Transcatheter Mitral Valve Repair With MitraClip® Therapy

What You and Your Family Should Know
About This Minimally Invasive Procedure

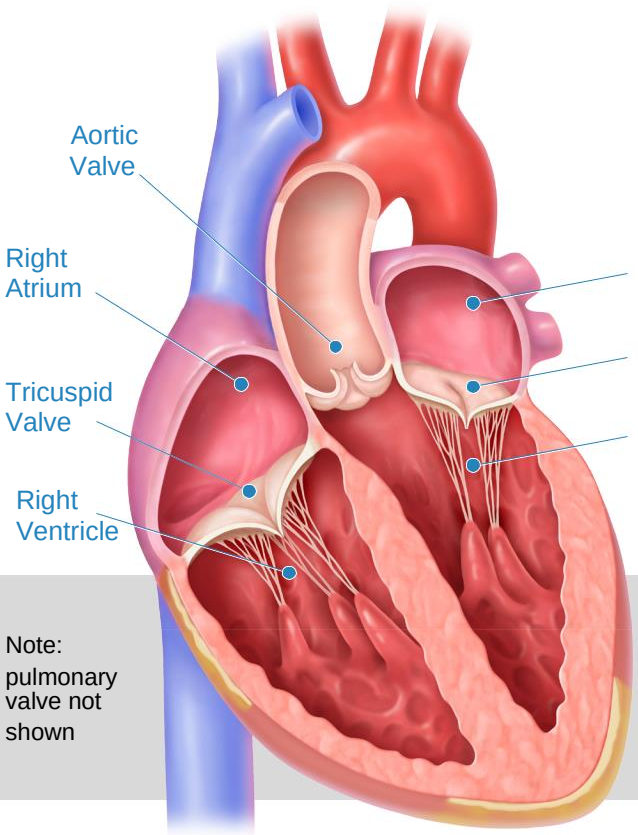
This guide provides you and your family with information about your heart and mitral regurgitation, a condition where the mitral valve does not seal completely and allows blood to leak backward inside the heart. Patients who have this problem and who are too sick to undergo open-heart surgery can also learn about a less-invasive treatment option called transcatheter mitral valve repair (TMVR) with MitraClip® therapy.

You can read an overview of the steps involved in TMVR and expectations for patients before, during, and after the TMVR procedure. It is important that you discuss your treatment options with your doctor, who will determine if this procedure is appropriate for you.

How Your Heart Works

Your heart beats thousands of times per day, pumping dozens of gallons of blood each hour. It pumps blood through your lungs to replenish it with oxygen, and then pumps the oxygen-rich blood back out to the rest of your body.

The heart has four chambers; the upper two chambers are called atria (each one is an atrium), and the lower two are called ventricles. There are four valves that function as the doorways between these chambers (see figure below). Each valve is made of thin but strong flaps of tissue called leaflets. The valves open in one direction to let blood pass from one chamber to the next, closing quickly between heartbeats so blood does not flow backward.



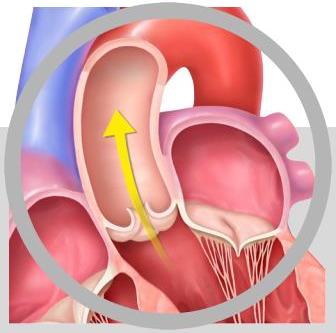
Note: pulmonary valve not shown

The Mitral Valve and Mitral Regurgitation

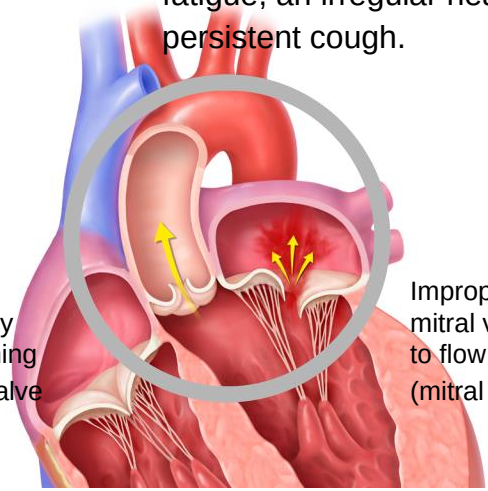
The mitral valve is the valve between the left atrium and left ventricle of your heart.

