Heart Failure
New Treatments & Developments

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Interventional Cardiology

Disclosures

- I am a consultant for/work with medical companies
  - Abbott, Medtronic, CHF Solutions, Respicardia, Relypsa
- I have received grants and travel funds from companies
  - Abbott, Abiomed, Syncardia

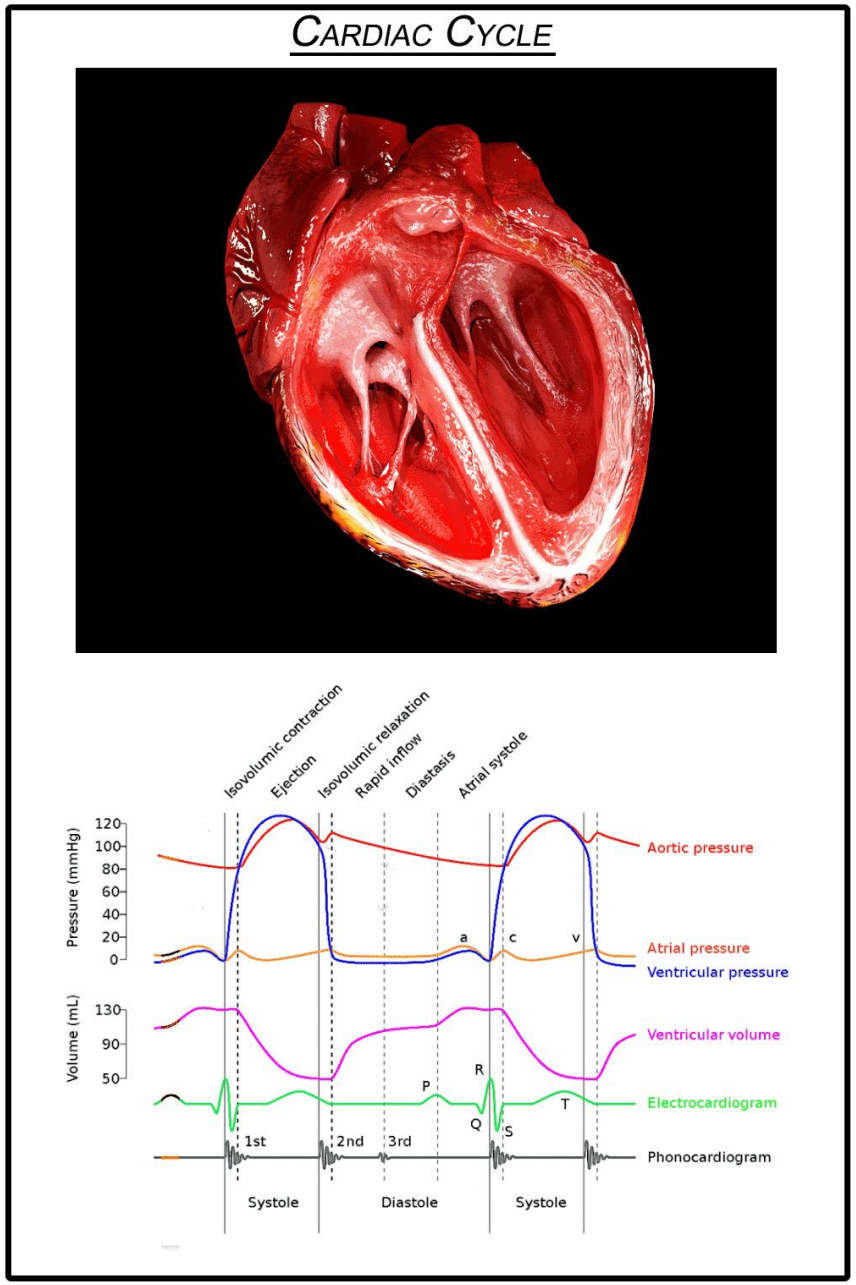
- I will not be promoting specific company products preferentially
- But I will be talking about newer therapies, experimental therapies, and ideas not yet approved for “prime time”

Review of basic physiology in heart failure

- HF is the result of cardiac dysfunction leading to inadequate forward blood flow to the rest of the body
- HF can have many causes
- The causes and resultant effects determine the best therapies

