces of the outer pouch are NONSTERILE and must not be placed in the sterile field.

The CLS is packaged in a double-pouch configuration. The CLS is sterile if the pouches are undamaged and unopened. The outer surfaces of the outer pouch are NONSTERILE and must not be placed in the sterile field. The CLS is sterilized with ethylene oxide gas.

7.2 Storage

Store the bioprosthesis at room temperature. Avoid exposing to extreme fluctuations of temperature. Avoid freezing. Appropriate inventory control should be maintained so that bioprostheses with earlier Use By dates are implanted preferentially. Store the catheter and CLS in a cool, dry environment.

8.0 ADDITIONAL EQUIPMENT

Note: While extensive, this equipment list is not meant to cover all possible scenarios.

Transesophogeal Echocardiogram (TEE) or Transthoracic Echocardiography (TTE) on stand by

Temporary pacer insertion

- temporary pacemaker catheter (4 Fr or 5 Fr), per hospital protocol
- sterile sleeve for pacemaker catheter
- hemostatic vessel introducer sheath
- temporary pacemaker generator
- sterile temporary pacemaker-to-generator cable

If indicated, pulmonary artery catheter insertion

- standard pulmonary artery catheter
- hemostatic vessel introducer sheath
- saline flush line connected to pressure transducer

Baseline aortography via radial, brachial, or femoral approach

- 5-Fr graduated pigtail angiographic catheter (with radiopaque markers)
- 6-Fr hemostatic vessel introducer sheath
- 2-port manifold with saline flush line and pressure tubing or transducer
- power injector syringe
- contrast media
- high-pressure power injector tubing

Predilatation of implant site

- 2-port manifold with saline flush and transducer
- 9-Fr and 18-Fr hemostatic vessel introducer sheaths
- standard length 0.035-in (0.889-mm) straight guidewire
- appropriate suture-mediated closure system, if applicable
- angiographic catheter
- 0.035-in (0.889-mm) x 260-cm standard high-support guidewire to be shaped with a pigtail loop
- balloon valvuloplasty catheters, ≤4 cm length x 18 mm, 20 mm, 22 mm or 23 mm, and 25 mm diameters
- inflation device or syringe and diluted 1:5 contrast media

Bioprosthesis implantation

- 18-Fr hemostatic vessel introducer sheath

Stand-by supplies (must be available in the room)

- pericardiocentesis tray
- 35-mm x 120-cm single loop snare
- 6-Fr coronary guide catheters
- 14-Fr and 16-Fr hemostatic vessel introducer sheaths
- standard cardiac catheterization lab equipment

9.0 INSTRUCTIONS FOR USE

Figure 4

1. Catheter tip
2. Capsule
3. Catheter shaft
4. Tube flush port
5. AccuTrak™ stability layer
6. Macro slider
7. Micro knob
8. Luer-lock connection flush port

9.1 Inspection and Bioprosthesis Loading Procedure

Caution: Once the bioprosthesis is removed from its container and the catheter and CLS are removed from their packaging, ensure all subsequent procedures are performed in a sterile field.

9.1.1 Inspection Prior to Use

1. Before removing the bioprosthesis, catheter, or CLS from its primary packaging, carefully inspect the packaging for any evidence of damage that could compromise the sterility or integrity of the device (e.g., cracked jar or lid, leakage, broken or missing seals, torn or punctured pouch).

   Caution: Do not use the product if there is evidence of damage.

2. Inspect the temperature indicator located within the packaging for the bioprosthesis to ensure it has not been activated.

   Caution: Do not use the bioprosthesis if the temperature indicator has been activated.

9.1.2 Preparation of the Catheter

3. Wipe the length of the catheter with a moist (saline) gauze.
4. Use the micro knob and macro slider on the handle to open and close the catheter (Figure 4).

5. Attach a stopcock to the first flush port. Attach a 10-mL syringe filled with saline to the stopcock on the first flush port and flush. Repeat step for the second flush port on the catheter (Figure 5).

Figure 5

6. Verify no catheter leakage is observed during any of the flushing steps. If leakage is observed, use a new system.
7. Attach a 10-mL syringe filled with saline to the third flush port on the handle on the catheter (Figure 6) and flush.

Figure 6

8. Fill a loading bath with cold, sterile saline (0°C to 8°C [32°F to 46°F]), and place the CLS components in the bath.

9.1.3 Bioprosthesis Rinsing Procedure

9. Fill each of 3 rinsing bowls with approximately 500 mL of fresh, sterile saline at ambient temperature between 15°C to 25°C (59°F to 77°F).
10. Confirm the integrity of the primary bioprosthesis container. Open the container and remove the bioprosthesis by carefully grasping one of the frame loops. Let any remaining solution drain from the bioprosthesis completely.

    Caution: The bioprosthesis should not be handled or manipulated with sharp or pointed objects. Use atraumatic blunt-tipped forceps only. DO NOT use the forceps to grasp the tissue portion of the bioprosthesis.

    Note: Retain the container with the original solution. **It may be needed to store and return a rejected bioprosthesis.**
11. Compare the serial number on the container with the serial number on the tag attached to the bioprosthesis.

    Caution: If the serial numbers do not match, DO NOT use the bioprosthesis.

12. Carefully remove the serial number tag from the bioprosthesis and retain the tag. Ensure that the suture that was used to secure the serial number tag to the bioprosthesis is completely removed from the bioprosthesis.
13. Immerse the entire bioprosthesis in a sterile rinsing bowl.
14. Gently agitate the bioprosthesis by hand for 2 minutes to remove the glutaraldehyde from the bioprosthesis.
15. Repeat steps 13 and 14 in each of the 2 remaining rinsing bowls to ensure complete removal of glutaraldehyde from the bioprosthesis.
16. Leave the bioprosthesis submerged in sterile saline until it is ready to be loaded.

9.1.4 Bioprosthesis Loading Procedure

Caution: Rapid capsule advancement can contribute to difficulties with loading the valve. Slowly advancing the capsule helps facilitate successful loading.

Caution: With the exception of attaching the bioprosthesis frame loops to the catheter tabs, do not touch the capsule or the transition between the capsule and the catheter shaft. To protect the capsule, handle the catheter using the catheter shaft or, during loading, the loading tools.

Note: If a capsule becomes damaged during loading or the capsule fails to close, replace the entire system (bioprosthesis, catheter, and CLS). Do not use a catheter with a damaged capsule.

Perform the bioprosthesis loading procedure while the bioprosthesis, CLS, capsule, and catheter tip are immersed in cold, sterile saline (0°C to 8°C [32°F to 46°F]).

17. To open the capsule, activate the macro slider and slide back.
18. Submerge and cool the bioprosthesis in a bath filled with cold, sterile saline.
19. Advance the outflow tube (tube with flared ends) over the catheter shaft toward the handle (Figure 7).

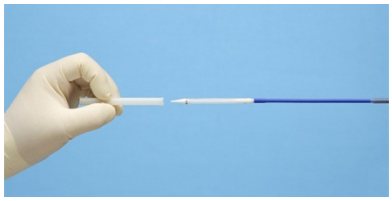

Figure 7

20. Gently squeeze the outflow part of the cold bioprosthesis frame and insert it into the outflow cone (Figure 8).

    Note: As applicable, all subsequent bioprosthesis loading steps should be performed under chilled (0°C to 8°C [32°F to 46°F]) saline.

Figure 8

21. Slowly continue to insert the frame into the outflow cone.
22. Once the bioprosthesis is fully inserted, secure the outflow cap onto the outflow cone (Figure 9).

Figure 9

23. Carefully insert the inflow tube (straight tube) into the outflow cap (Figure 10).

Figure 10

24. Gently continue to advance the inflow tube until the bioprosthesis frame loops begin to separate.
25. Insert the distal catheter tip into the inflow tube (Figure 11).

Figure 11

26. Carefully withdraw the inflow tube and attach the exposed frame loops to the catheter tabs (Figure 12).

Figure 12

27. Rotate the micro knob to advance the capsule to cover the bioprosthesis frame loops and the top of the outflow crowns (Figure 13).

    Note: Ensure that the capsule has covered all of the outflow crowns and the bioprosthesis frame loops are securely attached to the catheter tabs.

Figure 13

28. Advance the outflow tube over the radiopaque marker band of the capsule prior to advancing the capsule further (Figure 14).

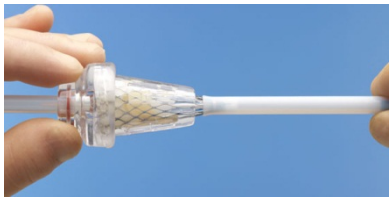

Figure 14

29. Remove the outflow cap and inflow tube from the outflow cone (Figure 15).

Figure 15

30. Move the outflow cone away from the bioprosthesis over the catheter toward the handle.
31. Advance the inflow cone over the bioprosthesis using the outflow tube (Figure 16).

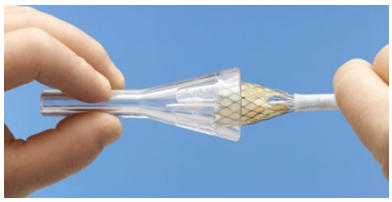

Figure 16

Note: Ensure the bioprosthesis frame axis is visually aligned (coaxial) with the inflow cone axis during the insertion of the bioprosthesis into the inflow cone (Figure 17). Complete the insertion of the bioprosthesis into the inflow cone in one uninterrupted movement.

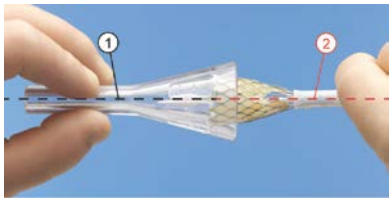

Figure 17

1. Inflow cone axis
2. Bioprosthesis frame axis

32. Continue to advance the bioprosthesis into the inflow cone until the outflow tube contacts the inside of the inflow cone (Figure 18).

Figure 18

33. Visually inspect the bioprosthesis within the inflow cone to verify there is no crease or infold in the frame beyond the second node from the inflow end. Ensure inspection is performed circumferentially around the entire bioprosthesis.

    Caution: If a crease or infold greater than 2 nodes long is noticed, do not use the bioprosthesis or catheter. Prepare a new bioprosthesis to load into a new catheter.

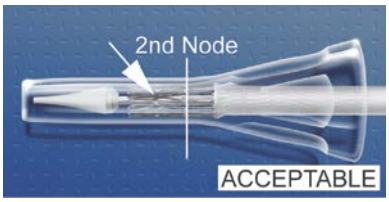

Figure 19

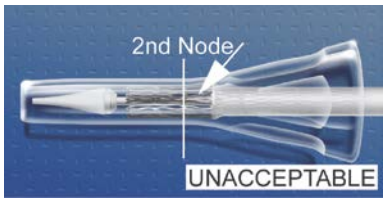

Figure 20

34. Hold the inflow cone against the outflow tube while slowly advancing the capsule over the bioprosthesis until the capsule comes within approximately 5 mm of the catheter tip (Figure 21). If the micro knob clicks, apply upward pressure to the macro slider and continue turning the micro knob (Figure 22).

Figure 21

Figure 22

35. With the catheter tip submerged in cold saline, flush both tube flush ports with saline.
36. Slowly advance the capsule over the bioprosthesis until the capsule contacts the catheter tip.
37. If the micro knob has fully advanced the capsule and a small gap remains between the end of the capsule and the catheter tip, stabilize the handle with one hand; position the other hand on the blue catheter shaft and gently advance the capsule manually to close the gap between the capsule and the catheter tip (Figure 23).

