Clinical Insights

SUMMARY OF CLINICAL DATA

MITRACLIP® TRANSCATHETER MITRAL VALVE REPAIR

REAL WORLD USE OF MITRACLIP THERAPY IN US — RESULTS FROM THE STS/ACC TVT REGISTRY

PERSPECTIVE

First published 1-year report from the STS/ACC TVT Registry on real world use of the MitraClip® System (Abbott, Menlo Park) in U.S. patients following FDA approval in 2013.[1] Demonstration of safety and effectiveness in commercial use is important to strengthen MitraClip therapy as the pioneer in transcatheter mitral valve repair.

HIGHLIGHTS

- **MitraClip therapy in real world use is safe and achieved meaningful mitral regurgitation (MR) reduction** (≤2+) in elderly and highly comorbid DMR patients who are unsuited for surgery.
- These real world results from the STS/ACC TVT registry are **consistent with earlier MitraClip studies, and affirm improved patient survival with reduced need for mitral valve interventions through 1-year** when severe MR is alleviated.[2]
- **Long-term patient outcomes** following MitraClip treatment can be monitored from the CMS claims database via links to the STS/ACC TVT registry.

WHAT IS THE STS/ACC TVT REGISTRY?

The Transcatheter Valve Therapy (TVT) registry is a joint initiative of the Society of Thoracic Surgery (STS) and American College of Cardiology (ACC) to create a national database of transcatheter valve replacement and repair procedures at participating US centers to:

- Perform post-market surveillance safety and outcomes
- Create benchmarks for hospital practices of such procedures
- Enable scientific research and publication of the registry data
- Satisfy requirements for CMS national coverage

Source: https://www.ncdr.com/webncdr/tvt/publicpage/home

STUDY DESIGN AND METHODS[1]

- 2,952 MitraClip patients from 145 hospitals who enrolled into the TVT registry from November 2013 to September 2015.
- Patients were predominantly symptomatic, primary degenerative MR (DMR) grade ≥3+, and STS-PROM ≥6% (MV repair) or ≥8% (MV replacement). All were deemed unsuitable for surgery by a site heart team.
- Baseline, procedural, and in-hospital results came from the Registry. Post-discharge outcomes for a subgroup of 1,867 patients came from links to the CMS national claims database.
- All site reported strokes, cardiac surgeries, and valve events were adjudicated by a board certified cardiologist from the Duke Clinical Research Institute.

COHORT BASELINE CHARACTERISTICS

This was an elderly cohort deemed unsuited for surgery, and highly comorbid with history of ischemia and atrial fibrillation, compromised LVEF, and documented mitral leaflet prolapse or flail in most patients.

- Median age of 82 years
- STS-PROM of 6.1% (repair) or 9.2% (replacement)
- 93.0% had Grade 3± or 4+ MR
- 85.9% had only degenerative MR, 8.6% had only functional MR, 8.9% had both
- 85% were at NYHA class III/IV prior to treatment
- 50.3% were deemed frail

PROCEDURAL RESULTS

- High acute procedural success of 91.8%.[3]
  - 82.8% of cases involved the A2-P2 segments
  - 34.5% received multiple Clips
  - 1.5% site-reported single-leaflet device attachment (SLDA) rate
- Majority were discharged directly to home (85.9%).
- Short median hospital stay of 2.0 days.

Indications:
The MitraClip® Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at high risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.

Abbott

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EFFECTIVENESS OUTCOMES

- 92.0% of patients had their MR reduced to ≤2+, increased from 86% in earlier trials.[2]
- Importantly, successful MR reduction (2+ or less) significantly improved patient prognosis [Figure 1]:
  - Lower in-hospital and 1-year mortality
  - Lower SLDA rate
  - Shorter hospital stay
  - Less need for reintervention with mitral valve surgery or MitraClip therapy
- Contrarily, less successful procedures led to poorer outcomes.
  - Much higher in-hospital mortality and doubling of 1-year death rates

SAFETY

- Low mortality, myocardial infarction, and stroke rates through 1-year [Table 1].
- Infrequent MV reinterventions. When needed, the MitraClip therapy was used more often than surgery.
- Mortality and heart failure (HF) rehospitalization at 1-year were 25.8% and 20.2%, consistent with the EVEREST II/ REALISM High Risk Cohort (22.8% and 19.8%).[3]
- Not unexpectedly in an elderly comorbid population, persistent risk of death was associated with age, residual MR, dialysis, lung disease, baseline LVEF, and severe tricuspid regurgitation (TR), which are also factors related to poor outcomes after mitral valve surgery [Figure 2].

