THE ALT-FLOW II TRIAL

ALT-FLOW II Trial for evaluation of the Edwards APTURE transcatheter shunt system

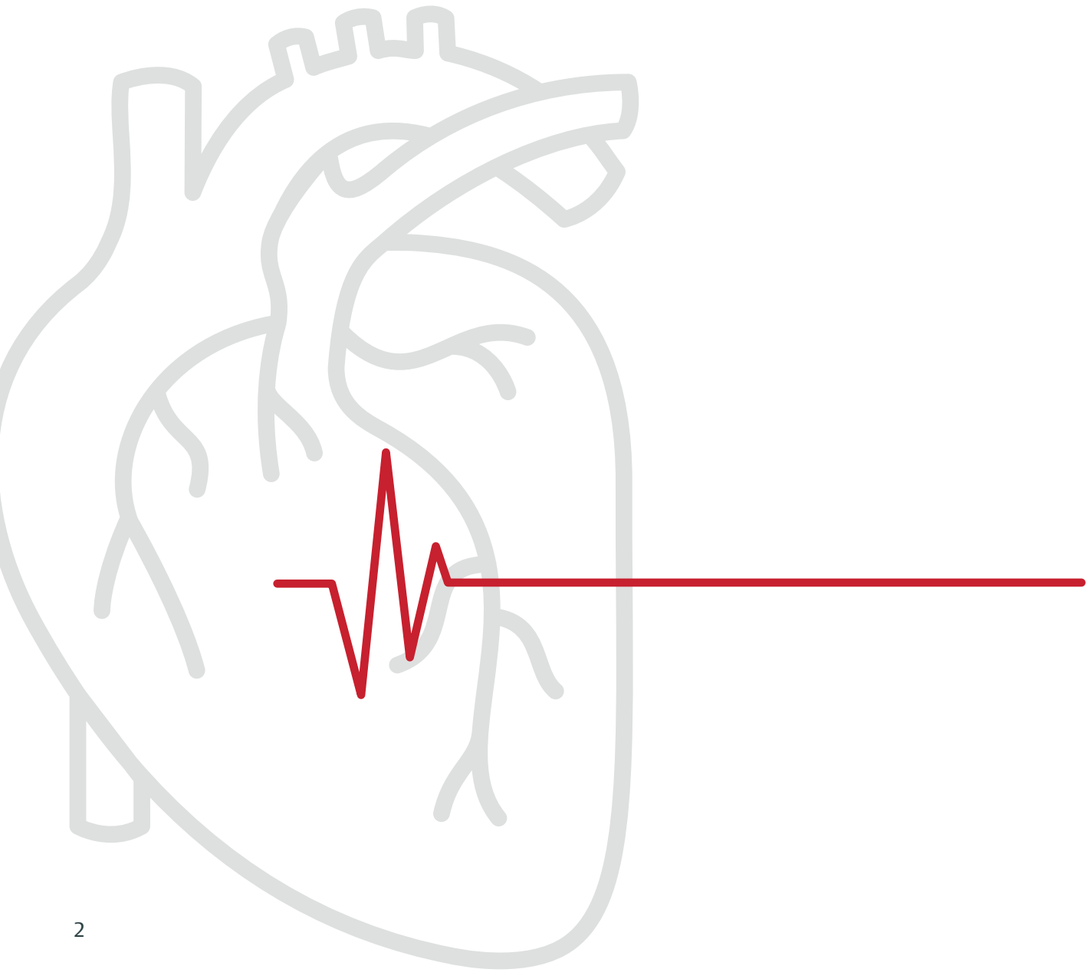
Understanding heart failure

Heart Failure (HF) is a chronic condition that occurs when the heart muscle is not working as well as it should.

If the heart becomes damaged by diseases such as high blood pressure, coronary artery disease, or diabetes, the heart may gradually change its shape over time. This may result in the heart wall becoming either thick and stiff or thin and weak. Heart failure can cause a variety of symptoms, including shortness of breath, fatigue, swelling in the legs and ankles, and difficulty exercising.