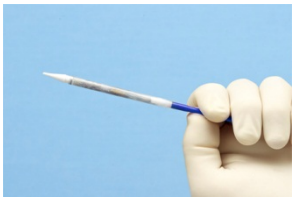

Figure 23

38. Remove the outflow cone and outflow tube from the catheter (Figure 24).

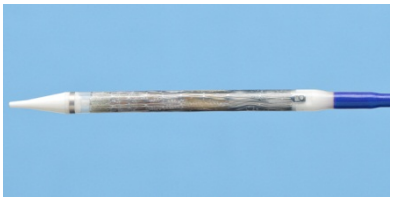

Figure 24

39. Conduct a final visual inspection of the loaded bioprosthesis to make sure the frame is free of creases or infolds beyond the second node from the inflow end. Ensure inspection is performed circumferentially around the entire bioprosthesis.

    Caution: If a crease or infold greater than 2 nodes long is noticed, do not use the bioprosthesis or catheter. Prepare a new bioprosthesis to load into a new catheter.

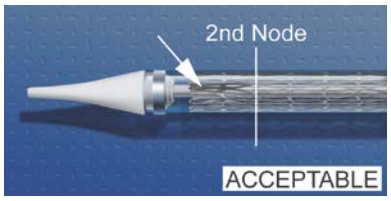

Figure 25

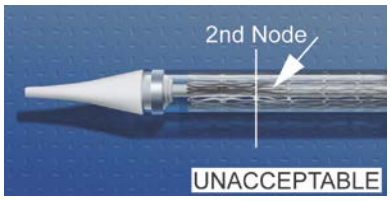

Figure 26

40. Leave the loaded bioprosthesis submerged in cold saline until implantation.

9.2 Bioprosthesis Implantation

9.2.1 Vascular Access

Note: Vascular access should be achieved per hospital protocol (either percutaneously or via surgical cutdown).

Note: The primary access artery will be used to introduce the CoreValve™ system and the balloon catheter; the secondary access artery will be used to introduce the reference pigtail.

1. Establish a central venous line. Insert a 4-Fr or 5-Fr temporary pacemaker catheter via the right internal jugular vein (or other appropriate access vessel) per hospital protocol.
2. Insert a 6-Fr introducer sheath into the secondary access artery.
3. Insert an 18-Fr introducer sheath into the primary access artery.
4. Administer anticoagulant according to hospital protocol. If heparin is administered as an anticoagulant, check the activated clotting time (ACT) after initial bolus of heparin and recheck every 30 minutes thereafter. Maintain ACT ≥250 seconds.

   Note: Anticoagulant may be administered at any time prior to this point, but avoid delaying beyond this point.

9.2.2 Crossing the Native Valve

5. Advance the graduated pigtail catheter to the ascending aorta and position the distal tip in the noncoronary cusp of the native aortic valve.
6. Identify the ideal annular viewing plane using contrast injections at various angiographic angles.

   Note: It is recommended that a dedicated individual prepare and operate the contrast injector.

7. Insert an angiographic catheter over a standard J-tip guidewire into the primary access sheath and advance to the ascending aorta.
8. Exchange the J-tip guidewire for a 0.035-in (0.889-mm) straight-tip guidewire. Advance the straight-tip guidewire across the native aortic valve into the left ventricle (LV).
9. After crossing the native aortic valve with the guidewire, advance the angiographic catheter into the LV.
10. Exchange the straight-tip guidewire for an exchange-length J-tip guidewire.
11. Exchange the angiographic catheter for a 6-Fr pigtail catheter.
12. Remove the guidewire and connect the catheter to the transducer. Using both catheters, record the aortic pressure gradient.
13. Using a right anterior oblique (RAO) projection, advance the previously pigtail-shaped, 0.035-in (0.889-mm) high-support guidewire through the pigtail catheter and position in the apex of the LV.
14. Remove the pigtail catheter while maintaining guidewire position in the LV.

9.2.3 Predilatation of the Implant Site

15. Insert the valvuloplasty balloon through the 18-Fr introducer sheath and advance it to the ascending aorta.
16. Reposition the angiographic equipment to the ideal viewing plane. Position the valvuloplasty balloon across the native valve, while maintaining strict fluoroscopic surveillance of the distal tip of the guidewire in the LV.
17. Perform balloon valvuloplasty per hospital protocol and remove the valvuloplasty balloon while maintaining guidewire position across the native aortic valve.

9.2.4 Deployment

18. Insert the device over the 0.035-in (0.889-mm) guidewire and advance it while maintaining strict fluoroscopic surveillance of the guidewire in the LV. Confirm the position of the macro slider prior to crossing the aortic arch.
19. When crossing the aortic arch, it is critical that the guidewire is controlled to prevent it from moving forward. Without proper management of the distal tip of the guidewire, the guidewire could move forward and cause trauma to the LV.
20. Advance the device through the native valve. Perform an angiogram to confirm that the pigtail catheter is in position within the noncoronary cusp of the aortic root. Fluoroscopically identify the appropriate landmarks.

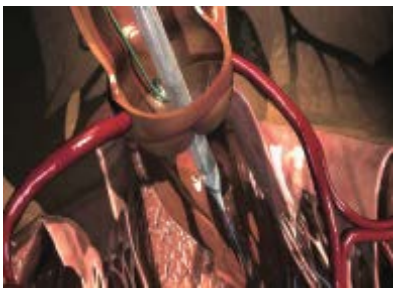

Figure 27

21. Note the radiopaque bands (Figure 28). Follow the diagrams in Figure 29 and Figure 32 for the optimal placement of the bioprosthesis. The bioprosthesis should be placed so that the skirt is within the aortic annulus (approximately 4 mm to 6 mm below the annulus). The annulus is defined as the angiographic floor of the aortic root.

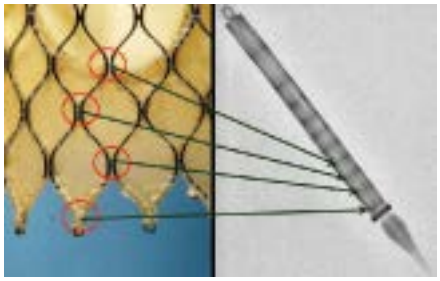

Figure 28

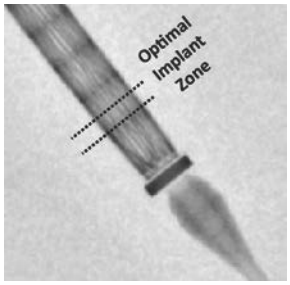

Figure 29

22. After attaining optimal catheter position, slowly turn the micro knob and begin to deploy the bioprosthesis. As the inflow aspect of the bioprosthesis starts to flare outward, monitor bioprosthesis position under fluoroscopy.

    Caution: During implantation, if resistance to deployment is encountered (e.g., the micro knob starts clicking or is tight or stuck), apply mild upward pressure to the macro slider while turning the micro knob (Figure 22). If the bioprosthesis still does not deploy, remove it from the patient and use another system.

Figure 30

23. Perform an angiogram. Once annular contact is made, the bioprosthesis should not be advanced into a lower position.

Note: The force required to move the bioprosthesis into a higher position becomes noticeably greater once annular contact is made.

24. Continue deploying rapidly to the 2/3 deployment point; stop turning the micro knob.

    Note: Shortly after annular contact, the blood pressure will be reduced until the 2/3 deployment point, when the bioprosthesis leaflets are exposed and are functioning.

Figure 31

25. Perform an angiogram to assess the location of the bioprosthesis. Refer to Figure 29 and Figure 32 for the optimal placement of the bioprosthesis skirt within the aortic annulus (approximately 4 mm to 6 mm below the annulus).

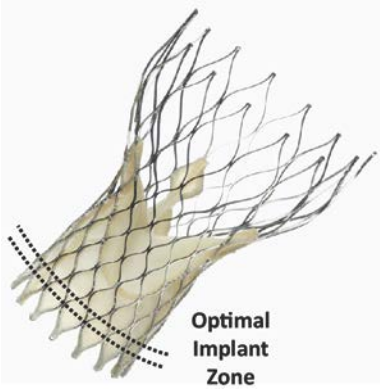

Figure 32

26. If the bioprosthesis is positioned low, slight repositioning of a partially deployed bioprosthesis (≤2/3 of the bioprosthesis length) can be achieved by carefully withdrawing the catheter.
27. When satisfactory position is achieved, withdraw the reference pigtail catheter to the ascending aorta. Continue to turn the micro knob until both frame loops disengage. Use orthogonal views under fluoroscopy to confirm that the frame loops have detached from the catheter tabs. If a frame loop is still attached to a catheter tab, do not pull on the catheter. Under fluoroscopy, advance the catheter slightly and, if necessary, gently rotate the handle clockwise (<180°) and then counterclockwise (<180°) to disengage the loop from the catheter tab.

9.2.5 Postdeployment

28. Under fluoroscopic guidance, confirm that the catheter tip is coaxial with the inflow portion of the bioprosthesis.
29. Withdraw the catheter to the aorta, while maintaining guidewire position.

    Note: For transfemoral access, withdraw the catheter until the catheter tip is positioned in the descending aorta. For direct aortic access and subclavian access, withdraw the catheter until the catheter tip is close to the distal tip of the introducer sheath.
30. Close the capsule and remove the catheter through the 18-Fr introducer sheath.

    Note: If the capsule does not close properly, gently rotate the catheter clockwise (<180°) and then counterclockwise (<180°) until the capsule closes.

    Caution: Ensure the capsule is closed before catheter removal. If increased resistance is encountered when removing the catheter 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/or harm to the patient. If the cause of resistance cannot be determined or corrected, remove the catheter and introducer sheath as a single unit over the guidewire, and inspect the catheter and confirm that it is complete.
31. Dispose of the device in accordance with local regulations and hospital procedures.
32. Advance a 6-Fr pigtail catheter over the guidewire into the LV.
33. Remove the guidewire and connect the pigtail catheter to the transducer.
34. Using both pigtail catheters, record aortic pressure gradient.
35. Remove the 6-Fr pigtail over a standard, J-tip guidewire.
36. Perform a postimplant aortogram with the reference pigtail to ensure coronary patency and assess aortic regurgitations.

    Note: In the event that valve function or sealing is impaired due to excessive calcification or incomplete expansion, a postimplant balloon dilatation of the bioprosthesis may be performed to improve valve function and sealing. To ensure patient safety, valve size and patient anatomy must be considered when selecting the size of the balloon used for dilatation. Refer to Table 3 for balloon size information. Refer to the specific balloon catheter manufacturer's instructions for use for instructions on the proper use of balloon catheter devices.
37. Remove the 18-Fr introducer sheath and complete the puncture site closure per hospital protocol.
38. Perform contrast angiography to verify the absence of any vascular complications.
39. Remove the reference pigtail catheter over a standard guidewire. Remove the 6-Fr introducer and close the access site per hospital protocol.
40. Administer anticoagulation and/or antiplatelet therapy as required according to hospital protocol.

10.0 RETURN OF EXPLANTED BIOPROSTHESES

Medtronic is interested in obtaining recovered bioprostheses. Specific pathological studies of the explanted bioprosthesis will be conducted under the direction of a consulting pathologist. A written summary of the findings will be returned to the physician. To obtain a product return kit, contact a Medtronic distribution center or a Medtronic Representative. If a kit is not available, place the explanted bioprosthesis in a container of glutaraldehyde or 10% buffered formalin immediately after excision. For further instructions on the return of an explanted device, contact a Medtronic Representative.

11.0 SUMMARY OF CLINICAL STUDY

The CoreValve™ U.S. Pivotal Trial Extreme Risk cohort was a prospective, non-randomized, unblinded, multi-center investigational study. All enrolled patients were assigned to transcatheter aortic valve replacement (TAVR) with the Medtronic CoreValve™ system. The purpose of this clinical study was to evaluate the safety and effectiveness of the Medtronic CoreValve™ system in the treatment of symptomatic severe aortic stenosis in patients requiring aortic valve replacement with predicted operative mortality or serious, irreversible morbidity risk of ≥50% at 30 days (Extreme Risk).