RESULTS BY MR ETIOLOGY

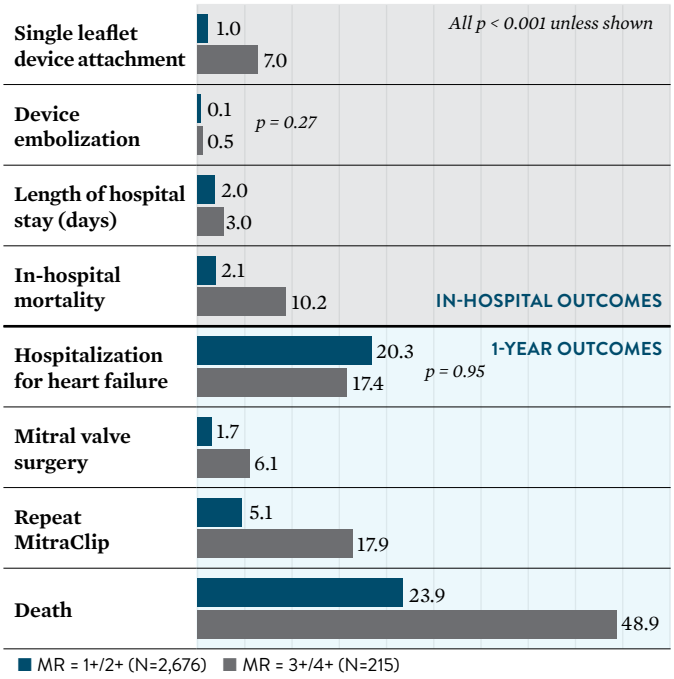
- MitraClip therapy was deemed by physicians to be suitable in some FMR patients from the CMS cohort (297/1,867).
- Given the small patient sample, no conclusions can currently be made regarding MitraClip therapy for FMR vs. DMR despite the higher 1-year mortality (31.2% versus 24.7%) and HF rehospitalization (32.6% versus 20.5%) rates reported.
- That answer lies in the COAPT RCT results expected in late 2018, which compares MitraClip therapy + optimal medical therapy to optimal medical therapy alone for HF patients with FMR.

CONCLUSIONS

- In the U.S., commercial transcatheter mitral valve repair with **MitraClip therapy demonstrates high procedural success (91.8%) with low incidences of in-hospital mortality (2.7%) and mitral valve surgery (0.7%)** for severely symptomatic MR patients with prohibitive surgical risk.
- Patient factors influencing long-term outcomes include age, LVEF, FMR, severe tricuspid regurgitation, moderate or severe lung disease, and post-procedural residual MR.

See Important Safety Information referenced within. AP2945413-US Rev A

FIGURE 1. OUTCOMES ACCORDING TO POST-IMPLANT MITRAL REGURGITATION



Patients who required conversion to open cardiac surgery (n = 20) are included in the patients with grade 3 or 4 post-implant MR.

Unless specified, all values are in %.

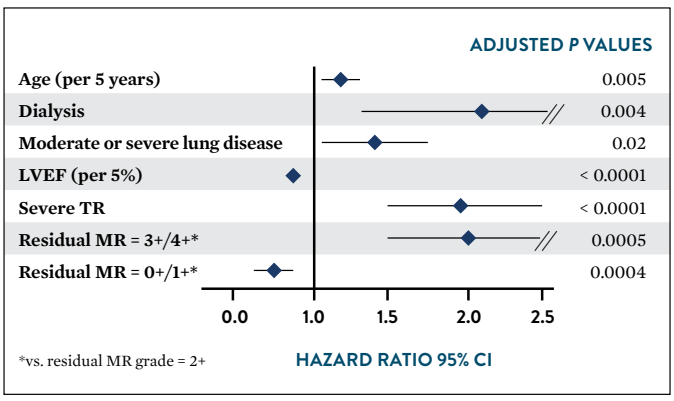
Adapted from Sorajja et al. *J Am Coll Cardiol.* 2017;70(19):2315-2327.