In a normally functioning mitral valve, blood flows in a single direction between the left atrium and left ventricle. However, when your mitral valve's two leaflets (or flaps) do not close properly, some blood flows backward through the valve back into the left atrium. This is called mitral regurgitation.

To make up for the backflow of blood, your left ventricle must pump harder to keep blood flowing through your body. This strain can enlarge and weaken your heart. Over time, the extra burden on your heart and lungs may lead to congestive heart failure, a condition that occurs when your heart can't pump enough blood to meet the needs of your body. This may cause you to have shortness of breath, fatigue, an irregular heartbeat, or a persistent cough.

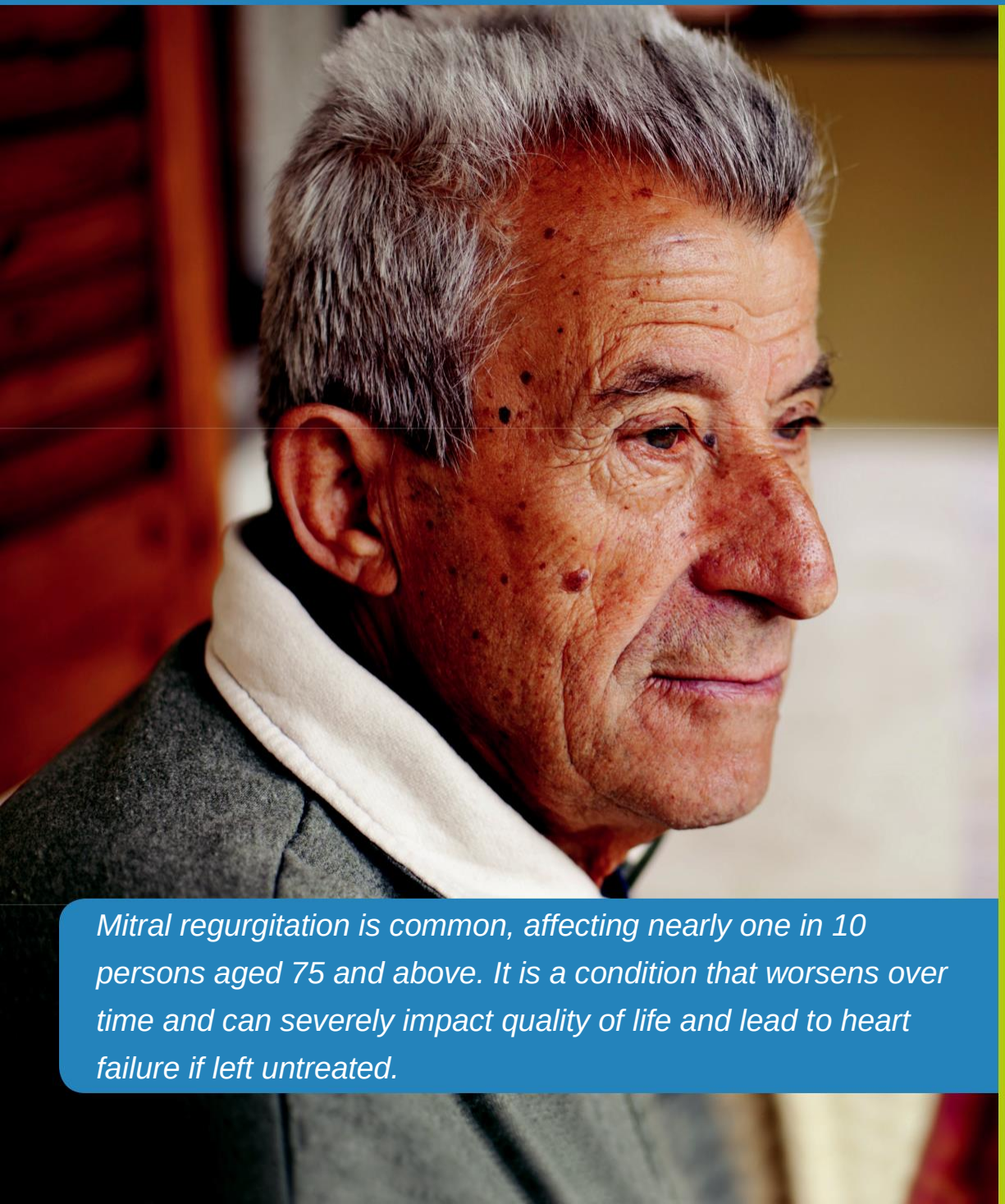


Normally functioning mitral valve



Improperly functioning mitral valve allowing blood to flow back into left atrium (mitral regurgitation)

What Is Significant, Symptomatic, Degenerative Mitral Regurgitation?