The Cardiac Cycle

- Two phases of heart function:
  - Systole (squeezing)
  - Diastole (filling)
- Squeezing function described by ejection fraction (EF)
- Dysfunction can occur in either phase
  - HF with reduced ejection fraction (HFrEF or systolic HF)
  - HF with preserved ejection fraction (HFpEF or diastolic HF)



Upload.wikimedia.org

Heart Failure Review

Inadequate forward flow can cause:

- Fatigue
- Low blood pressure
- Changes in other organs (such as kidneys)
- Back up of pressure/fluid
  - Shortness of breath
  - Swelling
  - Changes in appetite

Overview of current treatment options

- More proven therapies exist for HFrEF
  - Beta-blockers
  - ACEi/ARBs/ARNIs
  - Pacemakers/defibrillators
- Some therapies are used for both HFrEF and HFpEF
  - Diuretics (“water pills”, e.g. lasix)
  - Spironolactone

Other Important Factors

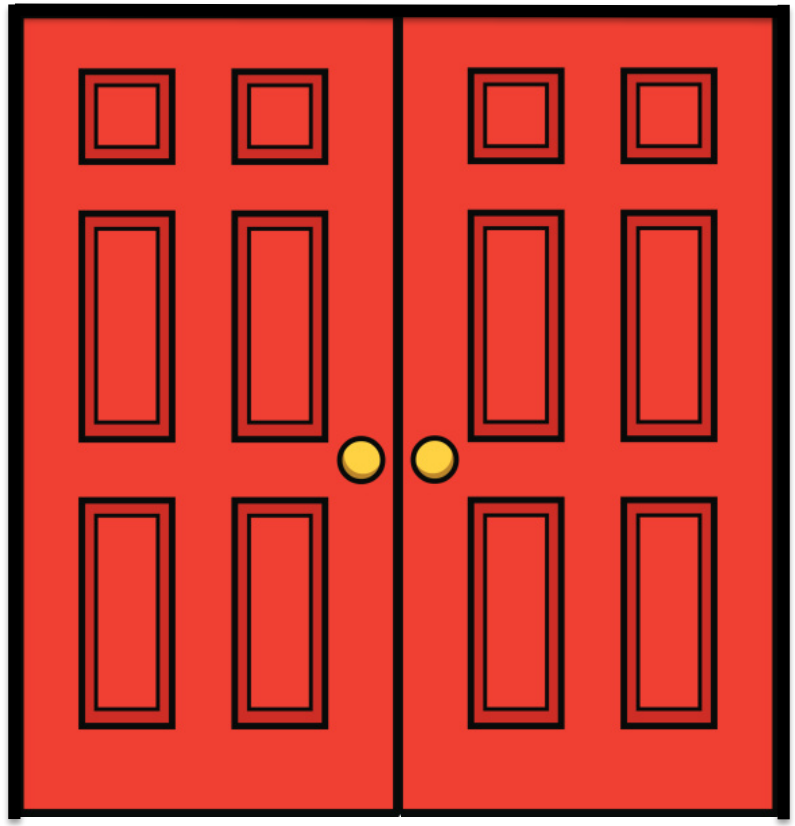
- Concurrent heart conditions
  - Rhythm disturbances
  - Valve disorders
  - Coronary Artery Disease
- Concurrent medical conditions
  - Diabetes
  - High blood pressure
  - Sleep Apnea

So What's New?

