Carillon® Mitral Contour System®

Clinical Compendium
Three prospective, multi-center trials involving more than 100 patients have shown that the Carillon Mitral Contour System is effective, efficient and flexible.

- **Effective**: 80% of patients demonstrate at least a 1 NYHA class improvement and a 50% reduction in regurgitant volume as a result of reversing annular dilation.²
- **Efficient**: Carillon has the best safety profile (with <3% MAEs) and shortest learning curve (with an implant time of <40 minutes) of any minimally invasive MR intervention.²
- **Flexible**: Carillon is a flexible treatment that does not limit future interventions.²

**Indications for Use**

Individual experiences, symptoms, situations and circumstances may vary. Please consult your physician or qualified healthcare provider regarding your condition and appropriate medical treatment.

CAUTION: The Carillon® Mitral Contour System® is CE-Marked and approved for sale in the European Union and elsewhere in the world.

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Improved Hemodynamics Demonstrated in Prospective, Multi-center Trials

Treatment of functional mitral regurgitation by percutaneous annuloplasty using the Carillon mitral contour system results in improved clinical efficacy – the TITAN II study


- This study treated 30 patients with dilated cardiomyopathy and moderate to severe FMR, EF <40%, New York Heart Association classification (NYHA class) II-IV, 6MWD 150-450 m and stable on heart failure (HF) medication.
- 83% successful implantation rate. 30-day MAE rate <3% with no device-related events.
- 40% improvement in FMR, 20% improvement in LV end systolic volume and 77.8m (294.1m vs. 381.6m) improvement in 6MWD at 12 months.
- 80% of patients had ≥1 NYHA class improvement at 12 months.

Key take away
Carillon has an excellent acute and long-term safety profile and results in significant improvement in FMR by invoking reverse remodeling to treat annular dilation.

Treatment of functional mitral regurgitation by percutaneous annuloplasty: results of the TITAN Trial


- In this study, 36 FMR patients were implanted with the Carillon Mitral Contour System and compared with a non-implanted cohort to evaluate safety and efficacy up to 24 months.
- The 30-day major adverse event (MAE) rate was 1.9%.
- After 12 months, the implanted group demonstrated significant reductions in FMR by regurgitant volume (49.6%; p<0.001) with a corresponding reduction in LV diastolic volume (14.2%; p=0.015) and systolic volume (20.5%; p=0.015) compared to baseline. Six-minute walk distance (6MWD) improved by 104m over baseline.
- 80% of patients experienced a 1 NYHA class reduction at 12 months.

Key take away
Carillon reduces MR and invokes remodeling, leading to a reduction in MR and an improvement in NYHA class and symptoms in FMR patients. Results are sustained for 24 months.

Percutaneous mitral annuloplasty for functional mitral regurgitation: results of the Carillon mitral annuloplasty device European Union study


- This study enrolled and completed six month follow-up on 30 patients with dilated cardiomyopathy, moderate to severe FMR, an ejection fraction <40%, and a 6MWD between 150 and 450 m. Patients were evaluated for FMR grade, functional capacity, NYHA class and QOL.
- At six months, the degree of FMR reduction among five different quantitative echocardiographic measures ranged from 22% to 32%.
- QOL, measured by the Kansas City Cardiomyopathy Questionnaire, improved from 47 at baseline to 69 points at six months (P <0.001). 6MWD increased by 96m at 6 months (p<0.001).
- 88% of patients improved to a NYHA class I or II at 6 months.

Key take away
Carillon is associated with a low MAE, and with improvement in QOL and functional capacity.
Effectiveness and safety of percutaneous coronary sinus-based mitral valve repair in patients with dilated cardiomyopathy (from the AMADEUS trial)\(^4\)


- This report presents the procedural results from the AMADEUS\(^TM\) trial. Acute FMR reduction and permanent implantation were achieved in 30 of 43 patients in whom an attempt was made.
- The coronary arteries were crossed in 36 patients (84%) however, arterial compromise contributed to a lack of implantation in only six patients (14%).
- No difference was found in the CS/great cardiac vein position relative to the mitral annulus between the patients who did and did not have a reduction in FMR.
- Additional measurements in patients with implants showed reductions in the vena contracta (33.3%, \(p<0.0001\)), effective regurgitant orifice area (42.4%, \(p<0.0001\)), regurgitant volume (40%, \(p=0.0005\)), and jet area/left atrial area (28.9%, \(p<0.0001\)).

**Key take away**

Carillon reduces FMR, and permanent implantation can be achieved in most eligible patients. Moreover, the position of the CS/great cardiac vein relative to the mitral annulus is not predictive of outcome.

The Carillon Mitral Contour transcatheter indirect mitral valve annuloplasty system\(^5\)

Goldberg, S. et al. EuroIntervention 2015;11W64-W66

- This paper presents a comprehensive summary of the device technology and clinical study data from development to ongoing clinical work.
- Carillon has undergone technical enhancements to ensure maximum safety and reliability of the design implanted at present demonstrated in the TITAN and TITAN II studies.
- REDUCE FMR is an ongoing prospective, double-blind, randomized clinical study comparing Carillon to guideline-directed medical therapy in symptomatic FMR patients.

**Key take away**

Technological enhancements to Carillon have resulted in a more effective device which is demonstrated in clinical trials.

