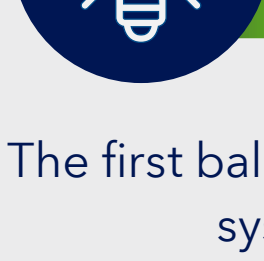


The Evolution of

Medtronic Self-Expanding TAVR in the United States

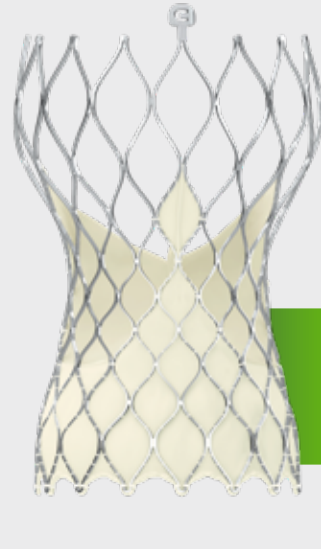
The original CoreValve™ self-expanding nitinol tissue valve was first introduced for the treatment of symptomatic, severe aortic stenosis (AS). Five generations and nearly a decade later, transcatheter aortic valve replacement (TAVR) using the self-expanding, supra-annular Evolut™ platform has helped revolutionize how aortic heart valves are replaced. Prior to TAVR, patients requiring aortic valve replacement had to undergo open heart surgery.

Severe aortic stenosis is one of the most serious forms of heart valve disease and can become life-threatening once symptoms develop. For AS patients, TAVR provides a minimally invasive option to restore function of their diseased valve.



2011

The first balloon-expandable TAVR system is Food and Drug Administration (FDA) approved only for patients who are too sick to undergo open-heart surgery, leading the way for new TAVR innovations.



2015

The Evolut™ R system is introduced. The first TAVR to offer implanters the ability to recapture and reposition the valve during deployment.



2017

FDA expands indication for self-expanding platform to intermediate risk patients with symptomatic, severe aortic stenosis.

Evolut™ PRO system incorporates a pericardial tissue wrap to the 23-29mm valve sizes. This adds surface area contact between the valve and the native aortic annulus to further advance valve sealing performance.



2022

Evolut FX system introduced to the market.

Redesigned delivery system to enhance ease-of-use and provide greater precision and control throughout the procedure.

Valve incorporates gold markers built into the frame as radiopaque markers to identify depth and commissure location during implant.

2014



Using a nitinol frame, the first self-expanding TAVR technology, the Medtronic CoreValve system, is approved for patients at extreme risk and high risk for surgery giving heart teams an additional treatment option in the U.S.

2016



The Evolut R system adds the 34mm valve size to the lineup, resulting in the largest treatable annulus range.*

*Broadest annulus range based on CT-derived diameters.

2019



The FDA approves an expanded indication of the Evolut platform to low risk patients with symptomatic, severe aortic stenosis.

Pericardial tissue wrap added to the 34mm valve.

Today



Today, due to the clinical and technological advances made, as well as the minimally-invasive nature of TAVR, more TAVR cases are performed than surgical aortic valve replacement for symptomatic severe aortic stenosis.²

To date, more than 450,000 patients worldwide have been treated with the Medtronic TAVR platform.

Medtronic data on file.

TAVR risks may include, but are not limited to, death, stroke, damage to the arteries, bleeding, and need for permanent pacemaker.

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¹ Ross J Jr, Braunwald E. Aortic stenosis. Circulation. 1968;38(1 Suppl):61-67.

² Carroll J, Mack M, Vemulapalli S, et al. STS-ACC TAVT Registry of Transcatheter Aortic Valve Replacement. J Am Coll Cardiol 2020;76:2492-516.

The Medtronic CoreValve™ Evolut™ R, Evolut™ PRO+, and Evolut™ FX Systems are indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be appropriate for the transcatheter heart valve replacement therapy.

The Medtronic CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems are indicated for use in patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (e.g., STS predicted risk of operative mortality score $\geq 8\%$ or at a $\geq 15\%$ risk of mortality at 30 days).