Mitral regurgitation is common, affecting nearly one in 10 persons aged 75 and above. It is a condition that worsens over time and can severely impact quality of life and lead to heart failure if left untreated.

One type of mitral regurgitation is called degenerative mitral regurgitation (also called primary or organic). It can be related to age, a birth defect, underlying heart disease, or a history of rheumatic fever.

To determine if you have degenerative mitral regurgitation and to assess the function and condition of your heart and mitral valve, your doctor may perform diagnostic tests including:

- Listening to your heart with a stethoscope
- Using an echocardiogram (ultrasound) to get a close look at your heart and mitral valve
- Taking a chest x-ray to see the size and shape of your heart and evaluate your lungs
- Evaluating you for symptoms of congestive heart failure (such as shortness of breath or fatigue) or other related heart conditions

If you have degenerative mitral regurgitation that allows a very large amount of blood to backflow in your heart, your doctor may diagnose you as having degenerative mitral regurgitation that is moderate to severe. If you also have symptoms of congestive heart failure or other related heart conditions, your disease may be classified as significant, symptomatic, degenerative mitral regurgitation.

Treatment Options for Significant, Symptomatic, Degenerative Mitral Regurgitation

Treatment for your degenerative mitral regurgitation depends on how severe it is and how sick you are. Your doctor may prescribe medications that reduce symptoms, such as fluid buildup in the lungs. However, these medications only treat the symptoms and do not address the underlying problem with your mitral valve that is causing your disease.

Degenerative mitral regurgitation itself can only be treated in two ways: mitral valve surgery or transcatheter mitral valve repair.

Mitral Valve Surgery

Mitral valve surgery is the preferred treatment for degenerative mitral regurgitation. There are two types of surgery to treat degenerative mitral regurgitation: mitral valve repair or mitral valve replacement. Repair of the natural valve is preferred over replacement. If the valve cannot be repaired, it is replaced with an artificial valve.

While open-heart surgery is an effective treatment for degenerative mitral regurgitation, your doctor may suggest an alternative treatment due to your age, advanced heart failure, or other serious medical conditions. Patients who are too sick for open-heart surgery (also referred to as being at “prohibitive risk” for surgery) may be candidates for transcatheter mitral valve repair, a less-invasive treatment option.

Patients who are too sick for open-heart surgery may be candidates for a less-invasive procedure called transcatheter mitral valve repair.

Transcatheter Mitral Valve Repair

Transcatheter mitral valve repair (TMVR) is a minimally invasive procedure that may be an option for patients with degenerative mitral regurgitation who are too sick for surgery. Unlike surgery, this procedure does not require opening the chest and temporarily stopping the heart.

Doctors place a thin tube (called a catheter) through your skin and into a large vein in your leg to reach your heart. A clip is then implanted onto the center of your mitral valve. This reduces mitral regurgitation, and the valve continues to open and close on either side of the clip, allowing blood to flow through.

To determine whether you are able to withstand mitral valve surgery or if you are a potential candidate for TMVR, you will be evaluated by a heart team. This team includes a cardiac surgeon and a cardiologist, who will review your medical history and perform a variety of tests.

The TMVR procedure is not right for everyone. In certain cases, the risks of the procedure may outweigh the benefits.

About the Transcatheter Mitral Valve Repair Procedure

Who Should Not Have the Procedure?

The MitraClip® device should not be used in patients who:

- Cannot tolerate medications that thin the blood or prevent blood clots from forming
- Have an active infection or inflammation of the mitral valve
- Have mitral valve disease as a result of rheumatic fever
- Have a blood clot in their heart or in the vessels that carry blood from the lower body to the heart

Your doctor should discuss with you if you have any of these issues that would prevent you from having the MitraClip® procedure. An evaluation of your heart will also confirm if your heart valve anatomy would allow for successful placement of the device.