This Extreme Risk cohort enrolled 656 patients with symptomatic severe aortic stenosis (500 iliofemoral and 156 non-iliofemoral patients) at 41 of the 43 activated centers in the United States with baseline characteristics described in Table 4. Severe aortic stenosis was defined as an aortic valve area of ≤0.8 cm^2 and a mean aortic valve gradient of >40 mm Hg. The primary endpoint was all-cause mortality or major stroke at 12 months. The primary analysis compared the primary endpoint against a pre-specified performance goal.

Patients received the CoreValve™ bioprosthesis either through the iliofemoral access route or through the non-illiofemoral (subclavian and direct aortic) access routes. An attempted implant was performed on 489 patients via iliofemoral access and who embody the Attempted Implant[6] iliofemoral cohort (n=489), which was the basis for assessment of the primary endpoint. Of the 489 attempted implants via iliofemoral access, 486 patients were implanted with the CoreValve™ bioprosthesis and embody the Implanted[7] iliofemoral cohort (n=486), which was the basis for secondary endpoints related to hemodynamic data.

An attempted implant was performed on 150 patients via non-iliofemoral access and these patients embody the Attempted Implant cohort. Of these 150 patients, 148 were implanted with the CoreValve™ bioprosthesis and embody the Implanted non-iliofemoral cohort. Per protocol, non-iliofemoral patients were not included in the primary analysis due to anticipated heterogeneity in patient selection and outcome. Compared with patients enrolled in the iliofemoral cohort, patients in the non-iliofemoral cohort were, generally, at a higher risk with respect to specific critical co-morbidities.

The following data summarize the results from the Extreme Risk cohort (iliofemoral and non-iliofemoral).

11.1 Patient Population

The patient characteristics analyzed for the iliofemoral and non-iliofemoral enrolled cohorts include demographics, clinical characteristics, medical history, and potentially prohibitive anatomic factors for surgical aortic valve replacement (SAVR) and assessments for co-morbidity, frailty, and disability (Table 4). The ability of a patient to obtain a functional recovery after SAVR is largely based on the presence of significant co-morbidities, frailties,

[6] The Attempted Implant population consisted of all patients with an attempted procedure, defined as when the patient was brought into the procedure room and any of the following had occurred: anesthesia administered, vascular line placed, TEE placed, or any monitoring line placed.

[7] The Implanted population consisted of all Attempted Implant patients who were actually implanted with the CoreValve™ bioprosthesis.

and disabilities, with the combination of the factors having higher weight than the individual factors alone. As detailed in Table 4, a high proportion of the CoreValve™ Extreme Risk patients had significant co-morbidities, frailties, or disabilities, which established the study population as "Extreme Risk." The mean age for patients participating in the trial was approximately 83 years old, and slightly less than 50% of patients were male. The mean Society of Thoracic Surgeons (STS) score was approximately 10. Greater than 90% of all patients were in NYHA classes III or IV.

Additionally, coronary artery disease was present in approximately 80% of patients, and greater than 30% of patients had previous MI. Peripheral vascular disease, COPD, and home oxygen use were more prevalent for non-iliofemoral patients.

Table 4: Baseline Characteristics and Echocardiographic Findings (All Enrolled)

Demographic	Iliofemoral N=500	Non-Iliofemoral N=156
Age (years)	83.1 ± 8.6 (500)	81.6 ± 7.7 (156)
Gender (Male)	48.0% (240/500)	44.9% (70/156)
NYHA Classification		
II	8.6% (43/500)	8.3% (13/156)
III	63.6% (318/500)	66.0% (103/156)
IV	27.8% (139/500)	25.6% (40/156)
STS Score (Risk of Mortality, %)	10.3 ± 5.5	10.5 ± 5.7
Coronary Artery Disease	81.8% (409/500)	78.8% (123/156)
Previous MI	31.0% (155/500)	31.4% (49/156)
Previous Interventions		
Coronary Artery Bypass Surgery	39.0% (195/500)	41.0% (64/156)
Percutaneous Coronary Intervention	37.4% (187/500)	30.1% (47/156)
Balloon Valvuloplasty	20.4% (102/500)	22.4% (35/156)
Cerebral Vascular Disease	24.0% (119/496)	28.4% (44/155)
Prior Stroke	13.6% (68/499)	14.2% (22/155)
Peripheral Vascular Disease	36.0% (179/497)	59.0% (92/156)
Chronic Lung Disease/COPD	59.6% (298/500)	69.9% (109/156)
Home Oxygen	30.8% (154/500)	41.7% (65/156)
Creatinine Level >2 mg/dl	4.6% (23/500)	2.6% (4/156)
Atrial Fibrillation/Atrial Flutter	47.4% (236/498)	48.4% (75/155)
Preexisting Permanent Pacemaker Placement/ICD	25.8% (129/500)	24.4% (38/156)
Aorta Calcification[1]: Severe/Porcelain		
Severe	16.6% (83/499)	17.5% (27/154)

Demographic	Iliofemoral N=500	Non-Iliofemoral N=156
Porcelain	5.2% (26/499)	7.8% (12/154)
Chest Wall Deformity	5.6% (28/500)	1.9% (3/156)
Hostile Mediastinum	12.0% (60/499)	9.0% (14/156)
Cirrhosis of the Liver	3.0% (15/500)	1.3% (2/156)
Wheelchair Bound	16.6% (83/500)	12.2% (19/156)
Echocardiographic Findings		
Ejection Fraction (Visual Estimate, %)	53.2 ± 13.6 (498)	54.3 ± 15.3 (156)
Aortic Valve Area (cm^2)	0.67 ± 0.25 (485)	0.62 ± 0.23 (153)
Mean Gradient across Aortic Valve (MGV_2, mm Hg)	47.72 ± 13.53 (498)	49.67 ± 16.85 (156)
Mitral Regurgitation: Moderate/Severe	24.2% (120/496)	23.2% (36/155)
1. Aorta Calcification is measured on screening CT Angiogram. Plus-minus values present the mean ± standard deviation.		

11.2 Procedure Data

Table 5 provides a summary of the transcatheter valve implantation procedures for the iliofemoral and non-iliofemoral cohorts, respectively. Overall device success rate was 84.6% for the iliofemoral cohort and 88.7% for the non-iliofemoral cohort. Procedure success was defined as device success and absence of in-hospital MACCE and procedure success rates were 77.6% and 77.5% for the iliofemoral and non-iliofemoral cohorts, respectively.

Table 5: TAVR Procedure Data (Attempted Implant)

	Iliofemoral N=489	Non-Iliofemoral N=150
Time to Procedure (days)	8.9 ± 12.3 (489)	10.2 ± 15.5 (150)
Total Time in Cath Lab or OR (min)	214.8 ± 64.9 (486)	258.7 ± 72.5 (148)
Total Procedure Time (min) (skin to skin)	66.1 ± 39.0 (484)	60.5 ± 46.5 (145)
General Anesthesia	94.4% (459/486)	99.3% (147/148)
Valve-in-Valve Procedure	2.5% (12/486)	0.7% (1/148)
Emergent Operation Due to Device or Procedure	0.0% (0/486)	0.0% (0/148)
Number of Devices Used		
0	0.6% (3/489)	1.3% (2/150)
1	93.3% (456/489)	94.7% (142/150)
2	6.1% (30/489)	4.0% (6/150)
Valve Size Implanted		

	Iliofemoral N=489	Non-Iliofemoral N=150
23 mm	2.5% (12/486)	6.1% (9/148)
26 mm	35.0% (170/486)	41.2% (61/148)
29 mm	58.4% (284/486)	49.3% (73/148)
31 mm	4.1% (20/486)	3.4% (5/148)
Device Success[1]	84.6% (397/469)	88.7% (125/141)
Procedure Success[2]	77.6% (370/477)	77.5% (110/142)

1. Device success is defined as deployment, only 1 valve implanted, only 1 valve in correct anatomic location, EOA >1.2cm^2 for 26, 29 and 31mm and ≥ 0.9 cm^2 for 23mm, mean gradient < 20mmHg, and aortic regurgitation < moderate.
2. Procedure success is defined as device success and absence of in-hospital MACCE.
Plus-minus values present the mean ± standard deviation.

11.3 Safety

The estimated K-M rate for all-cause mortality or major stroke at 12 months for the Attempted Implant iliofemoral cohort was 26.0% with an upper 2-sided 95% CI of 29.9%. The upper 95% CI was lower than the pre-specified Performance Goal rate of 43% for this primary endpoint ($p<0.0001$) (Figure 33).

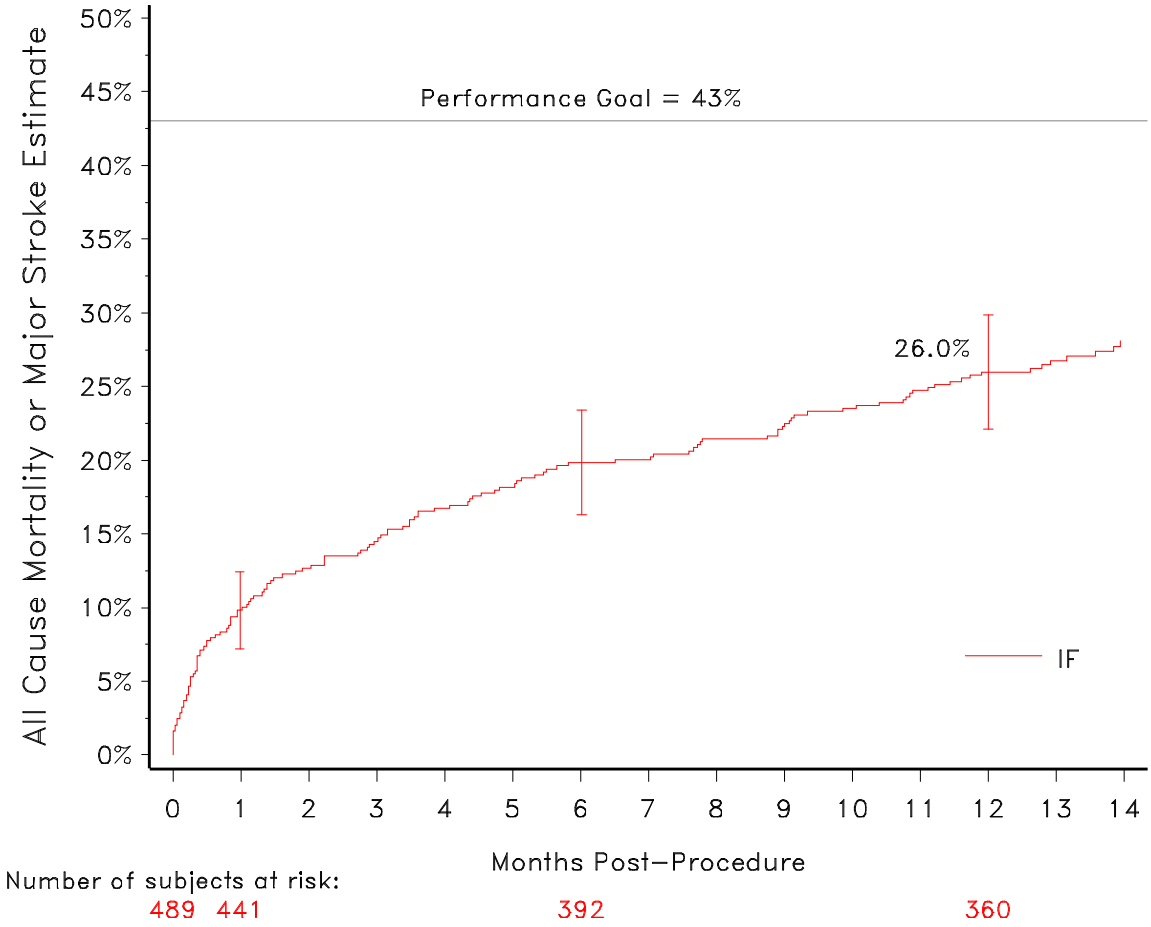

Figure 33: Primary Endpoint: All-Cause Mortality or Major Stroke Kaplan-Meier Event Rate — Iliofemoral Attempted Implant

Table 6 provides a summary of the adverse events (AEs) that occurred in this study for the iliofemoral and non-iliofemoral cohorts. AEs for the Attempted Implant populations are summarized and Kaplan-Meier (K-M) rates are provided.