Indications

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Contraindications

The CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems are contraindicated in patients who cannot tolerate Nitinol (titanium or nickel), gold (for Evolut FX Systems alone), an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

Warnings

General Information about the CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems should be performed only by physicians who have received Medtronic CoreValve Evolut R, Evolut PRO+, or Evolut FX training. This procedure should only be performed where emergency aortic valve surgery can be performed promptly. Mechanical failure of the delivery catheter system and/or accessories may result in patient complications. Transcatheter aortic valve (bioprostheses) Accelerated deterioration due to calcific degeneration of the bioprostheses may occur in: children, adolescents, or young adults; patients with altered calcium metabolism (e.g., chronic renal failure or hyperthyroidism).

Precautions

General Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up. The safety and effectiveness of the CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems have not been evaluated in the pediatric population. The safety and effectiveness of the bioprostheses for aortic valve replacement have not been evaluated in the following patient populations: Patients who do not meet the criteria for symptomatic severe native aortic stenosis as defined: (1) symptomatic severe high-gradient aortic stenosis – aortic valve area ≤ 1.0 cm² or aortic valve area index ≤ 0.6 cm²/m², a mean aortic valve gradient ≥ 40 mm Hg, or a peak aortic-jet velocity ≥ 4.0 m/s; (2) symptomatic severe low-flow, low-gradient aortic stenosis – aortic valve area ≤ 1.0 cm² or aortic valve area index ≤ 0.6 cm²/m², a mean aortic valve gradient < 40 mm Hg, and a peak aortic-jet velocity < 4.0 m/s; with untreated, clinically significant coronary artery disease requiring revascularization; with a preexisting prosthetic heart valve with a rigid support structure in either the mitral or pulmonary position (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (e.g., wire form fracture); partially detached leaflet that in the aortic position may obstruct a coronary ostium; stent frame with a manufacturer-labeled inner diameter < 17 mm. The safety and effectiveness of the bioprostheses for aortic valve replacement have not been evaluated in patient populations presenting with the following: Blood dyscrasias as defined as leukopenia (WBC $< 1,000$ cells/mm³), thrombocytopenia (platelet count $< 50,000$ cells/mm³), history of bleeding diathesis or coagulopathy, or hypercoagulable states; congenital unicuspid valve; 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 > 30 mm per the baseline diagnostic imaging or surgical bioprosthetic aortic annulus size < 17 mm or > 30 mm; transarterial access unable to accommodate an 18 Fr introducer sheath or the 14 Fr equivalent EnVeo InLine™ Sheath when using models ENVEOR-US/D-EVPROP2329US or Evolut FX Delivery Catheter System with InLine™ Sheath when using model D-EVOLUTFX-2329 or transarterial access unable to accommodate a 20 Fr introducer sheath or the 16 Fr equivalent EnVeo InLine Sheath when using model ENVEOR-N-US or transarterial access unable to accommodate a 22 Fr introducer sheath or the 18 Fr equivalent Evolut PRO+ InLine Sheath when using model D-EVPROP34US or Evolut FX Delivery Catheter System with InLine Sheath when using model D-EVOLUTFX-34; prohibitive left ventricular outflow tract calcification; sinus of Valsalva anatomy that would prevent adequate coronary perfusion; significant aortopathy requiring ascending aortic replacement; moderate to severe mitral stenosis; severe ventricular dysfunction with left ventricular ejection fraction (LVEF) $< 20\%$; symptomatic carotid or vertebral artery disease; and severe basal septal hypertrophy with an outflow gradient.