How Should You Prepare for Your Procedure?

In the days before your procedure, it is important that you:

- Take all your prescribed medications
- Tell your doctor if you are taking any other medications
- Make sure your doctor knows of any allergies you have
- Follow all instructions given to you by your doctor or nurse

What Is the MitraClip® Device and How Is It Used?

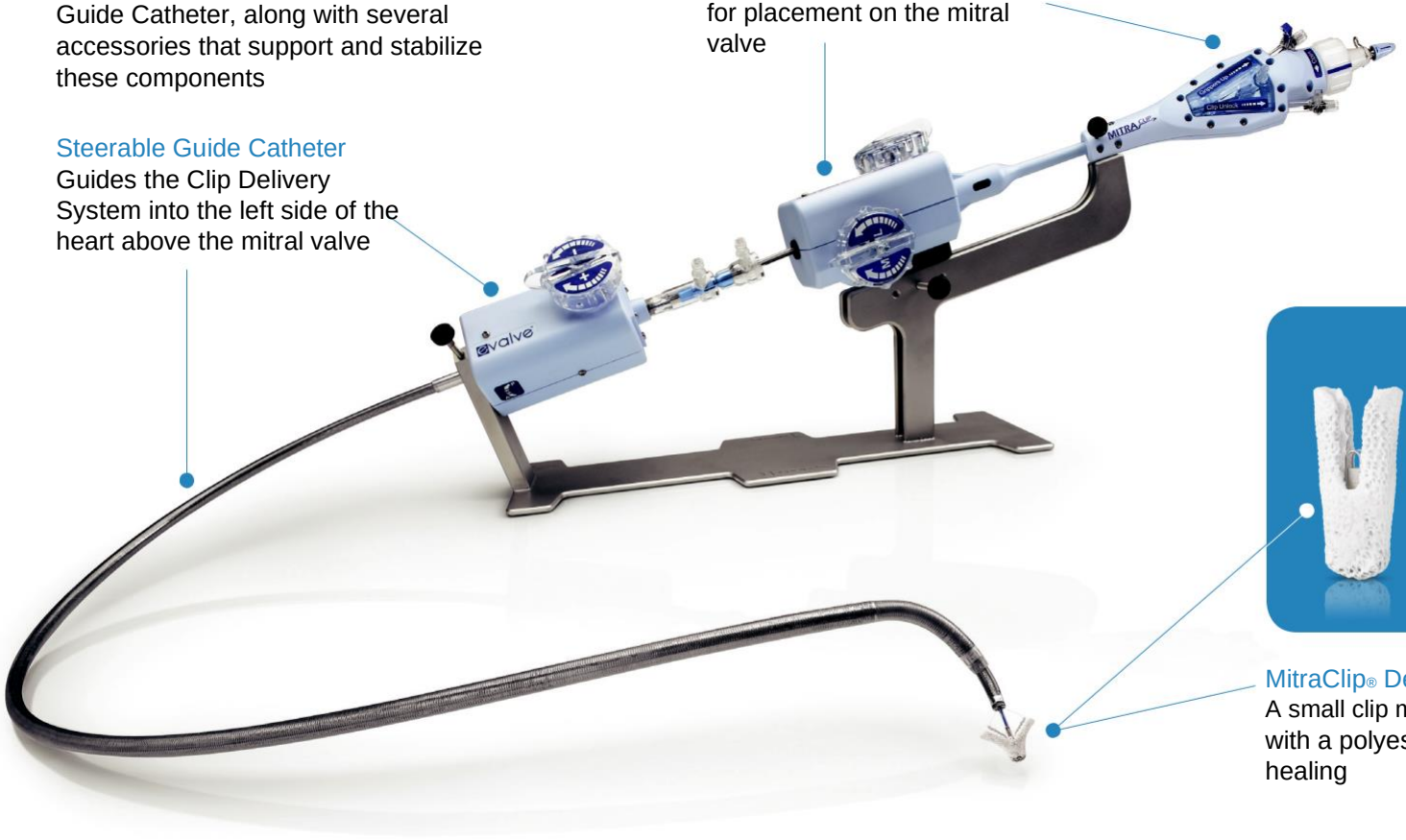
The MitraClip® device is a small clip (see figure below) that is implanted on your mitral valve. The clip is inserted through a catheter, without the need to temporarily stop your heart.