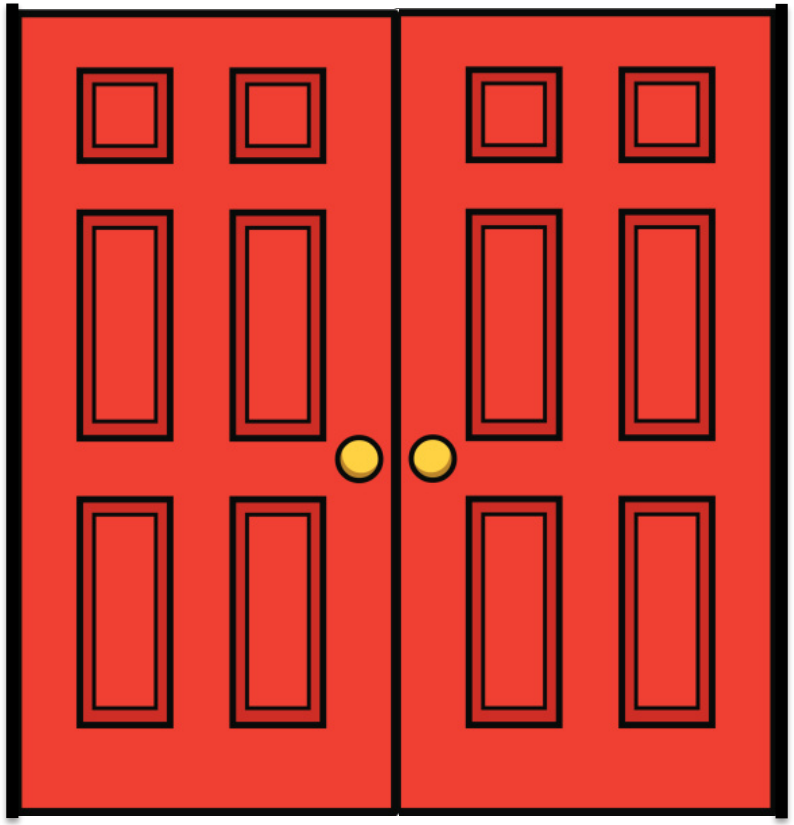
Valve Disease: Mitral Regurgitation

In many cases of HFrEF, MR can result from changes in the heart's shape

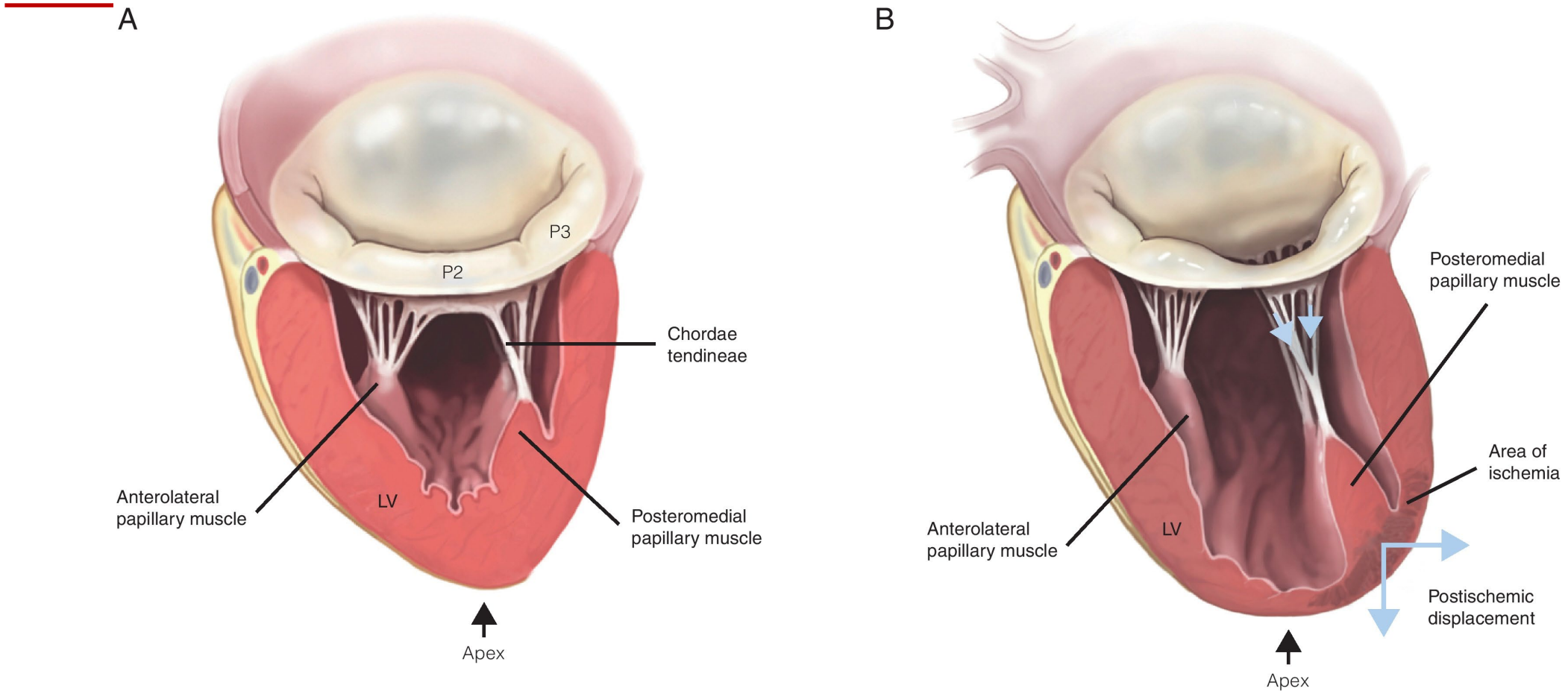
- Functional MR
- Think of a door frame stretching