Ejection Fraction (EF) is one element of a heart failure diagnosis. This measures how much blood the heart can pump out with each beat, and it is described as a percentage. A normal ejection fraction is typically between 50% to 70%.

There are different kinds of heart failure, including heart failure with preserved ejection fraction (HFpEF) and heart failure with mildly reduced ejection fraction (HFmrEF). You may hear these pronounced as “heff-peff” or “heff-mereff”.

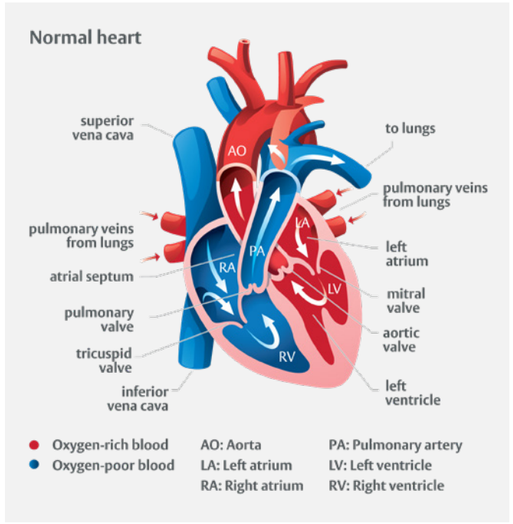


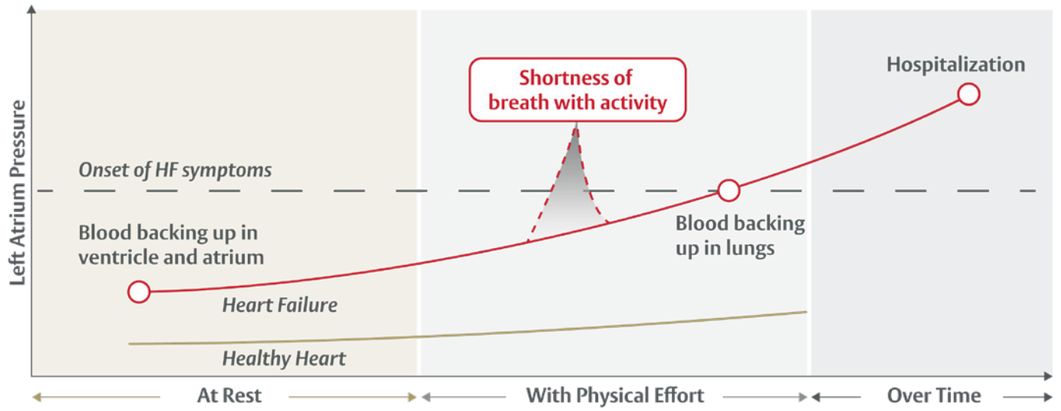
Understanding HFpEF and HFmrEF

HFpEF and HFmrEF are types of heart failure where the heart muscle becomes stiff and does not relax and fill properly. As a result, even though the EF remains close to normal, the amount of blood pumped with each beat may be smaller than normal.

The top of your heart is called the atrium, and the bottom of the heart is called the ventricle. In a healthy heart, oxygenated blood moves from your lungs to the left atrium. From there, blood enters the left ventricle where it is then pumped out to your body.

The left ventricle of a HFpEF heart is thick, making it hard for the ventricle to relax and fill with blood. When the ventricle cannot fill with blood, the blood may back up into the left atrium. This extra blood volume increases the pressure in the left atrium resulting in the atrium stretching and becoming stiff, reducing the ability of the left atrium to contract and relax properly. As the left atrial pressure increases, blood begins to back up into the lungs and may lead to shortness of breath and other heart failure symptoms.





Adapted from: Adamson PB. Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: new insights from continuous monitoring devices. Curr Heart Fail Rep. 2009 Dec;6(4):287-92.

The ALT-FLOW II Trial

Your provider thinks you may be a candidate for the ALT-FLOW II trial.

