An Initial Evaluation of the Carillon Mitral Contour System for Treatment of Atrial Functional Mitral Regurgitation

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The objective of this prospective, multi-center trial is to assess the effectiveness of the Carillon Mitral Contour System in treating patients with moderate-to-severe atrial functional mitral regurgitation (aFMR).

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51133

Source
ToetsingOnline

Brief title
AFIRE

Condition

- Other condition
- Cardiac valve disorders

Synonym
heart failure

Health condition

heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Cardiac Dimensions
Source(s) of monetary or material Support: Funded by the industry Sponsor of the study;Cardiac Dimensions Pty Ltd

Intervention

Keyword: atrial functional mitral regurgitation, Carillon Mitral Contour System

Outcome measures

Primary outcome

Primary Endpoint:

Change in mitral regurgitant volume (mL) associated with the Carillon device at

6 months post-implant, as compared to baseline

Secondary outcome

Secondary Endpoints:

* MR severity as assessed by echocardiography at Day One, 1 month, 6 months and

12 months, in accordance with American Society of Echocardiography guidelines,

compared to baseline. Semi-quantitative parameters to be assessed include vena

contracta width, MV EVmax, pulmonary vein flow). Quantitative MR variables to

be assessed include regurgitant volume (mL), regurgitant fraction (%) and

effective regurgitant orifice area (cm2, EROA) by Proximal Isovelocity Surface

Area (PISA).

* Change in Left Atrial Area, Diameter and LA Volume Index at 1, 6 and 12

months over baseline

* Change in Left Atrial Diameter and Area at 1, 6 and 12 months over baseline

* Change in Left Ventricular End Diastolic Volume (LVEDV) at 1, 6 and 12 months

over baseline

* Change in Left Ventricular End Systolic Volume (LVESV) at 1, 6 and 12 months over baseline

* Change in Pulmonary Artery Systolic Pressure at 1, 6 and 12 months over baseline

* Change in Right Ventricular size (base and mid) at 1, 6 and 12 months over baseline

* Change in 6 Minute Walk Test (6MWT) distance at 1, 6 and 12 months over baseline

* Change in Quality of Life (QoL) score as measured by Kansas City Cardiomyopathy Questionnaire (KCCQ) at 1, 6 and 12 months over baseline

* Change in Quality of Life (QoL) score as measured by Short Form-36 (SF-36) at 1, 6 and 12 months over baseline

* Change in New York Heart Association (NYHA) Functional Classification at 1, 6 and 12 months over baseline

* Hospitalization for heart failure at 1, 6 and 12 months

* Stroke, myocardial infarction, cardiovascular and all-cause mortality at 1, 6 and 12 months

* Need for mitral valve intervention or surgery at 1, 6 and 12 months

Study description

Background summary

The purpose of this clinical study is to evaluate the Carillon Mitral Contour System in people who have a specific type of mitral regurgitation called atrial functional mitral regurgitation. The Carillon Mitral Contour System is used during a non-surgical procedure to repair the mitral valve so that the mitral

valve no longer leaks (regurgitation), or leaks less. The Carillon implant is an approved device that has been used in humans over 1000 times, and the purpose of this study is to gather data on the subset of patients that includes atrial functional mitral regurgitation.

Study objective

The objective of this prospective, multi-center trial is to assess the effectiveness of the Carillon Mitral Contour System in treating patients with moderate-to-severe atrial functional mitral regurgitation (aFMR).

Study design

The AFIRE Trial is a prospective, multi-center clinical trial.
The centers will utilize pre-screening of existing medical records to identify potentially eligible subjects. Once informed consent has been obtained, the subject will undergo baseline assessments, which include: Transthoracic echocardiography, transesophageal echocardiography, and functional assessments (Six-Minute Walk Test, NYHA, and Quality of Life Questionnaires). Following final eligibility determination, eligible subjects will under the index procedure to implant the Carillon device (includes coronary sinus venogram). Subject will be discharged following one-night in-hospital stay and discharge assessments.
Subjects who have the Carillon implant procedure attempted but were not successfully implanted (Non-Implanted subjects) will be followed through discharge or resolution of safety events, whichever is longer, and then discharged from the trial.
Implanted subjects will have follow-up assessments performed at 1 month, 6 months, and 12 months post index procedure. Follow-up assessments will include transthoracic echocardiography, Six-Minute Walk Test, and Quality of Life Questionnaires.

Intervention

Carillon Mitral Contour System® (CMCS) - Model XE2
The CMCS received CE-Mark on 3 August 2011.
In Australia the CMCS received approval from TGA on 25 August 2020.

Study burden and risks

Any study of a medical device or procedure may have unknown, as well as known, side effects, discomforts and risks. Every effort has been made to minimize the risks involved with this study, however, complications may occur.