Improved Hemodynamics Demonstrated in Single-center Experience

Mitral Annuloplasty Device Implantation for Non-Surgical Treatment of Mitral Regurgitation: Clinical Experience after the Approval Studies\(^6\)


- 17 patients were implanted with the Carillon device in a prospective, single-center, non-randomized study.
- Patients experienced a one grade reduction of MR acutely (2.8 to 1.9, \(p<0.005\)) with an additional improvement at 3 months (1.5, \(p<0.005\)).
- In 41.2% of patients an acute reduction of coronary artery flow was detected intra-operatively and in all except one patient this could be easily managed such that the patients successfully received the implant.

**Key take away**

Potential coronary artery compromise can be managed safely and effectively in all patients with 95% successfully implanted.

Functional assessment of patients after percutaneous mitral valvuloplasty with Carillon device: a preliminary report\(^7\)


- This study enrolled 14 consecutive patients who underwent Carillon implantation.
- Echocardiographic parameters, 6MWD, Naughton treadmill exercise test, NYHA class and QOL were assessed at baseline and after one month.
- All measurements demonstrated statistically significant improvement at one month from baseline.
• Echocardiographic MR parameters were observed immediately after the procedure and during the one month follow up; these parameters included vena contracta (0.36cm after procedure and 0.31cm at one month vs. 0.65cm at baseline, both p<0.001) and effective regurgitant orifice area (0.18cm² after procedure and 0.20cm² at one month vs. 0.28cm² at baseline, p<0.05 and p<0.005, respectively).

• One month after the procedure the 6MWT (25%, p<0.001), Naughton treadmill exercise test (45.0%, p<0.005) and NYHA classifications (34.1%, p<0.005) were significantly improved.

Key take away
Carillon increased functional capacity and improved echocardiographic parameters in FMR patients.

Echocardiographic evaluation of percutaneous valve repair in patients with mitral regurgitation using the Carillon system

• In this study, nine patients were enrolled and successfully implanted with the Carillon device.

• One month post-implant, vena contracta, the ratio of the jet area to the left atrial area, and other echocardiographic parameters were assessed relative to baseline.

• Vena contracta and jet area to left atrial area improved (p<0.05 and p<0.005, respectively).

Key take away
Carillon improved echocardiographic parameters in functional mitral regurgitation patients.

Restoration of normal left ventricular geometry after percutaneous mitral annuloplasty: case report and review of literature
Soofi, M.A., Alsamadi F. Catheterization and Cardiovascular Interventions. 2014.

• Case report of a NYHA class IV patient who presented with severe dyspnea progressing to orthopnea and paroxysmal nocturnal dyspnea. He was found to have severe functional mitral regurgitation Grade 4 and severe left ventricle systolic dysfunction. Surgical mitral intervention was not considered suitable and percutaneous mitral annuloplasty was performed with Carillon Mitral Contour System.

• From baseline to 6-months following implantation of Carillon the patient experienced a 70% reduction in vena contracta (0.25cm vs. 0.84cm), 90% reduction in regurgitant volume (29ml vs. 291ml). MR Grade was reduced from a grade 4 to grade 2 and NYHA class improved from IV to I.

• Remodeling of the left ventricle was observed and resulted in an absolute improvement in ejection fraction of 30% (from 20% to 50%).

• The patient's symptoms improved so significantly that he was no longer considered an immediate candidate for CRT.

Key take away
In patients with severe heart failure and mitral regurgitation, Carillon can be successfully used as a first line medical device intervention and may delay or negate the need for further intervention.

Carillon Compatible with Cardiac Resynchronization Therapy

Percutaneous mitral annuloplasty device leaves free access to cardiac veins for resynchronization therapy

• Three patients meeting current guidelines for cardiac resynchronization therapy (CRT) included in the AMADEUS trial underwent CRT implantation 7-8 months after implantation of a mitral valve annuloplasty device.

• Access to the coronary sinus and placement of the left ventricular lead into a posterolateral cardiac vein was not at all compromised by the mitral valve annuloplasty device in any patient.

Key take away
Carillon can be implanted prior to a CRT device in HF patients with low ejection fraction, wide QRS and FMR.
Cardiac resynchronization therapy after percutaneous trans-coronary-venous mitral annuloplasty


- Case study of a 45 year-old male with ischemic heart failure who underwent successful implantation of a Carillon device.
- The procedure resulted in clinical improvements and a decrease in FMR.
- Fifteen months post implant, the patient was a candidate for CRT and underwent successful implantation, which resulted in further improvement of clinical and echocardiographic parameters.

Key take away
Carillon can be implanted prior to CRT and may provide additional benefit to HF patients with FMR, low ejection fraction and wide QRS.

Carillon Cost Effectiveness

Cost-utility analysis of percutaneous mitral valve repair in inoperable patients with functional mitral regurgitation in German settings

Borisenko, O., et al. BMC Cardiovascular Disorders. 2015.

- Cost-utility analysis of Carillon Mitral Contour System was performed based on the TITAN trial results using a combination of a decision tree and Markov process. The analysis was performed from the German statutory health insurance perspective over 10-year time horizon.
- Carillon provided additional benefits to patients with an 1.15 incremental quality-adjusted life years (QALY) and an 1.41 incremental life years. The procedure was cost-effective in comparison to optimal medical therapy (OMT) with an incremental cost-effectiveness ratio of €15,533/QALY. With a willingness-to-pay threshold of €35,000/QALY, PMVR had a 84% probability of being cost-effective.

Key take away
Percutaneous mitral valve repair may be cost-effective in patients with FMR due to heart failure.

References

Peer-reviewed Publications on Mitral Regurgitation, Mitral Valve and Anatomy


Pre-Clinical Publications on Carillon


German Peer-reviewed Clinical Publications


Non-peer reviewed publications on Carillon

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