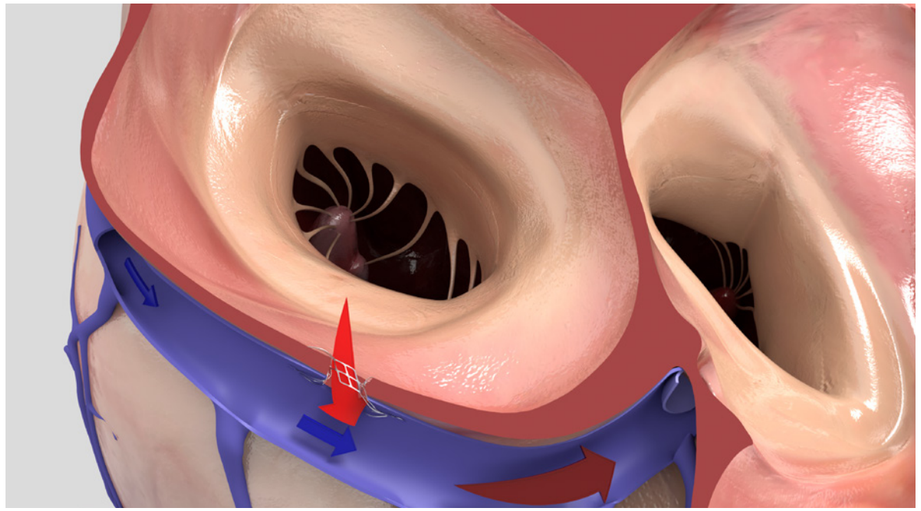
This trial is primarily designed to further test the safety and performance of an investigational device called the Edwards APTURE transcatheter shunt. The APTURE shunt is a metal device that is placed in the heart, creating a channel to allow a small amount of blood to flow from the left atrium to the right atrium via the coronary sinus. The device is designed to lessen some of the pressure that has built up in the left atrium. It is currently unknown whether this or other shunts provide reductions in shortness of breath, severe episodes of heart failure, or the risk of death in patients like you. Your participation in the trial will begin to provide the information needed to answer these questions.

You may be eligible for this trial if:

You are experiencing symptoms related to heart failure with high pressures in the heart

You experience symptoms despite being on medications as recommended by optimal guideline-directed medical therapy

Your provider will perform a series of tests to see if you meet certain criteria for this trial.



The Edwards APTURE transcatheter shunt system

Am I guaranteed to receive the APTURE shunt if I qualify for enrollment?

- When enrolling in a randomized trial you will be assigned by chance to one of two groups; each group undergoes different treatments. Neither the researcher nor the participants choose which group you are assigned to.
- One group will receive the APTURE shunt implant, the other group will not receive the APTURE shunt implant. The procedure for both groups will include general anesthesia followed by a contrast injection in your heart to see if your anatomy is suitable for the APTURE shunt. After this, you will be randomized to receive the APTURE shunt or not.
- After the procedure, both groups will continue to receive guideline-directed medical therapy and monitoring for heart failure symptoms. You, your family, and your providers managing your care after the procedure will not know if you've received the implant. This is an important part of this trial and will provide the most reliable evidence regarding whether treatment of people with the APTURE shunt provides any additional benefits.
- If you are randomized to the sham-control group, you may be eligible to receive the APTURE shunt when:
  - the last patient reaches their 6-month follow-up
  - you've completed your one-year follow up visit
  - FDA approves control patients receiving the investigational device