The risks listed below are associated with this study and include the risks associated with diagnostic coronary angiography, as well as the risks

associated with the delivery, permanent placement, and recapture of the Carillon implant in the coronary venous system, and any risks associated with study related testing (e.g., echocardiogram (TTE), 6MWT, blood collections). As the study device has to be permanently implanted, the majority of the risks listed below could occur shortly after the procedure to implant the device. The risks in this section include known risks that have occurred in prior trials, as well as possible risks based on similar types of therapy and what is known about heart failure.

Potential adverse events are categorized by frequency of occurrence and severity as follows:

Severity (how serious is the event):
* Mild: awareness of a sign or symptom but easily tolerated
* Moderate: discomfort that may interfere with usual activity or affect clinical status
* Severe: requiring intervention or treatment

The anticipated side effects specifically for the Carillon Mitral Contour System include, but are not limited to:

Occurring in approximately 5 out of 100 people:
* Mild: bleeding or damage to the blood vessels.
* Moderate: abnormal heart rhythms, worsening of mitral regurgitation, or tearing of the blood vessels.

Occurring in approximately 1 out of 100 people, or rarer:
* Mild: infection
* Moderate: chest pain associated with your heart or blood vessel spasm
* Severe: blockage in your vessels by air, blood clot, tissue or the device, heart attack, blockage of blood flow to the heart, which could require a cardiac procedure to increase flow, fluid collection around the heart

Other risks are possible by participating this trial. They are listed below, and are related to the assessments required for your participation in the trial, as well as related to your ongoing diagnosis of heart failure.

Occurs in approximately 15 out of 100 people:
* Mild: tiredness, headache, nausea, vomiting, pain, or weakness.
* Moderate: heart failure worsening or hospitalization.

Occurring in approximately 5 out of 100 people:
* Mild: bleeding, abnormal blood pressure, damage to the blood vessels, bruising, or shortness of breath.
* Moderate: abnormal heart rhythms, worsening of mitral regurgitation, or tearing of the blood vessels.

Occurring in approximately 3 out of 100 people:
* Mild: infection, physical injury, damage to blood vessels, or swelling.
* Moderate: chest pain associated with your heart, ballooning of an area of a blood vessel which weakens the vessel, abnormal blood clotting, abnormal blood counts, inflammation around your heart, abnormal kidney lab tests, infection of blood or urinary system, fainting, blood vessel spasms, or hardening of the blood vessels.
* Severe: pressure on the heart from fluid collection around it, injury to the major blood vessel in your neck, blockage in your vessels by air, blood clot, tissue or the device, heart attack, blockage of blood flow to the heart, which could require a cardiac procedure to increase flow, fluid collection around the heart, collapsed lung, lung infection, kidney failure, respiratory failure, multi system organ failure, fluid in the lungs, or breathing issues.

Occurring in approximately 1 out of 100 people, or rarer:
* Mild: allergic reaction to contrast, injury to neck
* Moderate: abnormal twisting of a blood vessel, damage to teeth, depression, device malfunction or failure, loss of blood flow to arms or legs, or abnormal movement of the mitral valve.
* Severe: decline in urine output, hardening and narrowing of the major artery of the body, nerve damage, clotting in your arms, legs, or lungs, device placement or shifting of device placement that blocks blood flow of a blood vessel in the heart, abnormal electrical activity in the heart, inflammation to the lining of the heart, throat injury, narrowing or injury of your mitral valve, a hole poked through tissue during procedure, cardiac arrest, skin rash from x-ray exposure, reduced blood flow to the brain that has short or long term damages, surgical removal of the device, or wearing down of blood vessels.

In an effort to minimize all the risks mentioned above, the doctors conducting the study have been specially trained to perform the study-related procedures. In the event of any complication, appropriate treatment will be provided to you. This may include medical and/or surgical treatment.

Taking part in the study can have pros and cons. We will list them below.

The Carillon Mitral Contour System is an approved medical device Australia and in Europe (CE marked). You may benefit from being in this study and as a result of the procedure. You may also be helping patients with a similar problem benefit from the knowledge gained from your participation in this study. Potential benefits of the Carillon Mitral Contour System include, but may not be limited to, the following: a decrease in your mitral regurgitation, an increase in your ability to exercise, and overall improvement in your symptoms of heart failure.

Taking part in the study can have these cons:
- You may experience the side effects or adverse effects of an angiographic

procedure, as described.
- There may be some discomfort from the measurements during the study. For example: taking a blood sample can be a little painful. Or you could get a bruise as a result.
- Taking part in the study will cost you extra time.
- You have to comply with the study agreements.