The rates of all-cause mortality or major stroke (the primary endpoint of the trial) were 26.0% and 39.4% at 1 year for the iliofemoral and non-iliofemoral cohorts, respectively. Mortality was the primary driver of the primary endpoint for both the iliofemoral and noniliofemoral cohorts and cardiovascular mortality made up the majority of all deaths experienced in both cohorts. The greater event rate of all-cause mortality or major stroke in the non-iliofemoral cohort was expected based on the comorbidities identified in this group of patients.

Several important periprocedural complications including acute kidney injury, myocardial infarct, and major vascular complications generally occurred at similar rates for iliofemoral and non-iliofemoral patients. Bleeding complications were the most frequently observed early adverse events. Early (within 30 days) permanent pacemaker implantation (PPI) occurred in a significant minority of patients in both cohorts.

Table 6: Clinical Outcomes at 30 Days and 1 Year (Attempted Implant)

Event	30 Days				1 Year			
	Iliofemoral N=489		Non-Iliofemoral N=150		Iliofemoral N=489		Non-Iliofemoral N=150	
	# Patients	K-M rate	# Patients	K-M rate	# Patients	K-M rate	# Patients	K-M rate
All-Cause Mortality or Major Stroke	48	9.8%	23	15.3%	127	26.0%	59	39.4%
All-Cause Mortality	41	8.4%	17	11.3%	119	24.3%	54	36.0%
Cardiovascular	41	8.4%	17	11.3%	88	18.3%	42	28.8%
All Strokes	19	4.0%	13	8.8%	31	7.0%	18	13.0%
Major Strokes	11	2.3%	11	7.5%	19	4.3%	13	9.1%
TIA	3	0.6%	2	1.4%	5	1.1%	3	2.3%
Bleeding Event	179	36.7%	87	58.3%	206	42.8%	96	65.1%
Life-threatening or Disabling	62	12.7%	36	24.2%	83	17.6%	43	29.4%
Major Bleed	121	24.9%	55	37.1%	136	28.5%	60	41.9%
Major Vascular Complication	40	8.2%	13	8.7%	41	8.4%	14	9.5%
Acute Kidney Injury	57	11.8%	21	14.2%	57	11.8%	21	14.2%
MI	6	1.2%	3	2.1%	9	2.0%	3	2.1%
Aortic Valve Hospitalization	31	6.7%	12	8.7%	94	21.6%	27	21.2%
New Permanent Pacemaker Implant[1]	104	21.6%	24	16.4%	123	26.2%	30	21.5%
Permanent Pacemaker Implant[2]	104	29.4%	24	22.0%	121	34.9%	30	28.8%

1. Patients with pacemaker or ICD at baseline are included in the denominator.
2. Patients with pacemaker or ICD at baseline are excluded from the numerator and denominator. Note 2 patients with baseline pacemaker/ICD received new pacemaker/ICD between 31-365 days.

Patients with unsuitable iliofemoral anatomy for placement of an 18-Fr sheath are at a higher risk with respect to specific critical co-morbidities including peripheral vascular disease, cerebrovascular disease, and chronic lung disease. While at a higher risk, these non-iliofemoral patients with suitable axillary/subclavian or direct aortic access may be treated with the CoreValve™ device. Given the unavailability of any viable treatment option, the overall performance of the device and the associated benefits of treatment outweigh the risks for this non-iliofemoral Extreme Risk patient population.

The estimated K-M rate of all-cause mortality or major stroke at 12 months for the Attempted Implant non-iliofemoral cohort was 39.4% with an upper 95% CI of 47.2%, which was higher than for the iliofemoral cohort (Figure 34).

Table 7 provides a summary of the K-M estimate of event free rates of key outcomes for both the iliofemoral and non-iliofemoral cohorts. As shown in Table 7, the non-iliofemoral cohort reported higher rates of all-cause death and all-stroke, which resulted in higher MACCE and MAE rates compared to the iliofemoral cohort.

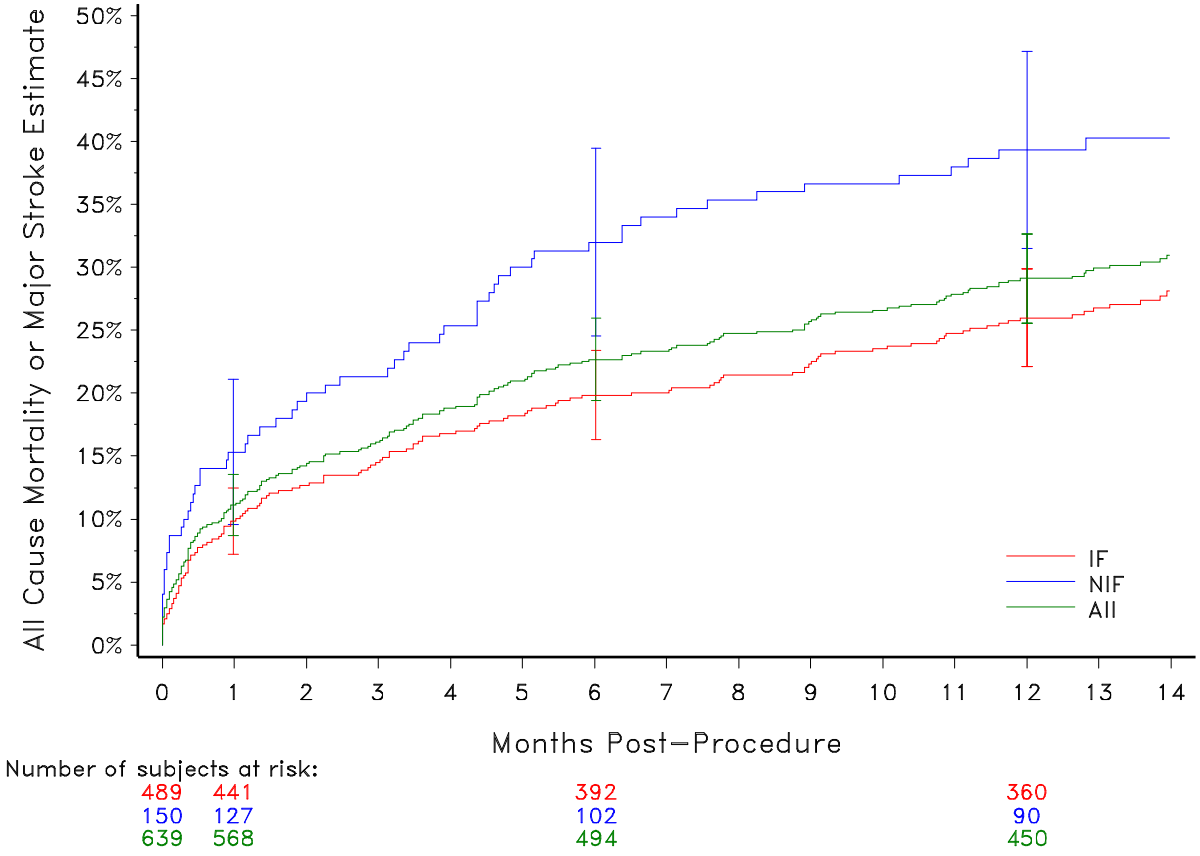

Figure 34: All-Cause Mortality or Major Stroke Kaplan-Meier Event Rate Attempted Implant (IF: iliofemoral; NIF: non-iliofemoral)

Table 7: Kaplan-Meier Estimate of Event-Free Rates: Results by IF (N=489) and NIF (N=150) Cohorts

Event	Access Site	Days post Attempted Implant			*p*-value*
		30 days	6 months (183 days)	12 months (365 days)	
MACCE	IF	87.7	77.5	70.8	0.004
	NIF	82.7	65.3	58.6	
All-Cause Death	IF	91.6	81.4	75.7	0.004
	NIF	88.7	71.3	64.0	
Myocardial Infarction	IF	98.8	98.5	98.0	0.861
	NIF	97.9	97.9	97.9	
All Stroke	IF	96.0	94.8	93.0	0.015
	NIF	91.2	88.0	87.0	
Reintervention	IF	98.9	98.5	98.2	0.408
	NIF	100.0	100.0	99.0	
MAE	IF	46.2	40.1	37.2	<0.001
	NIF	30.7	24.0	20.0	
*_p_-value from Log-Rank test comparing freedom from curves through 365 days					

A *post hoc* analysis was conducted to compare the K-M event rates for all-cause mortality or major stroke at 12 months between Attempted Implant iliofemoral patients in different Society of Thoracic Surgeons (STS) risk score categories (<5%, 5–15%, >15%). The STS risk score calculates the risk of operative mortality and morbidity of adult cardiac surgery on the basis of patient demographic and clinical variables. The Log-rank p-value for the K-M analysis was 0.042, indicating a statistically significant difference in the event rate between different STS score categories (Figure 35).

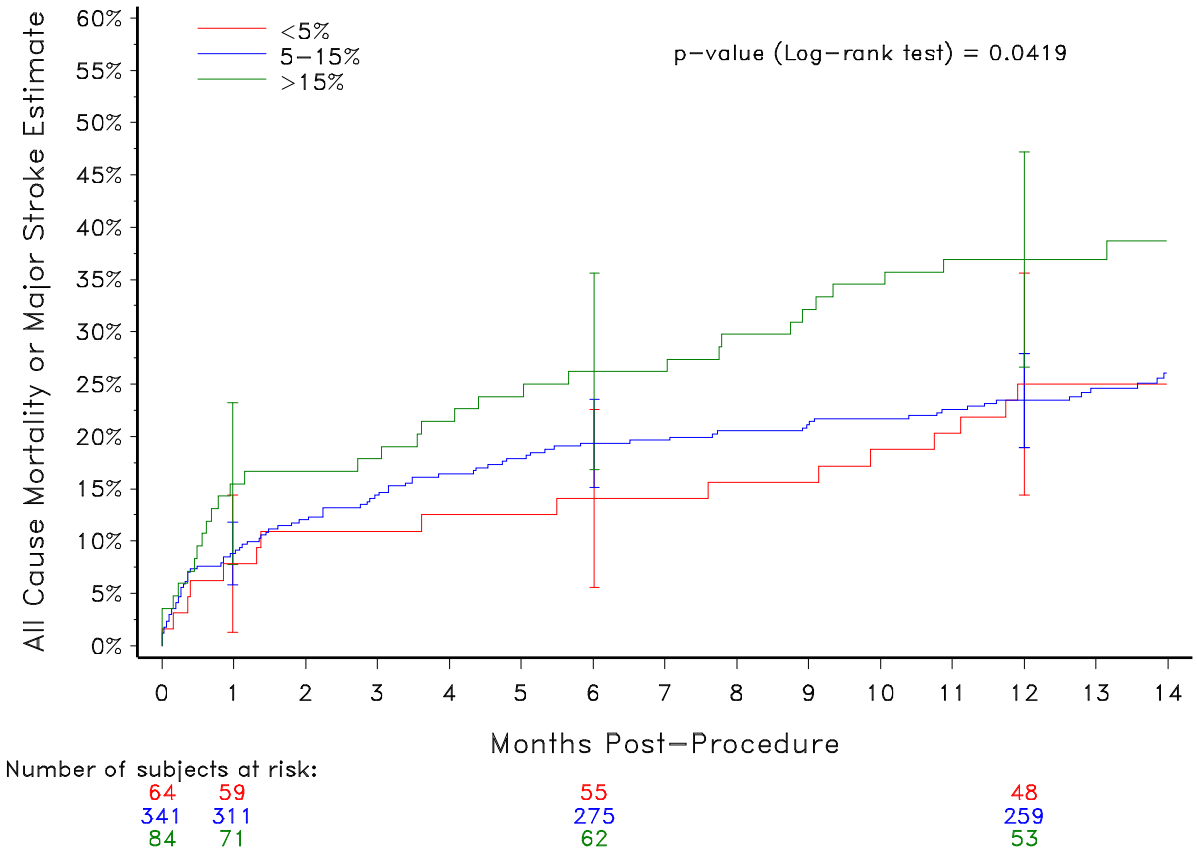

Figure 35: Primary Endpoint: All-Cause Mortality or Major Stroke Stratified by STS Score – Attempted Implant Iliofemoral