Screening tests and follow-up visits

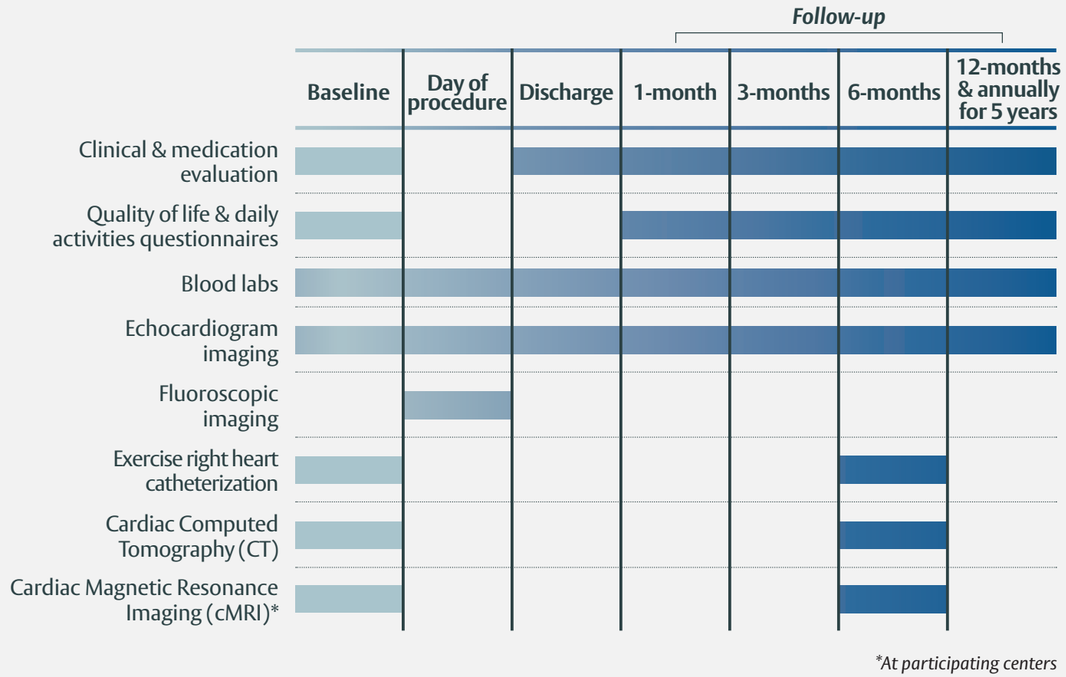
The ALT-FLOW II trial involves comprehensive screening before you can enroll. Testing includes:

- Exercise right heart catheterization
- Cardiac imaging including echocardiogram and Computer Tomography (CT)
- Blood work
- Questionnaires and surveys
- Other medical tests*

*See ALT-FLOW II Trial consent form for a current and complete list of required screening tests for this trial.

After the procedure, there are follow-up visits where some of the same tests will be repeated to assess safety and response to the therapy.

These assessments will be scheduled to occur at: 1 month, 3 months, 6 months, and annually for 5 years.



*At participating centers

FPO – See Pocket Flap on Page 9

Edwards APTURE transcatheter shunt

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.

THE ALT-FLOW II TRIAL

Questions to ask your Provider

- √ What are the risks and benefits of enrolling in a randomized clinical trial?
- √ Do you think enrolling in the ALT-FLOW II trial is an option for me?
- √ If I qualify for the ALT-FLOW II trial, will there be any changes to the medications I take now?
- √ What are the potential risks of participating in the ALT-FLOW II trial?
- √ What do the researchers hope to learn about doing this research trial?
- √ What if I'm admitted to the hospital once I'm enrolled in the trial, how will my care providers know if I've received the implant or not?
- √ Why is it important that I do not know if I've received the implant or not?
- √ Will not knowing which group I am in be important for my healthcare?
- √ How will I let my other doctors know that I am participating in this trial?
- √ Will patients randomized to the sham control be able to access the device?

Learn more about the ALT-FLOW II Trial

www.edwards.com/TheALTFLOWIITrial

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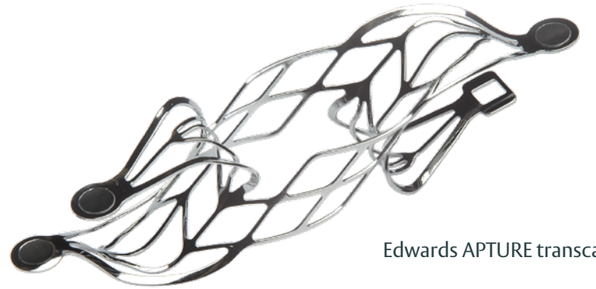
Pocket Flap



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Glue Flap