The MitraClip® device treats mitral regurgitation by closing the center of the mitral valve. The valve continues to open and close on either side of the clip. This allows blood to flow on both sides of the clip into the left ventricle while reducing or preventing blood from flowing back into the left atrium.

The MitraClip® System consists of the Clip Delivery System and the Steerable Guide Catheter, along with several accessories that support and stabilize these components

Clip Delivery System
Delivers the MitraClip® device for placement on the mitral valve

Steerable Guide Catheter
Guides the Clip Delivery System into the left side of the heart above the mitral valve



MitraClip® Device
A small clip made of metal and covered with a polyester fabric to promote healing

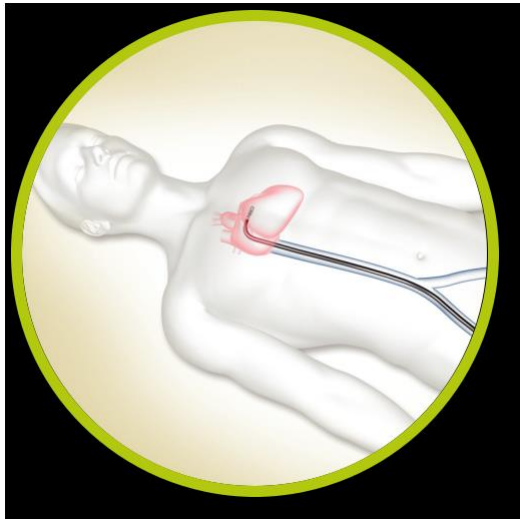
About the Transcatheter Mitral Valve Repair Procedure *(continued)*

What Will Happen During Your Procedure?

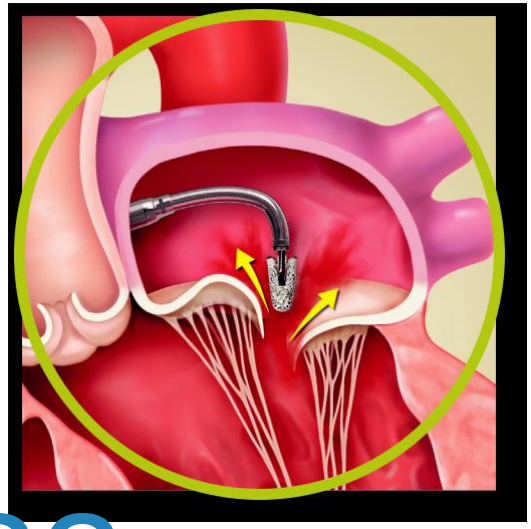
Your procedure will most likely be performed in a specialized room at the hospital called a “cath lab.” During the procedure, you will be placed under general anesthesia to put you in a deep sleep, and a ventilator will be used to help you breathe. Your doctor will use fluoroscopy (a type of X-ray that delivers radiation to you) and echocardiography (a type of ultrasound) during the procedure to visualize your heart.

On average, the time required to perform the TMVR procedure is between 3 to 4 hours. However, the length of the procedure can vary due to differences in anatomy.

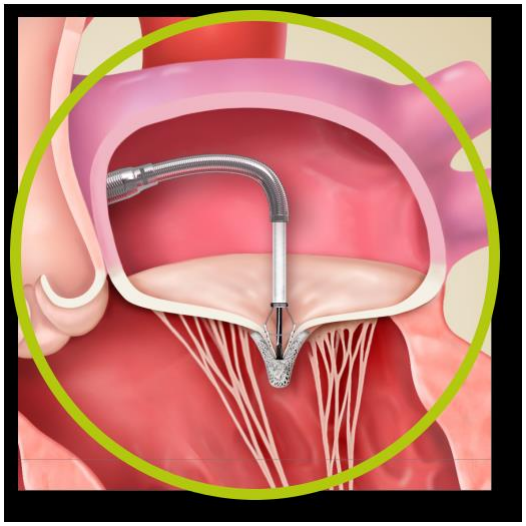
The following steps provide a general overview of the TMVR procedure with the MitraClip® device—your experience may be different. Your doctor will explain the procedure to you and can provide you with specific details and answer any questions you may have.