11.4 Effectiveness

Improvement in NYHA functional classification was evaluated for Implanted iliofemoral and non-iliofemoral patients. An evaluation of cardiac symptom severity based on NYHA classification was conducted at several evaluation time points through the first year of follow-up (Figure 36). Change from baseline to 12 months was evaluated for measures of forward flow hemodynamic performance (EOA and mean gradient) for iliofemoral and non-iliofemoral patients (Figure 37 and Figure 38).

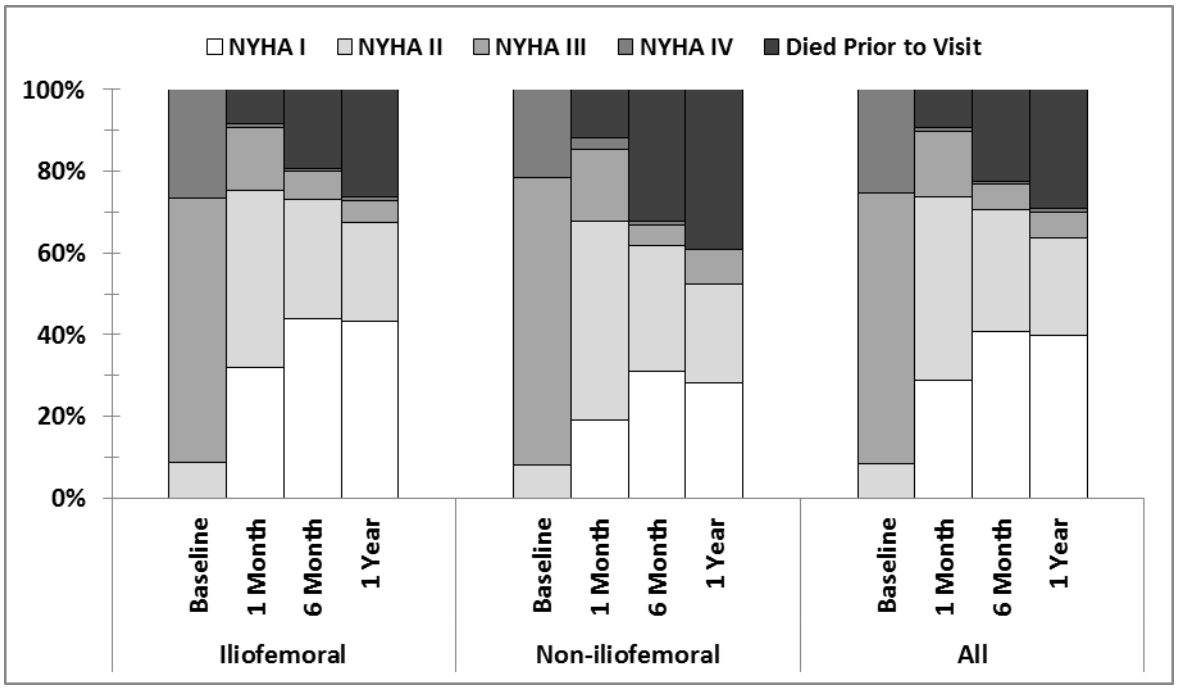

Figure 36: NYHA Classification by Visit – Attempted Implant

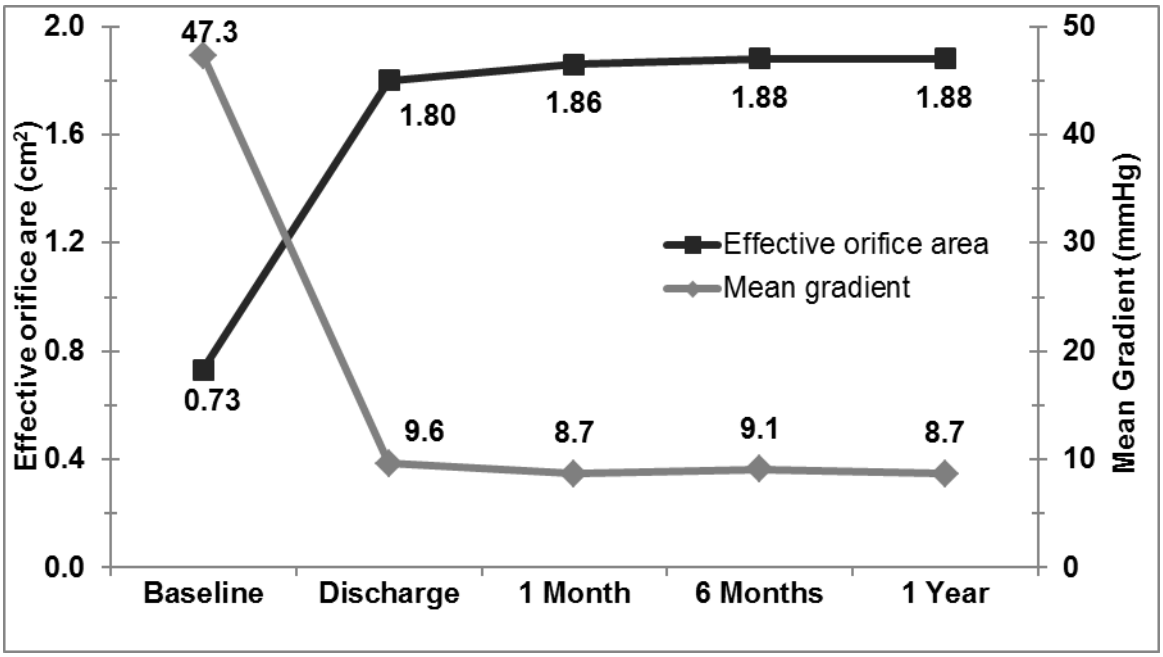

Figure 37: EOA and Mean Gradient by Visit – Iliofemoral Implanted

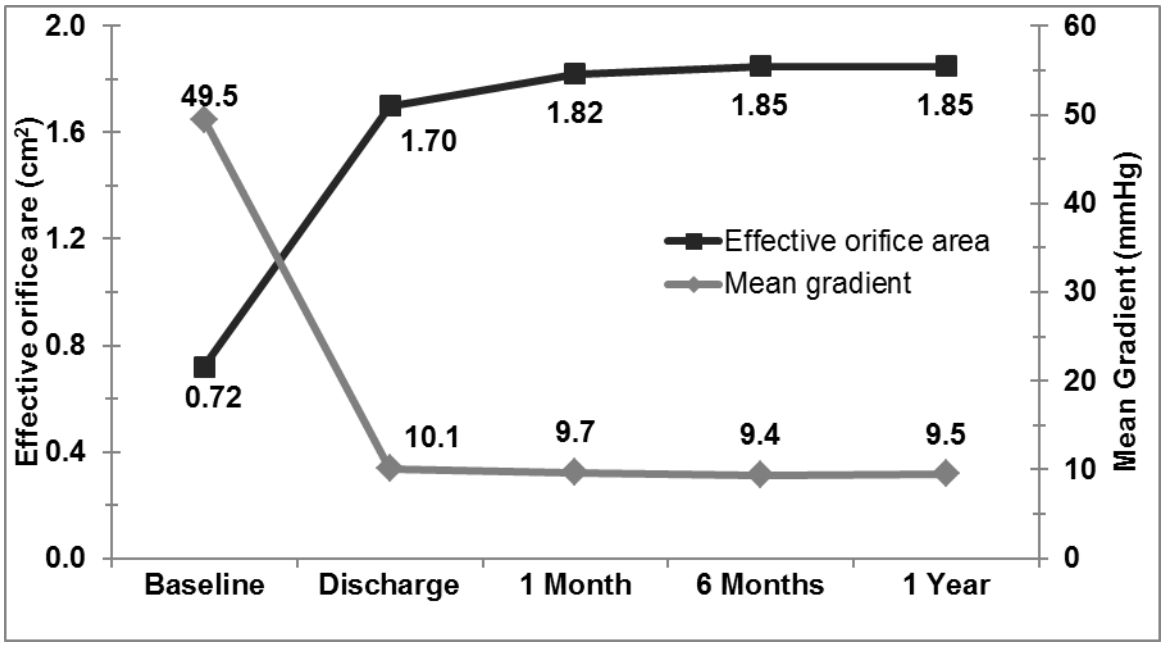

Figure 38: EOA and Mean Gradient by Visit – Non-Iliofemoral Implanted

Figure 39 shows total aortic regurgitation (AR) severity over time in the Implanted iliofemoral population. These data are presented per valve size as well as for all sizes combined. Considering all valve sizes, the majority of patients presented at 1, 6, and 12 months with AR severity classified as trivial or mild. Over time, the percentage of patients with moderate or severe AR decreased to 0% at 12 months. The number of patients with no AR increased over time to 21.3% at 12 months.

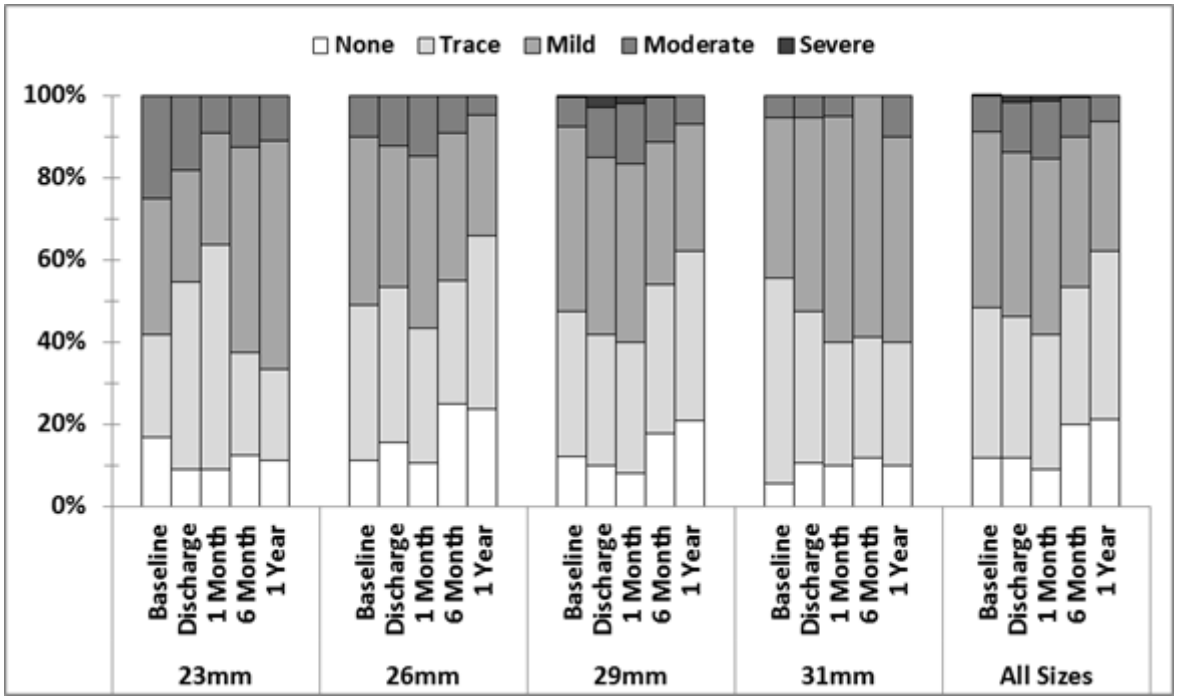

Figure 39: Total Aortic Regurgitation by Visit – Iliofemoral Implanted

Figure 40 shows total AR severity over time in the Implanted non-iliofemoral population. Considering all valve sizes, the majority of patients presented at 1 month with AR severity classified as mild or less. Over time, the percentage of patients with no AR increased to 39.0% at 12 months.