TABLE 1. CLINICAL OUTCOMES: IN-HOSPITAL, 30-DAY, AND 1-YEAR

PARAMETER, %	IN-HOSPITAL	30 DAYS	1 YEAR
Death	2.7	5.2	25.8
Myocardial infarction	0.1	0.2	2.5
Stroke			
Any stroke	0.4	1.0	2.7
Hemorrhagic	0.03	0.4	0.6
Heart failure hospitalization	–	4.7	20.2
Mitral valve surgery	–	0.4	2.1
Repeat MitraClip	–	1.3	6.2

Adapted from Sorajja et al. *J Am Coll Cardiol.* 2017;70(19):2315-2327.

FIGURE 2: MULTIVARIATE PREDICTORS OF 1-YEAR MORTALITY[1]



Rx ONLY

MITRACLIP® NT CLIP DELIVERY SYSTEM

INDICATION FOR USE

The MitraClip® NT Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.

CONTRAINDICATIONS

The MitraClip® NT Clip Delivery System is contraindicated in DMR patients with the following conditions:

- Patients who cannot tolerate procedural anticoagulation or post procedural anti-platelet regimen
- Active endocarditis of the mitral valve
- Rheumatic mitral valve disease
- Evidence of intracardiac, inferior vena cava (IVC) or femoral venous thrombus

WARNINGS

- **DO NOT use MitraClip® NT outside of the labeled indication. Treatment of non-prohibitive risk DMR patients should be conducted in accordance with standard hospital practices for surgical repair and replacement.**
- MitraClip® NT is intended to reduce mitral regurgitation. The MitraClip® NT procedure is recommended to be performed when an experienced heart team has determined that reduction of MR to ≤2+ is reasonably expected following the MitraClip® NT. If MR reduction to ≤2+ is not achieved, the benefits of reduced symptoms and hospitalizations, improved quality of life, and reverse LV remodeling expected from MitraClip® NT may not occur.
- The MitraClip® NT Device should be implanted with sterile techniques using fluoroscopy and echocardiography (e.g., transesophageal [TEE] and transthoracic [TTE]) in a facility with on-site cardiac surgery and immediate access to a cardiac operating room.
- Read all instructions carefully. Failure to follow these instructions, warnings and precautions may lead to device damage, user injury or patient injury. Use universal precautions for biohazards and sharps while handling the MitraClip® NT System to avoid user injury.
- Use of the MitraClip® NT should be restricted to those physicians trained to perform invasive endovascular and transseptal procedures and those trained in the proper use of the system.
- The Clip Delivery System is provided sterile and designed for single use only. Cleaning, re-sterilization and/or reuse may result in infections, malfunction of the device or other serious injury or death.

PRECAUTIONS

- Patient Selection:
  - Prohibitive risk is determined by the clinical judgment of a heart team, including a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, due to the presence of one or more of the following documented surgical risk factors:
    - 30-day STS predicted operative mortality risk score of
      - ≥8% for patients deemed likely to undergo mitral valve replacement or
      - ≥6% for patients deemed likely to undergo mitral valve repair
    - Porcelain aorta or extensively calcified ascending aorta.
    - Frailty (assessed by in-person cardiac surgeon consultation)
    - Hostile chest
    - Severe liver disease/cirrhosis (MELD Score >12)
    - Severe pulmonary hypertension (systolic pulmonary artery pressure >2/3 systemic pressure)
    - Unusual extenuating circumstance, such as right ventricular dysfunction with severe tricuspid regurgitation, chemotherapy for malignancy, major bleeding diathesis, immobility, AIDS, severe dementia, high risk of aspiration, internal mammary artery (IMA) at high risk of injury, etc.
  - Evaluable data regarding safety or effectiveness is not available for prohibitive risk DMR patients with an LVEF < 20% or an LVESD > 60mm. MitraClip® NT should be used only when criteria for clip suitability for DMR have been met.
  - The major clinical benefits of MitraClip® NT are reduction of MR to ≤2+ resulting in reduced hospitalizations, improved quality of life, reverse LV remodeling and symptomatic relief in patients who have no other therapeutic option. No mortality benefit following MitraClip® NT therapy has been demonstrated.
- The heart team should include a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease and may also include appropriate physicians to assess the adequacy of heart failure treatment and valvular anatomy.
- The heart team may determine an in-person surgical consult is needed to complete the assessment of prohibitive risk. The experienced mitral valve surgeon and heart team should take into account the outcome of this surgical consult when making the final determination of patient risk status.
- For reasonable assurance of device effectiveness, pre-procedural evaluation of the mitral valve and underlying pathologic anatomy and procedural echocardiographic assessment are essential.
- Note the "Use by" date specified on the package.
- Inspect all product prior to use. Do not use if the package is open or damaged, or if product is damaged.