1 Your cardiologist will make a small incision in your upper leg, where a guide catheter (a hollow, flexible tube slightly larger than the diameter of a pencil) will be inserted through a vein to reach your heart.



22 The MitraClip® device, which is attached to the end of a clip delivery system, will be guided to your mitral valve through the catheter. Your cardiologist will use imaging equipment to guide the placement of the clip.



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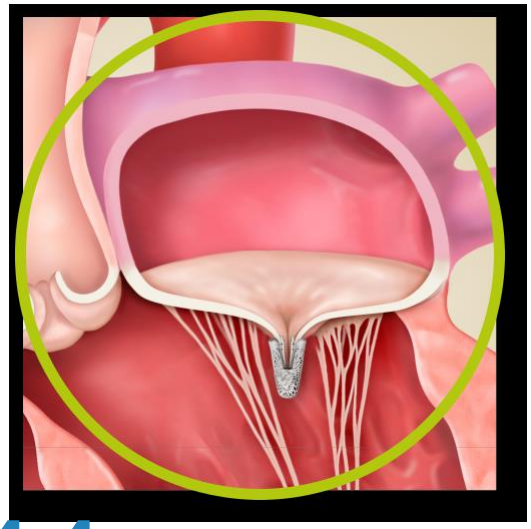
Your cardiologist will implant the clip at the appropriate position on your mitral valve. The clip will grasp the mitral valve leaflets to close the center of the mitral valve and reduce mitral regurgitation.

Your cardiologist will then perform tests to confirm that the clip is working properly. In some cases, your cardiologist may implant a second clip for further reduction of mitral regurgitation.



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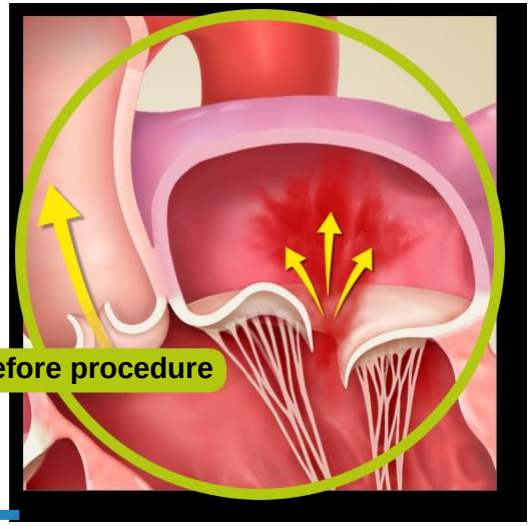
Once the clip is in place and working properly, it will be disconnected from the clip delivery system. The clip delivery system and the guide catheter will then be removed from your body and the incision in your leg will be closed.



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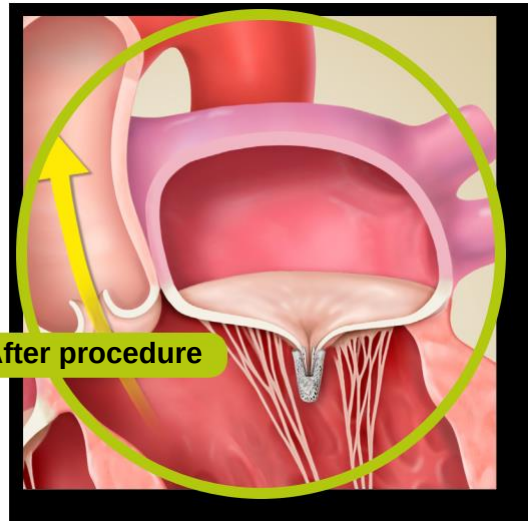
The implanted clip will become a permanent part of your heart, allowing your mitral valve to close more tightly and reduce the backward flow of blood.



About the Transcatheter Mitral Valve Repair Procedure *(continued)*

What Will Happen After Your Procedure?

Your hospital stay following the procedure will likely range from one to five days, depending on your recovery and overall health. You should experience relief from your symptoms of mitral regurgitation soon after your procedure. Most patients will not need special assistance at home following discharge from the hospital, outside of ongoing needs for any unrelated health conditions.

While in the hospital, you will be closely monitored and your doctor will perform various tests to evaluate your heart function. You may be prescribed blood-thinning medications to help reduce the risk of developing a dangerous blood clot after the procedure. Your doctor or nurse will give you instructions about your medications before you leave the hospital.