This research study involves exposure to a small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The additional effective dose from this study procedure is about 22 mSv. The dose from this study is comparable to that received from several computer tomography X-ray (CT) and nuclear medicine procedures. The benefits from the study should be weighed against the possible detrimental effects of radiation, including increased risk of fatal cancer. In this particular study, the risk is moderate, and the estimated risk of such harm is about 1 in 900. For comparison, this risk is about 225 times lower than the cancer mortality rate in the general population of about one case in every four people and theoretically is approximately equivalent to 11 years of background radiation. If you are pregnant, you SHOULD NOT participate in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Moderate-to-severe non-primary Mitral Regurgitation (as assessed by qualitative, semi-quantitative and/or quantitative echocardiographic assessment in the setting of all of the following:
a. Severe left atrial (LA) dilatation as defined by at least two (2) of the following:
i. LA area * 41cm2
ii. Indexed LA volume > 48mL/m2
iii. LA diameter * 52 mm for men and * 46 mm for women
b. Preserved left ventricular contractility (Left Ventricular Ejection Fraction *50% by Simpson*s biplane technique)
c. No more than mild left ventricular dilatation as defined by:
i. LV diastolic volume/BSA (mL/m2) <90 mL/m2 for men and <71 mL/m2 for women
ii. LV systolic volume/BSA (mL/m2) <39 mL/m2 for men and <33 mL/m2 for women
2. New York Heart Association (NYHA) Class II, III or ambulatory IV heart failure
3. Stable heart failure medication regimen for at least 30 days prior to index procedure including antihypertensives and/or diuretics to achieve controlled BP (< 140 mmHg systolic) and adequate heart rate control (<100 bpm resting HR)
4. Patient deemed appropriate candidate for transcatheter mitral valve repair by the local multidisciplinary heart team
5. Subject meets anatomic screening criteria as determined by angiographic screening at the time of the index procedure to ensure that implant can be sized and placed in accordance with the Instructions for Use
6. Female subjects of child-bearing potential must have a negative serum *HCG test
7. Age * 18 years old
8. The subject has read the informed consent, agrees to comply with the requirements, and has signed the informed consent to participate in the study

Exclusion criteria

1. Hospitalization in past three (3) months due to myocardial infarction, coronary artery bypass graft surgery, and/or unstable angina
2. Evidence of transient ischemic attack or stroke within three (3) months prior to intervention

3. Percutaneous coronary intervention in the last 30 days
4. Subjects expected to require any cardiac surgery, including surgery for coronary artery disease or for pulmonic, aortic, or tricuspid valve disease within one (1) year
5. Subjects expected to require any percutaneous coronary intervention within 30 days of the index procedure.
6. Pre-existing device (e.g., pacing lead) in coronary sinus (CS) / great cardiac vein (GCV), or anticipated need for cardiac resynchronization therapy (CRT) within twelve (12) months
7. Presence of a coronary artery stent under the CS / GCV in the implant target zone
8. Presence of left atrial appendage (LAA) clot.
9. Presence of primary renal dysfunction or significantly compromised renal function as reflected by a serum creatinine > 2.2 mg/dL (194.5 *mol/L) OR estimated Glomerular Filtration Rate (eGFR) < 30 ml/min
10. Poorly controlled atrial fibrillation or flutter, with poor ventricular rate control (> 100 bpm resting HR), or other poorly controlled symptomatic brady- or tachy-arrhythmias
11. Uncontrolled hypertension (BP > 180 mmHg systolic and/or >105 mmHg diastolic) or hypotension (BP < 90 mmHg systolic) at baseline
12. Presence of severe mitral annular calcification
13. Prior mitral valve surgery
14. Presence of a mechanical mitral heart valve, mitral bio-prosthetic valve or mitral annuloplasty ring
15. Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
16. Active endocarditis
17. Severe aortic stenosis (aortic valve area <1.0 cm2) or severe aortic regurgitation
18. Infiltrative cardiomyopathies (e.g., amyloidosis, hemochromatosis, sarcoidosis)
19. Hypertrophic cardiomyopathy, restrictive cardiomyopathy, constrictive pericarditis, or any other structural heart disease causing heart failure other than atrial functional mitral regurgitation
20. Subjects with echocardiographic documentation of non-compaction cardiomyopathy with associated hypercontractility of the cardiac structures supporting the mitral annulus
21. Hemodynamic instability requiring inotropic support or mechanical heart circulatory support
22. Active infections requiring current antibiotic therapy
23. Severe right ventricular failure or severe tricuspid regurgitation
24. History of bleeding diathesis or coagulopathy, or subject who refuses blood transfusions
25. Significant organic mitral valve pathology (e.g., moderate or severe myxomatous degeneration, with or without mitral leaflet prolapse, rheumatic disease, full or partial chordal rupture)
26. Allergy to contrast dye that cannot be pre-medicated
27. Pregnant or planning pregnancy within next 12 months.

28. Chronic severe pathology limiting survival to less than 12-months in the judgement of the investigator
29. Anticipated need of left ventricular assist device within twelve (12) months
30. Currently participating or has participated in another investigational study where the study primary endpoint was not reached at the time of screening
31. Patient requires emergent/emergency treatment for mitral regurgitation

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	25
Type:	Anticipated

Medical products/devices used

Generic name:	Carillon Mitral Contour System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	26-07-2021
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04529928
CCMO	NL76947.099.21