Functional MR



Functional MR



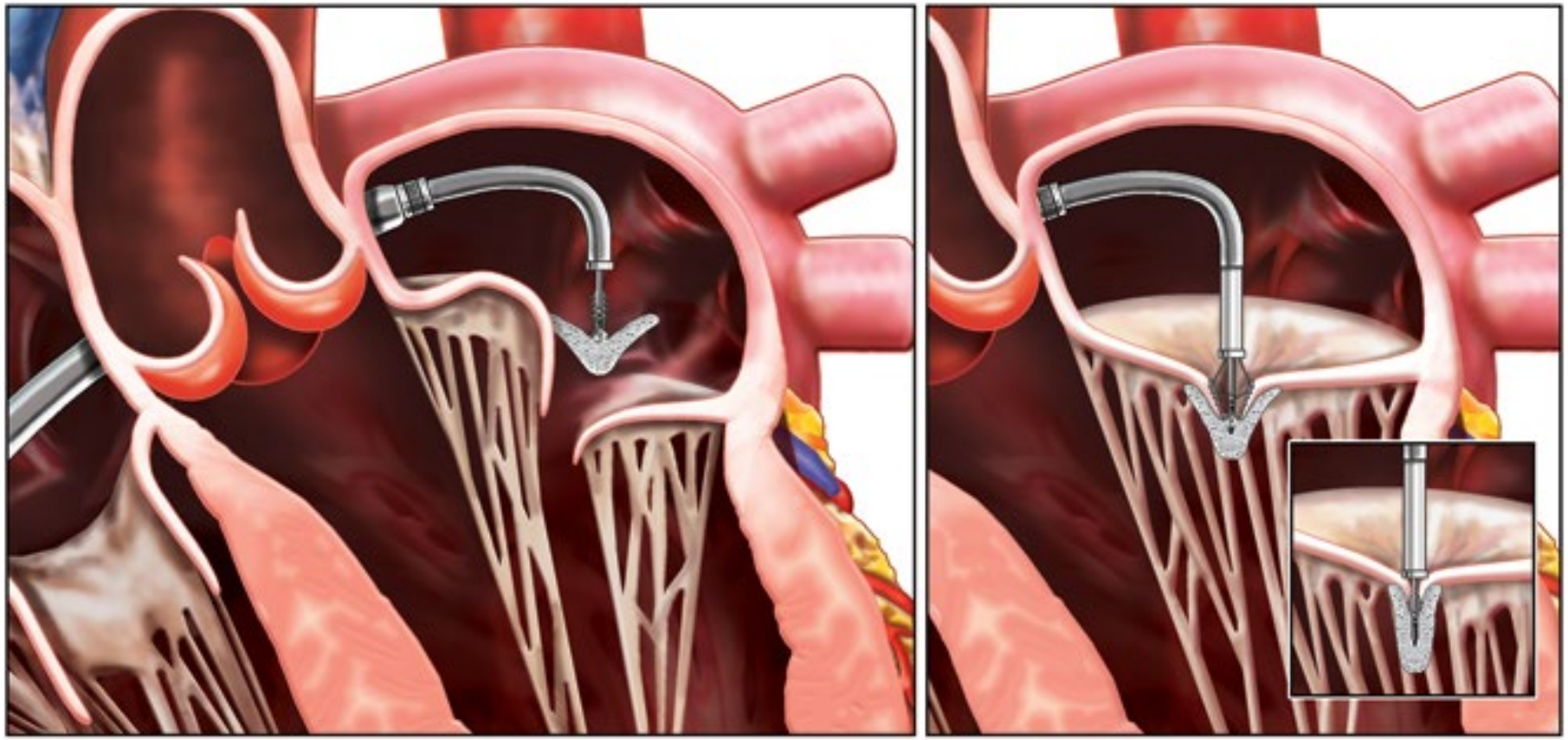
Castillo JG, *et al*, *Rev Esp Cardiol* 2011