You will be discharged to the care of your cardiologist or family doctor, who will ask you to return for follow-up visits. It is important that you keep all appointments for follow-up care and follow your doctor's instructions. If you do not carefully follow your doctor's instructions, you will greatly increase your risk of complications and the possibility that your mitral regurgitation will return. **If you experience any pain or other problems that may be related to your procedure or the return of any symptoms related to mitral regurgitation, notify your doctor immediately.**

After being discharged from the hospital, it is important that you:

- Limit strenuous physical activity (such as jogging or activities that cause breath-holding, grunting, or straining such as lifting heavy objects) for at least 30 days, or longer if your doctor thinks it is necessary
- Carefully follow your doctor's instructions regarding medications you need to take, especially if blood-thinning drugs are prescribed
- Call your doctor if you cannot keep taking your medications because of side effects, such as rash, bleeding, or upset stomach
- Notify your doctor before any medical or dental procedure; you may need to be prescribed antibiotics to avoid potential infection

Failure to follow these instructions will increase your risk for complications and may result in the return of your mitral regurgitation or cause the MitraClip® device to not work properly. Notify your doctor immediately if you experience any pain or other problems that may be related to your procedure or the return of any symptoms related to mitral regurgitation.

Clinical Information on Benefits and Risks

The safety and effectiveness of the MitraClip® device were studied in 127 patients with degenerative mitral regurgitation (DMR) who were considered to be too sick for open-heart surgery due to their age, advanced heart failure, or other serious medical conditions. This group of “prohibitive risk” patients (referred to as the PR DMR Cohort) was part of two large studies of the MitraClip® device in a broader patient population.

Overall, more than 1,200 patients in the United States have been treated with the MitraClip® device in several clinical studies, with over 900 patients who have been followed for one year.

What Are the Possible Benefits and Risks 30 Days After the Procedure?

Clinical data from DMR patients treated with the MitraClip® device demonstrate an immediate reduction of mitral regurgitation. You should experience improvement in your symptoms of mitral regurgitation and quality of life soon after your procedure.

As with any treatment, there are risks associated with MitraClip® therapy. Your doctor will discuss how the risks of MitraClip® therapy compare with other options that may be available to you.

The most common serious risks observed within 30 days of the MitraClip® procedure in patients enrolled in the PR DMR Cohort include:

- **Death from any cause** occurred in 8 out of 127 patients (6.3%)
- **Stroke** occurred in 3 out of 127 patients (2.4%). Stroke is a condition where lack of blood flow to the brain causes rapid loss of brain function
- **Ventilation longer than 48 hours** occurred in 4 out of 127 patients (3.1%). This means that the use of a ventilator was required more than two days to help a patient breathe
- **Major vascular complications** occurred in 7 out of 127 patients (5.5%). Examples include a hematoma (large blood clot under the skin) or damage to the artery and surrounding veins where the catheter was inserted that requires surgical repair
- **Bleeding events** occurred in 16 out of 127 patients (12.6%). This refers to a loss of blood related to the procedure that required a blood transfusion of 2 or more units

Clinical Information on Benefits and Risks *(continued)*

What Are the Possible Benefits and Risks 1 Year After the Procedure?

Benefits

Patients with DMR studied one year after the MitraClip® procedure continued to experience reduced mitral regurgitation, resulting in the following benefits:

- **Improved heart function**: reducing mitral regurgitation decreases the burden placed on the heart, resulting in a reversal of heart enlargement and allowing the heart to pump blood more efficiently
- **Improvement in symptoms**: patients experienced significant improvement in how they feel during physical activity as measured by the New York Heart Association (NYHA) system, which places patients in 1 of 4 classes
  - 88% of patients had improved by at least 1 class and 36% had improved by at least 2 classes
- **Fewer hospitalizations**: a 73% reduction in hospitalizations for heart failure was observed in the year following the MitraClip® procedure compared to the year prior
- **Improved quality of life**: patients experienced meaningful improvements in physical and mental function as measured by a standardized quality of life survey

Risks

The most common serious risks observed within 1 year of the MitraClip® procedure in patients enrolled in the PR DMR Cohort include:

- **Death from any cause** occurred in 30 out of 127 patients (23.6%)
- **Stroke** occurred in 3 out of 127 patients (2.4%). Stroke is a condition where lack of blood flow to the brain causes rapid loss of brain function
- **Ventilation longer than 48 hours** occurred in 6 out of 127 patients (4.7%). This means that the use of a ventilator was required more than two days to help a patient breathe
- **Major vascular complications** occurred in 9 out of 127 patients (7.1%). Examples include a hematoma (large blood clot under the skin) or damage to the artery and surrounding veins where the catheter was inserted that requires surgical repair
- **Bleeding events** occurred in 25 out of 127 patients (19.7%). This refers to a loss of blood related to the procedure that required a blood transfusion of 2 or more units
- **Kidney failure** occurred in 5 out of 127 patients (3.9%)
- **Gastrointestinal complications** occurred in 3 out 127 patients (2.4%)
- **Septicimia** occurred in 6 out of 127 patients (4.7%). Septicemia is a serious infection of the blood often caused by bacteria

The following table is a summary of the clinical risks observed within 30 days and 1 year of the MitraClip® procedure in patients enrolled in the PR DMR Cohort.

Risks Within 30 Days and 1 Year After the MitraClip® Procedure		
	30 Days	1 Year
Death (from any cause)	6.3% (8 out of 127 patients)	23.6% (30 out of 127 patients)
Myocardial infarction (heart attack)	0.8% (1 out of 127 patients)	0.8% (1 out of 127 patients)
Re-operation for failed surgical repair	0	0
Heart surgery required for complications	0.8% (1 out of 127 patients)	0.8% (1 out of 127 patients)
Stroke	2.4% (3 out of 127 patients)	2.4% (3 out of 127 patients)
Kidney failure	1.6% (2 out of 127 patients)	3.9% (5 out of 127 patients)
Deep wound infection	0	0
Ventilation longer than 48 hours	3.1% (4 out of 127 patients)	4.7% (6 out of 127 patients)
Gastrointestinal complication requiring surgery	0.8% (1 out of 127 patients)	2.4% (3 out of 127 patients)
New onset of permanent atrial brillation (fast, irregular heart rhythm)	0	0
Septicemia (serious blood infection)	0	4.7% (6 out of 127 patients)
Bleeding event (transfusion of 2 or more units of blood)	12.6% (16 out of 127 patients)	19.7% (25 out of 127 patients)
Major vascular complications	5.5% (7 out of 127 patients)	7.1% (9 out of 127 patients)

Warnings and Precautions

Warnings

- **MitraClip® therapy should only be used in patients with significant, symptomatic, degenerative mitral regurgitation who are too sick for mitral valve surgery.**
- MitraClip® therapy is intended to reduce mitral regurgitation. If mitral regurgitation is not reduced enough, you may not get the full treatment benefits of reduced hospitalizations and improvement in heart failure symptoms and quality of life expected from MitraClip® therapy.

Precautions

- MitraClip® therapy should only be used in patients considered to be too sick for surgery. This 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, based on the presence of one or more surgical risk factors.
- The major clinical benefits of MitraClip® therapy are reduction of mitral regurgitation, resulting in reduced hospitalizations and improvement in heart failure symptoms and quality of life.
  No benefit on how long a patient survives following MitraClip® therapy has been demonstrated.
- How long the MitraClip® device will last is unknown at this time.
- The first MitraClip® device was implanted in 2003 and laboratory testing supports durability of the device over a period of 15 years. Regular medical follow-up is essential to evaluate how the MitraClip® device is performing. Notify your doctor immediately if you experience the return of any symptoms related to mitral regurgitation.
- Patients who have undergone MitraClip® therapy should receive prophylactic antibiotic therapy before any medical or dental procedure to minimize the possibility of infection.
- **The safety and effectiveness of MitraClip® therapy have not been established in patients who have functional (also called secondary) mitral regurgitation.**
- The safety and effectiveness of MitraClip® therapy have not been established in patients who have specific mitral valve anatomy that may interfere with proper placement and positioning of the MitraClip® device:
  - A mitral valve opening that is too small
  - Calcified mitral valve leaflets
  - A cleft of the mitral valve leaflet
  - A leaflet flail width or leaflet flail gap that is too large
- MitraClip® therapy has not been tested in pregnant women or children or infants, and the device may not work for these patients.