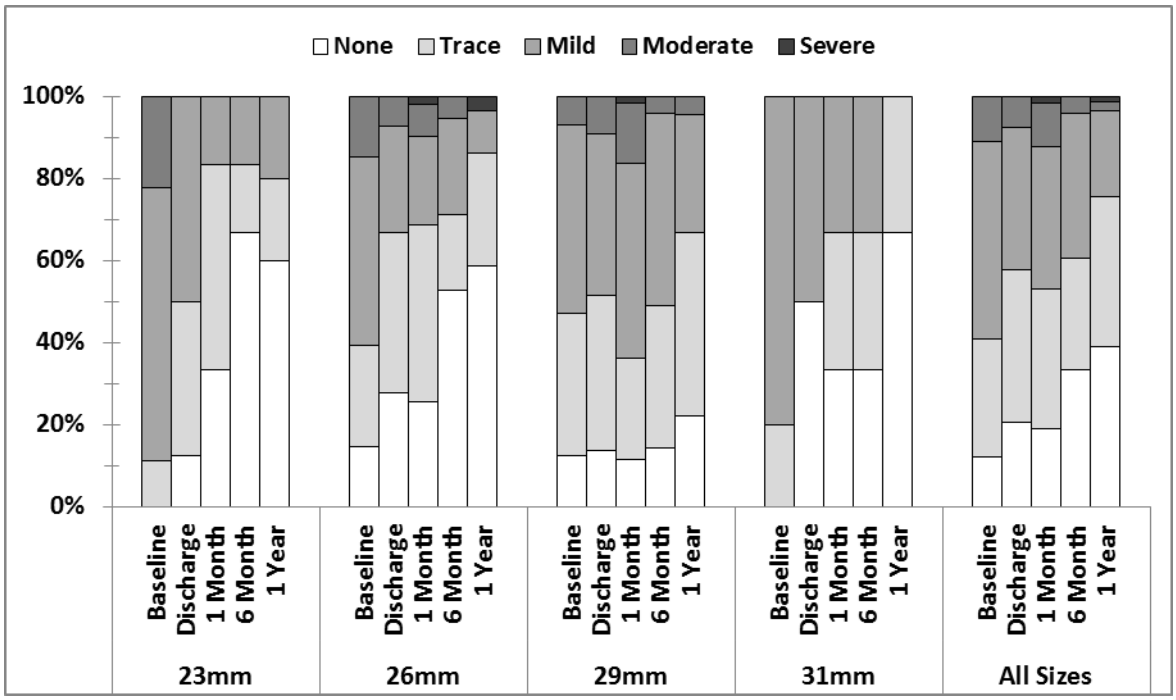

Figure 40: Total Aortic Regurgitation by Visit – Non-Iliofemoral Implanted

12.0 DISCLAIMER OF WARRANTY

The Following Disclaimer of Warranty Applies to United States Customers Only:

DISCLAIMER OF WARRANTY

ALTHOUGH THE MEDTRONIC COREVALVE™ TRANSCATHETER AORTIC VALVE (MODELS MCS-P4-23-AOA, MCS-P3-26-AOA, MCS-P3-29-AOA, AND MCS-P3-31-AOA), DELIVERY CATHETER SYSTEM (MODELS DCS-C4-18FR-23 AND DCS-C4-18FR), AND COMPRESSION LOADING SYSTEM (MODEL CLS-3000-18FR), HEREAFTER REFERRED TO AS "PRODUCT", HAVE BEEN MANUFACTURED UNDER CAREFULLY CONTROLLED CONDITIONS, MEDTRONIC HAS NO CONTROL OVER THE CONDITIONS UNDER WHICH THIS PRODUCT IS USED. MEDTRONIC THEREFORE DISCLAIMS ALL WARRANTIES, BOTH EXPRESS AND IMPLIED, WITH RESPECT TO THE PRODUCT, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. MEDTRONIC SHALL NOT BE LIABLE TO ANY PERSON OR ENTITY FOR ANY MEDICAL EXPENSES OR ANY DIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES CAUSED BY ANY USE, DEFECT, FAILURE OR MALFUNCTION OF THE PRODUCT, WHETHER A CLAIM FOR SUCH DAMAGES IS BASED UPON WARRANTY, CONTRACT, TORT OR OTHERWISE. NO PERSON HAS ANY AUTHORITY TO BIND MEDTRONIC TO ANY REPRESENTATION OR WARRANTY WITH RESPECT TO THE PRODUCT.

The exclusions and limitations set out above are not intended to, and should not be construed so as to, contravene mandatory provisions of applicable law. If any part or term of this DISCLAIMER OF WARRANTY is held by any court of competent jurisdiction to be illegal, unenforceable or in conflict with applicable law, the validity of the remaining portion of the DISCLAIMER OF WARRANTY shall not be affected, and all rights and obligations shall be construed and enforced as if this DISCLAIMER OF WARRANTY did not contain the particular part or term held to be invalid.

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M333433D001 Rev. 1B

Medtronic

CoreValve®

TRANSCATHETER AORTIC VALVE REPLACEMENT (TAVR) PLATFORM

An approach to treat severe aortic stenosis for those who cannot have open heart surgery.

Is CoreValve Transcatheter Aortic Valve Replacement (TAVR) Right for You?

CoreValve TAVR may be right for you if you feel sick from severe aortic stenosis and your doctor has determined that you are not a candidate for open heart valve replacement surgery. Your doctor can help decide if CoreValve is the appropriate treatment option for you.

This brochure provides information about the heart, severe aortic stenosis (AS) and the Medtronic CoreValve TAVR procedure that can treat this disease.

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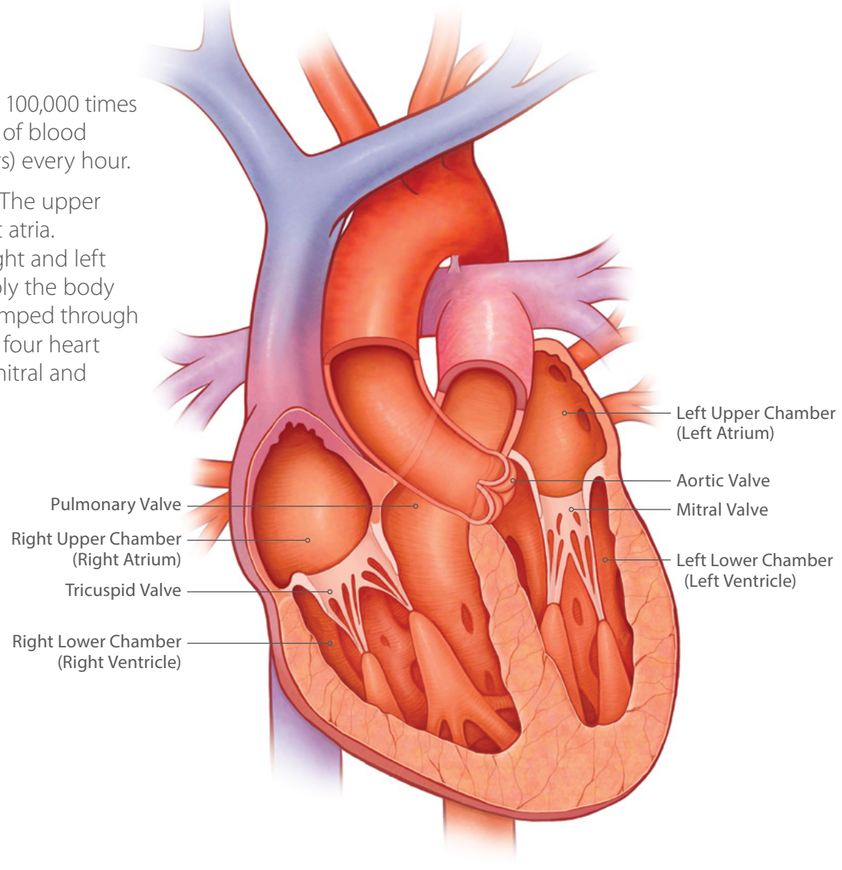
This booklet is provided to help you and loved ones learn more about CoreValve Transcatheter Aortic Valve Replacement. Please discuss any questions with your heart doctor. Only a doctor can decide if CoreValve is the right treatment for you.

About the Heart

How the Heart Works

A healthy heart beats approximately 100,000 times a day and pumps about five quarts of blood each minute, or 75 gallons (284 liters) every hour.

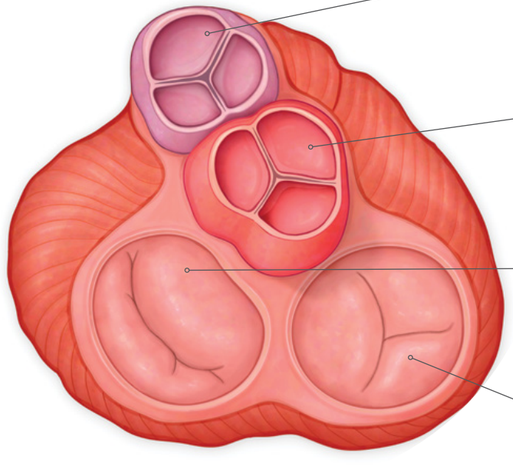
A normal heart has four chambers. The upper two chambers are the right and left atria. The lower two chambers are the right and left ventricles. The heart's job is to supply the body with oxygen-rich blood. Blood is pumped through the four chambers with the help of four heart valves—the tricuspid, pulmonary, mitral and aortic valves.



About the Heart

What Heart Valves Do

Heart valves open when the heart pumps to allow blood to flow forward, and close quickly between heartbeats to make sure blood does not flow backward. Any disruption in this normal flow will make it difficult for the heart to effectively pump the blood where it needs to go.



The **pulmonary valve** directs blood flow from the right lower chamber (right ventricle) into the pulmonary artery, which splits into two arteries so that the blood from the body can get to both lungs.

The **aortic valve** directs blood from the left lower chamber (left ventricle) into the aorta. The aorta is the major blood vessel that leads from the left lower chamber out to the rest of the body.

The **mitral valve** sits between the left upper chamber (left atrium) and left lower chamber. The mitral valve directs blood flow from the left upper chamber into the left lower chamber.

The **tricuspid valve** sits between the right upper chamber (right atrium) and right lower chamber (right ventricle). The tricuspid valve directs blood flow from the right upper chamber to the right lower chamber.