Before Use Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and

throat. Avoid prolonged or repeated exposure to the vapors. Damage may result from forceful handling of the catheter. Prevent kinking of the catheter when removing it from the packaging. The bioprosthesis size must be appropriate to fit the patient's anatomy. Proper sizing of the devices is the responsibility of the physician. Refer to the Instructions for Use for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed below. Patients must present with transarterial access vessel diameters of ≥ 5 mm when using models ENVEOR-US/D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 5.5 mm when using model ENVEOR-N-US or ≥ 6 mm when using models D-EVPROP34US/D-EVOLUTFX-34, or patients must present with an ascending aortic (direct aortic) access site ≥ 60 mm from the basal plane for both systems. 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 $> 30^\circ$ for right subclavian/axillary access or $> 70^\circ$ for femoral and left subclavian/axillary access. For subclavian access, patients with a patent left internal mammary artery (LIMA) graft must present with access vessel diameters that are either ≥ 5.5 mm when using models ENVEOR-L-US/D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 6 mm when using model ENVEOR-N-US or ≥ 6.5 mm when using models D-EVPROP34US/D-EVOLUTFX-34. Use caution when using the subclavian/axillary approach in patients with a patent LIMA graft or patent RIMA graft. For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft. For transfemoral access, use caution in patients who present with multipanar curvature of the aorta, acute angulation of the aortic arch, an ascending aortic aneurysm, or severe calcification in the aorta and/or vasculature. If ≥ 2 of these factors are present, consider an alternative access route to prevent vascular complications. Limited clinical data are available for transcatheter aortic valve replacement in patients with a congenital bicuspid aortic valve who are deemed to be at low surgical risk. Anatomical characteristics should be considered when using the valve in this population. In addition, patient age should be considered as long-term durability of the valve has not been established.

During Use After the procedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis. After the procedure, administer anticoagulation and/or antiplatelet therapy per physician/clinical judgment. Excessive contrast media may cause renal failure. Prior to the procedure, 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 a CoreValve Evolut R, Evolut PRO+, or Evolut FX bioprosthesis implanted within a transcatheter bioprosthesis have not been demonstrated.

Potential adverse events

Potential risks associated with the implantation of the CoreValve Evolut R, Evolut PRO+, or Evolut FX transcatheter aortic valve may include, but are not limited to, the following:

- death
- myocardial infarction, cardiac arrest, cardiogenic shock, or cardiac tamponade
- coronary occlusion (obstruction, or vessel spasm (including acute coronary closure)
- cardiovascular injury (including rupture, perforation, tissue erosion, or dissection of vessels, ascending aorta trauma, ventricle, myocardium, or valvular structures that may require intervention)
- emergent surgical or transcatheter intervention (e.g., coronary artery bypass, heart valve replacement, valve explant, percutaneous coronary intervention [PCI], balloon valvuloplasty)
- prosthetic valve dysfunction (regurgitation or stenosis) due to fracture; bending (out-of-round configuration) of the valve frame; underexpansion 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 – prosthetic valve migration/embolization
- prosthetic valve endocarditis
- prosthetic valve thrombosis
- delivery catheter system malfunction resulting in the need for additional recrossing of the aortic valve and prolonged procedural time
- delivery catheter system component migration/embolization
- stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits
- individual organ (e.g., cardiac, respiratory, renal (including acute kidney failure)) or multi-organ insufficiency or failure
- major or minor bleeding that may require transfusion or intervention (including life-threatening or disabling bleeding)
- vascular access-related complications (e.g., dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, or stenosis)
- mitral valve regurgitation or injury
- conduction system disturbances (e.g., atrioventricular node block, left bundle-branch block, asystole), which may require a permanent pacemaker
- infection (including septicemia)
- hypotension or hypertension
- hemolysis
- peripheral ischemia
- General surgical risks applicable to transcatheter aortic valve implantation:
- bowel ischemia
- abnormal lab values (including electrolyte imbalance)
- allergic reaction to antiplatelet agents, contrast medium, or anesthesia
- exposure to radiation through fluoroscopy and angiography
- permanent disability.

Please reference the CoreValve Evolut R, Evolut PRO+, and Evolut FX Instructions for Use for more information regarding indications, warnings, precautions, and potential adverse events.

Caution: Federal Law (USA) restricts these devices to the sale by or on the order of a physician.

The commercial name of the Evolut™ R device is Medtronic CoreValve™ Evolut™ R System, the commercial name of the Evolut™ PRO+ device is Medtronic Evolut™ PRO+ System, and the commercial name of the Evolut™ FX device is Medtronic Evolut™ System.

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