POTENTIAL COMPLICATIONS AND ADVERSE EVENTS

The following ANTICIPATED EVENTS have been identified as possible complications of the MitraClip® NT procedure.

Allergic reaction (anesthetic, contrast, Heparin, nickel alloy, latex); Aneurysm or pseudo-aneurysm; Arrhythmias; Atrial fibrillation; Atrial septal defect requiring intervention; Arterio-venous fistula; Bleeding; Cardiac arrest; Cardiac perforation; Cardiac tamponade/Pericardial Effusion; Chordal entanglement/rupture; Coagulopathy; Conversion to standard valve surgery; Death; Deep venous thrombus (DVT); Dislodgement of previously implanted devices; Dizziness; Drug reaction to anti-platelet/anticoagulation agents/contrast media; Dyskinesia; Dyspnea; Edema; Emboli (air, thrombus, MitraClip® NT Device); Emergency cardiac surgery; Endocarditis; Esophageal irritation; Esophageal perforation or stricture; Failure to deliver MitraClip® NT to the intended site; Failure to retrieve MitraClip® NT System components; Fever or hyperthermia; Gastrointestinal bleeding or infarct; Hematoma; Hemolysis; Hemorrhage requiring transfusion; Hypotension/hypertension; Infection; Injury to mitral valve complicating or preventing later surgical repair; Lymphatic complications; Mesenteric ischemia; MitraClip® NT erosion, migration or malposition; MitraClip® NT Device thrombosis; MitraClip® NT System component(s) embolization; Mitral stenosis; Mitral valve injury; Multi-system organ failure; Myocardial infarction; Nausea/vomiting; Pain; Peripheral ischemia; Prolonged angina; Prolonged ventilation; Pulmonary congestion; Pulmonary thrombo-embolism; Renal insufficiency or failure; Respiratory failure/atelectasis/pneumonia; Septicemia; Shock, Anaphylactic or Cardiogenic; Single leaflet device attachment (SLDA); Skin injury or tissue changes due to exposure to ionizing radiation; Stroke or transient ischemic attack (TIA); Urinary tract infection; Vascular trauma, dissection or occlusion; Vessel spasm; Vessel perforation or laceration; Worsening heart failure; Worsening mitral regurgitation; Wound dehiscence

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1. Sorajja P et. al., Outcomes with Transcatheter Mitral Valve Repair in the United States: An STS/ACC TVT Registry Report. JACC 2017: 70 (19):2315-2327
2. Glower DD et al. Percutaneous Mitral Valve Repair for Mitral Regurgitation in High-Risk Patients. Results of EVEREST II study. JACC 2014; 64:172–81
3. Acute procedure success defined as acute reduction in MR to grade 2 or less, without conversion to cardiac surgery and without in-hospital mortality

Caution: This product is intended for use by or under the direction of a physician. Prior to use, reference the Instructions for Use provided inside the product carton (when available), at eifu.abbottvascular.com or at Manuals.sjm.com for more detailed information on Indications, Contraindications, Warnings, Precautions and Adverse Events.

Illustrations are artist's representations only and should not be considered as engineering drawings or photographs. Photos on file at Abbott.

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