Severe Aortic Stenosis

Severe Aortic Stenosis

Severe aortic stenosis (AS) occurs when the aortic valve doesn't open properly. This forces your heart to work harder to pump blood throughout your body. Over time, the heart muscle weakens. This affects your overall health and keeps you from participating in normal daily activities.

Left untreated, severe AS is a very serious, life-threatening condition, leading to heart failure and increased risk for sudden cardiac death.

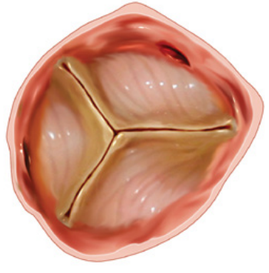
Severe AS is often not preventable, causes narrowing of the aortic valve, and may be related to the following:

- Age
- A buildup of mineral (calcium) deposits that narrows the aortic valve (stenosis)
- Radiation therapy
- A history of a bacterial infection of the heart (rheumatic fever)
- Increased fat in the blood vessels (high cholesterol)

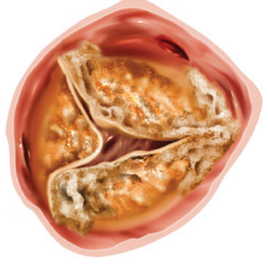
Symptoms of Severe AS

Signs and symptoms of severe AS can include:

- Chest pain or tightness
- Feeling faint or fainting with activity
- Dizziness
- Fatigue
- Shortness of breath
- Irregular heart beat (palpitations)
- Unusual sound heard during a heartbeat (murmur)



Normal Valve



Stenotic Valve

Treatment Options for Severe AS

Medical Management and Balloon Valvuloplasty

Medicines for severe AS focus on treating problems that can occur as a result of your diseased aortic heart valve. For example, patients with severe AS may take **medicines** that help control irregular heartbeats or prevent blood clots. These medicines may help control your symptoms for a period of time; however, without aortic valve replacement, severe AS could worsen to a more serious condition.

In addition to medications and if your physician determines appropriate, a procedure called **Balloon Valvuloplasty** can be performed to relieve symptoms. It is a non-surgical procedure that is performed by placing a balloon into the aortic valve and inflating the balloon. A thin, flexible tube (catheter) is first inserted through an artery in the groin or arm and threaded into the heart. Once the tube reaches the narrowed aortic valve, a balloon located on the tip of the catheter is quickly inflated. The balloon presses against the narrowed valve leaflets, which separates and stretches the valve opening and allows more blood to flow through the heart. This procedure does not require open-heart surgery.

Risks

Because risks will vary depending on your medical management, talk about adverse risk events with your doctor.

CoreValve® Transcatheter Aortic Valve Replacement (TAVR)

The CoreValve transcatheter aortic heart valve is made of natural tissue obtained from the heart of a pig. The leaflets that control the flow of blood are secured to a flexible, self-expanding metal frame (nickel-titanium) for support. The CoreValve aortic heart valve is available in four sizes with different diameters. Your doctor will determine which valve size is right for you.

The CoreValve aortic valve is implanted via a thin, flexible tube (catheter). It is a less invasive treatment option than open heart valve surgery.

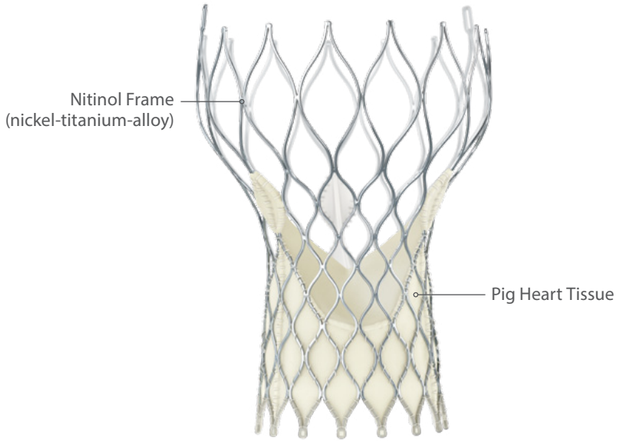


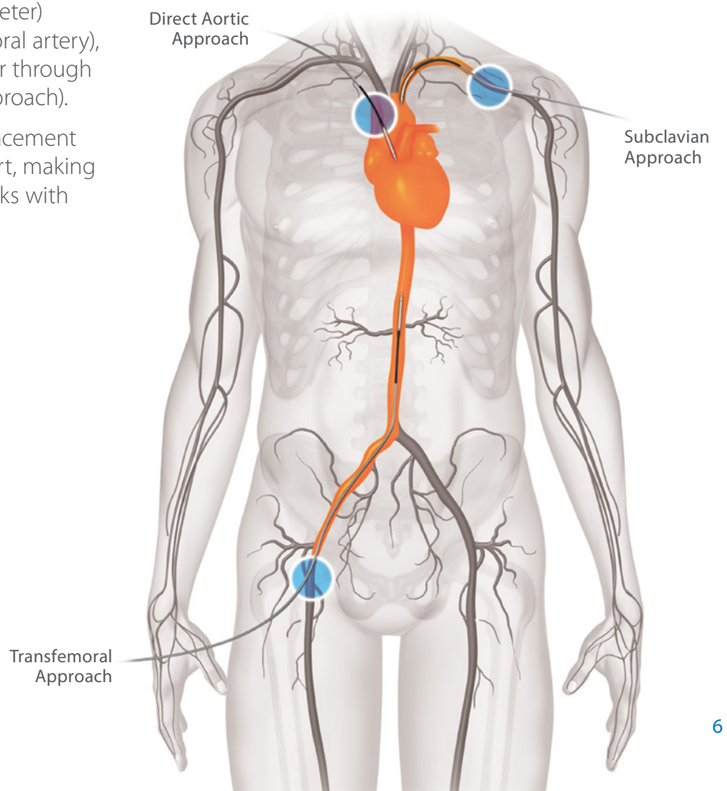
Image is bigger than actual valve

Treatment of Severe AS Using CoreValve

Where Does the Catheter, Which Holds the Valve, Enter My Body?

Depending on your vessel anatomy, your doctor will determine if the thin, flexible tube (catheter) should enter via the artery in your leg (femoral artery), the artery in your neck (subclavian artery), or through a space between your ribs (direct aortic approach).

The direct aortic approach for CoreValve placement involves additional steps to access your heart, making the procedure more invasive. Discuss the risks with your physician.



What You Can Expect

During the Procedure

Patients may be sedated during the 1-3 hour procedure. You may first have a test that uses sound waves to take a closer look at the inside structures of the heart. Your doctor will decide what sites are best for inserting the thin, flexible tube (catheter) required for the procedure. Additionally, your doctor will decide if performing a surgical incision to any of the sites is necessary. With CoreValve TAVR, a small incision is made and a thin, flexible tube (catheter) holding the CoreValve aortic heart valve is guided to the heart. Special imaging equipment is used to guide positioning and placement of the CoreValve aortic heart valve.

After the Procedure

Following CoreValve TAVR, you will be moved to an intensive care unit or cardiac care unit. Patients typically are able to be up and walking within 24-48 hours after their procedure. Your doctor will determine when you are ready to move to a standard hospital room. The typical hospital stay for CoreValve TAVR is approximately 9 days.

Summary of CoreValve TAVR

- Local numbing or sedation (local or general anesthesia)
- Heart pumps normally during procedure
- Catheter delivers CoreValve into the heart
- Valve replaced during 1-3 hour procedure (typical)
- Approximately 9 day hospital stay (typical)

Understanding the CoreValve Procedure

A Typical CoreValve® Transcatheter Procedure

1. Patients are normally sedated during the approximately 1-3 hour procedure. Because each patient is different, your doctor may determine whether or not you should be fully asleep for the procedure.
2. The interventional cardiologist or cardiac surgeon will make an incision and guide a long, hollow tube (sheath) into your blood vessel.
3. Using special imaging equipment to look at your arteries, a thin, flexible tube (catheter) with a balloon on the tip is threaded through the sheath and into your heart. If you're not fully sedated, you may have a "fluttering" feeling in your chest.
4. When the end of the balloon is in your aortic valve, the balloon will be inflated and will force your narrowed aortic valve open to prepare it for your CoreValve aortic heart valve.
5. Again, using the special imaging equipment, your doctor will place the CoreValve aortic heart valve in position over your own diseased aortic valve. **(Figures 1 and 2)**
6. Your new CoreValve aortic heart valve will begin opening and closing; the doctor will conduct a test to confirm it is working properly. **(Figure 3)**
7. The thin, flexible tube will be removed, the incision will be closed, and the procedure will be complete.

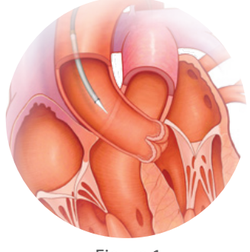


Figure 1

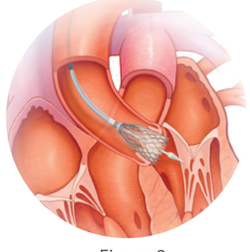


Figure 2

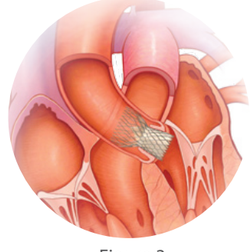


Figure 3

Transcatheter Aortic Valve Replacement is Not Right for Everyone

The CoreValve Transcatheter Aortic Valve Should NOT be Used for the Following People:

- Patients who have an infection in the heart or elsewhere
- Patients who have an artificial (mechanical) aortic valve
- Patients who cannot take aspirin, heparin and bivalirudin, ticlopidine (Ticlid), clopidogrel (Plavix), or have sensitivity to Nitinol (Titanium or Nickel) or contrast media (fluid used during the procedure to see internal structures)

If the CoreValve transcatheter aortic valve is used in the patients mentioned above, it may not work properly. This could make you feel very sick or even cause death.

For some patients the risk of the TAVR procedure may outweigh the benefits. See pages 11-16 for the risks associated with the CoreValve procedure.

CoreValve Clinical Experience

Experience from the Medtronic CoreValve US Pivotal Trial

The Medtronic CoreValve US Pivotal Trial evaluated the safety and effectiveness of the Medtronic CoreValve System in 639 patients (489 transfemoral and 150 direct aortic and subclavian access) who were treated at 41 different hospitals in the United States. These patients all had severe aortic stenosis and had been determined by their doctors to be unable to have open heart surgery to treat their illness. All patients were treated with the Medtronic CoreValve transcatheter heart valve and were examined 30 days, 6 months, and 1 year after the procedure, and will continue to be examined each year for 5 years. Study results for the CoreValve device were compared statistically with alternative therapies (other than TAVR) for safety and performance. The comparison demonstrated that the CoreValve device met its success criteria.

The following pages summarize the risks experienced by patients in the trial, divided according to access route.

Risks You Should Know

What are the Potential Risks 30 Days After CoreValve Implantation?

As with any major medical procedure, there is a risk of complications after the Medtronic CoreValve transcatheter valve implantation procedure.

The major risks 30 days after this procedure are as follows:

- **Death from any cause** - death due to any cause, whether heart related or not.
- **Stroke** - a condition when decreased blood flow to the brain causes death of the brain cells, which results in disability.
- **Major vascular complications** - a condition affecting the blood vessels, including blood collecting under the skin (hematoma), or a tear or hole in a blood vessel.
- **Major bleeding** - a bleeding event causing abnormal lab values or requiring blood to be put back into the body.

The following table summarizes the potential risks 30 days after CoreValve implantation and is divided by access site. The access site that applies to you is determined by your doctor. Talk to your doctor about these risks.

Risks – 30 days After TAVR Procedure	Access through an artery in your leg (transfemoral)	Access through a space between your ribs or an artery in your neck (direct aortic and subclavian)
Death from any cause	8 out of 100 patients	11 out of 100 patients
From a heart related cause	8 out of 100 patients	11 out of 100 patients
From a heart valve related cause	3 out of 100 patients	3 out of 100 patients
All stroke	4 out of 100 patients	9 out of 100 patients
Major stroke	2 out of 100 patients	7 out of 100 patients
Bleeding event	37 out of 100 patients	58 out of 100 patients
Major bleed	25 out of 100 patients	37 out of 100 patients
Life threatening or disabling bleed	13 out of 100 patients	24 out of 100 patients
New permanent device to help regulate the heart (pacemaker)	21 out of 100 patients	16 out of 100 patients
Major vascular complication	8 out of 100 patients	9 out of 100 patients
Acute kidney injury	12 out of 100 patients	14 out of 100 patients
Hospitalization due to complications with aortic valve	6 out of 100 patients	8 out of 100 patients
Heart attack (myocardial infarction)	1 out of 100 patients	2 out of 100 patients
Need for additional procedures on your aortic valve	1 out of 100 patients	0 out of 100 patients
Surgical aortic valve replacement	0 out of 100 patients	0 out of 100 patients
Less invasive procedure (not including replacement)	1 out of 100 patients	0 out of 100 patients
Valve inflammation or infection (endocarditis)	0 out of 100 patients	1 out of 100 patients

Risks You Should Know

What are the Potential Risks 1 Year After CoreValve Implantation?

The major risks associated with this procedure include:

- **Death from any cause** - death due to any cause, whether heart related or not.
- **Stroke** - a condition when decreased blood flow to the brain causes death of the brain cells, which results in disability.
- **Major vascular complications** - a condition affecting the blood vessels, including blood collecting under the skin (hematoma), or a tear or hole in a blood vessel.
- **Major bleeding** - a bleeding event causing abnormal lab values or requiring blood to be put back into the body.

The following table summarizes the potential risks 1 year after CoreValve implantation and is divided by access site. The access site that applies to you is determined by your doctor. Talk to your doctor about these risks.

Risks Within 1 Year After Your TAVR Procedure

Risks – 1 year After TAVR Procedure	Access through an artery in your leg (transfemoral)	Access through a space between your ribs or an artery in your neck (direct aortic and subclavian)
Death from any cause	24 out of 100 patients	36 out of 100 patients
From a heart related cause	18 out of 100 patients	28 out of 100 patients
From a heart valve related cause	5 out of 100 patients	5 out of 100 patients
All stroke	6 out of 100 patients	12 out of 100 patients
Major stroke	4 out of 100 patients	9 out of 100 patients
Bleeding event	42 out of 100 patients	64 out of 100 patients
Major bleed	28 out of 100 patients	40 out of 100 patients
Life threatening or disabling bleed	17 out of 100 patients	29 out of 100 patients
New permanent device to help regulate the heart (pacemaker)	25 out of 100 patients	20 out of 100 patients
Major vascular complication	8 out of 100 patients	9 out of 100 patients
Acute kidney injury	12 out of 100 patients	14 out of 100 patients
Hospitalization due to complications with aortic valve	19 out of 100 patients	18 out of 100 patients
Heart attack (myocardial infarction)	2 out of 100 patients	2 out of 100 patients
Need for additional procedures on your aortic valve	2 out of 100 patients	1 out of 100 patients
Surgical aortic valve replacement	0 out of 100 patients	0 out of 100 patients
Less invasive procedure (not including replacement)	2 out of 100 patients	1 out of 100 patients
Valve inflammation or infection (endocarditis)	1 out of 100 patients	1 out of 100 patients

Other Potential Risks Associated with the CoreValve TAVR

- Cardiogenic shock - failure of the heart to pump enough blood to the body organs
- Perforation of the myocardium or vessel - a hole in the heart muscle or a blood vessel
- Cardiac Tamponade - the constriction or inability of the heart to pump due to build up of blood or fluid around the lining of the heart
- Ascending aorta trauma - injury to the large blood vessel leading blood away from the heart
- Embolism - an abnormal particle (air, blood clots) floating in the blood stream or attached to an object, including the valve
- Thrombosis (including valve thrombosis) - blood clot, including a blood clot on the valve
- Valve migration - upward or downward movement of the device from where it was originally placed
- Valve dysfunctions of the CoreValve including but not limited to:
  - Break (fracture) in the valve frame
  - Bending of the valve frame
  - The valve frame does not open (expand) all the way
  - Build up of minerals on the valve (calcification)
  - Pannus - the formation of scar tissue that may cover or block the valve from functioning normally
  - Wear, tear or movement forward (prolapse) or backward (retraction) from the normal position of the valve leaflets
  - The valve leaflets do not close together
  - A break in the stitches (sutures) of the valve frame or leaflets
  - Leakage through or around the valve or valve frame
  - Incorrect size of the valve implanted
  - Incorrect position of the valve, either too high or too low
  - Regurgitation - backward flow of blood through the valve
  - Stenosis - narrowing of the opening of the valve
- Mitral valve regurgitation - a leaking valve between the left upper (left atrium) and left lower (left ventricle) chambers of the heart where blood flows backward through the valve
- Hypotension or hypertension - low or high blood pressure
- Unfavorable reaction by the body (allergic reaction) to:
  - antiplatelet agents - drugs that keep blood clots from forming
  - contrast medium - a substance used to increase the visualization of body structures such as x-ray dye
- Bowel ischemia - decreased blood supply to the intestines
- Complications at the area where the doctor opened the skin or related to opening the skin, including but not limited to:
  - pain
  - bleeding
  - hematoma - blood collecting under the skin
  - pseudoaneurysm - blood collecting on the outside of a vessel wall causing a balloon-like widening
  - irreversible nerve damage - permanent damage to nerves
  - compartment syndrome - squeezing of nerves and muscles in a closed space that could cause muscle or nerve damage
  - stenosis - narrowing of a vessel (artery)

In addition, you may experience other problems that have not been previously observed with this procedure.

Benefits

Symptom Relief

Most patients receiving a CoreValve heart valve can expect immediate symptom relief. The table below shows the number of patients who showed improvement 30 days and 1 year after their procedure using a standard tool (New York Heart Association heart failure class) to measure how much better they felt.

Quality of Life Improvements

The clinical trial assessed quality of life using a combination of standardized tools* to determine the improvement in patients' health after the procedure. These assessments showed substantial improvement in patients' health 30 days after the procedure and patients continued to experience the improvement at 1 year. Patients reported significant improvements in many quality of life measurements including; reduced pain and anxiety, and increased ability to take care of themselves and participate in everyday activities.

Access through an artery in your leg (transfemoral)		Access through a space between your ribs or an artery in your neck (direct aortic and subclavian)	
30 Days	1 Year	30 Days	1 Year
8 out of 10 patients	7 out of 10 patients	7 out of 10 patients	5 out of 10 patients

* Kansas City Cardiomyopathy Questionnaire (KCCQ) and EuroQol/EQ-5D

What You Should Do After the Procedure

Follow-up Care

Your doctor will provide you with more specific care instructions as well as any restrictions you may have. You will still need to take medications as prescribed and have your heart and valve function checked from time to time. Ask your heart doctor or nurse about your follow-up appointment schedule or any other questions you have about living with your new heart valve.

As a precaution, you'll want to inform your dentist and other doctors about your heart valve before any dental or medical procedure. If you require a magnetic resonance imaging (MRI) scan, tell the doctor or MRI technician that you have had a heart valve procedure. Failure to do so could result in damage to your implanted heart valve or death.

You will receive a patient card that has information about your heart valve. It is important to keep this card with you and to show it to any medical personnel who may be treating you. If you do not receive a card after your CoreValve procedure, contact your doctor.

It is not known at this time how long your CoreValve heart valve will last. The CoreValve device has been tested in a laboratory to simulate 5-year durability.

Because of the uniqueness of each heart patient, it is difficult to predict how long the CoreValve aortic heart valve will last.

It is important to keep appointments with your heart doctor and to follow recommended daily care to ensure the best possible results.

Warnings and Precautions

Warnings

Patients who have a known blood disorder that causes them to have more minerals (calcium) in their blood may cause the CoreValve device to wear (deteriorate) faster.

The safety of the CoreValve has only been established in patients who:

- have severe aortic stenosis which is causing them to feel sick
- are not able to have their heart valve replaced surgically

Precautions

- Long term durability has not been established for the CoreValve aortic heart valve. Follow-up appointments with your doctor are recommended to evaluate your heart valve over time.
- Antibiotics are recommended after the CoreValve procedure for patients who are at risk of infections.
- Patients should stay on blood-thinning medication after the procedure, as directed by their doctor. Patients who do not take blood-thinning medication after the procedure have an increased chance of developing a blood clot, which could lead to a stroke.
- If you require a magnetic resonance imaging (MRI) scan, tell the doctor or MRI technician that you have had a heart valve procedure. Failure to do so could result in damage to your implanted heart valve or death.

The safety of the CoreValve aortic heart valve has not been established in the following:

- Patients who are not sick from aortic stenosis
- Children
- Patients who were born with an aortic valve that has only one or two leaflets
- Patients who have a blood clot or an abnormal growth
- Patients who have an infection in the heart or elsewhere
- Patients who have aortic stenosis along with moderate or severe aortic regurgitation (when your valve does not fully close and allows blood to leak backwards through the valve)
- Patients who have severe disease with their mitral valve (the heart valve that allows blood to fill the left lower chamber/ left ventricle)
- Patients whose left lower chamber (left ventricle) does not pump enough blood out of the heart
- Patients whose aortic valve diameter is either too small or too big for the device
- Patients whose vessels cannot accommodate the device
- Patients whose aortic anatomy may prevent proper blood supply to the heart after CoreValve implant
- Patients whose blood vessels that supply blood to the heart (coronary arteries) are not working and need to be treated
- Patients who are sick from problems with the blood vessels that supply blood to the brain (carotid or vertebral arteries)
- Patients who have severe problems with bleeding or blood clotting
- Patients who have a severe kidney disease and require mechanical assistance to work properly
- Patients who can have open heart surgery
- Patients who have an artificial heart valve already implanted in any of their four heart valves
- Patients who have a condition in which the heart muscle becomes thick and makes it difficult for the heart to pump blood
- Patients who have a condition in which the heart muscle becomes thick and blocks the heart from pumping blood

If the CoreValve transcatheter aortic valve is used in the patients mentioned above, it may not work properly. This could make you feel very sick or even cause death.

For some patients the risk of the TAVR procedure may outweigh the benefits. See pages 11-16 for the risks associated with the CoreValve procedure.

FAQs

Frequently Asked Questions

Are physical activities safe?

Discuss your activity level with your heart doctor to determine what is best for you.

Is it safe to have an x-ray with a CoreValve aortic heart valve?

The CoreValve aortic heart valve is completely safe with x-ray examinations.

Is it safe to have an MRI with a CoreValve aortic heart valve?

The CoreValve can be safely scanned under certain conditions. If you have had a CoreValve procedure, inform your physician about your implanted transcatheter valve prior to having an MRI. Failure to do so could result in damage to the valve or death.

How will I know if my CoreValve aortic heart valve is working properly?

Your heart doctor will schedule regular follow-up appointments to check your valve.

Resources

For More Information on the CoreValve TAVR

Please contact your physician or nurse for more information. For product information, visit **www.CoreValve.com**.

For Technical Support Information

Toll-free phone number in the USA: **1-877-526-7890**

Phone number from outside the USA: **1-763-526-7890**

Email address: **rs.cstechsupport@medtronic.com**

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

The CoreValve transcatheter aortic valve has been approved by FDA for specific patient populations only. Refer to the Instructions for Use for a full list of warnings, precautions, indications, and adverse events.

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