Treating Functional MR

- Surgical options
  - Repair
  - Replacement
- Minimally invasive “repair”
  - MitraClip*
  - Percutaneous ring annuloplasty*
- Transcatheter MV Replacement*

*under investigation

MitraClip



Feldman T, Young A, *JACC* 2014

Results of the COAPT Trial (MitraClip)

In highly-selected HFrEF patients, MitraClip:

- Reduced the risk of HF hospitalization
- Improved survival
- Also improved size of the heart

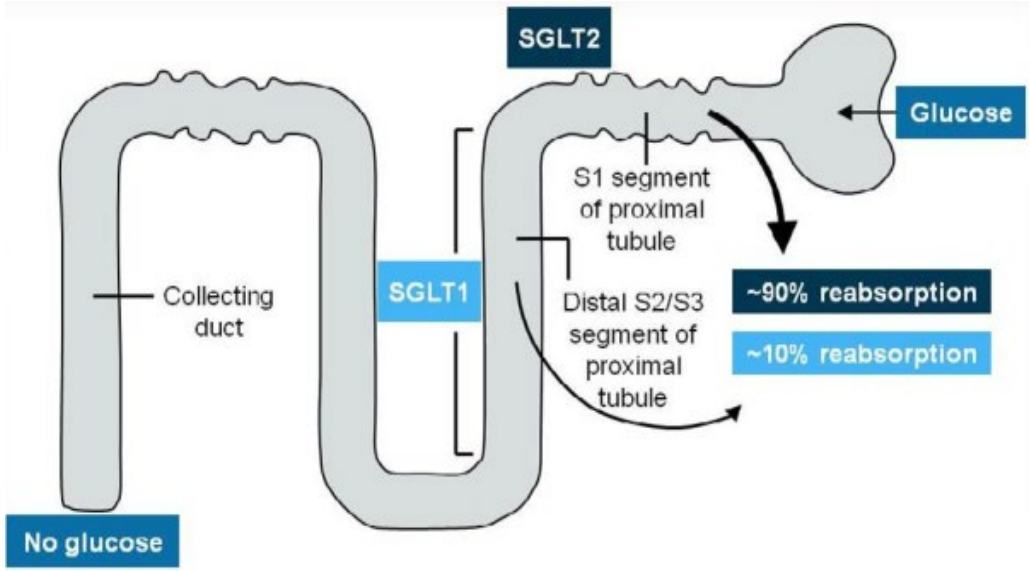
Stone GW, et al, *NEJM* 2018

Other FMR treatment options

- Minimally invasive MV replacement options (tMVR)
- Several designs being tested

Diabetes: SGLT2 Inhibitors

- Sodium-glucose Cotransporter-2 Inhibitors (SGLT2-I's)
- Approved lower blood sugar in patients with T2DM
  - Canagliflozin (Invokana)
  - Dapagliflozin (Farxiga)
  - Empagliflozin (Jardiance)
  - Sotagliflozin (*under development)
- Prevent glucose reabsorption in kidney
  - Urinate out excess sugar



www.fda.gov
www.diabetesincontrol.com

SGLT Inhibitors and Heart Disease

In T2DM patients at high risk for cardiac complications, SGLT2 inhibitors:

- Did not reduce the risk of heart attack
- But reduced the rate of cardiac hospitalization
  - The benefit seemed to focus on HF hospitalizations
  - Unclear if benefit was for HFrEF, HFpEF, or both
- Improved cardiac survival

Zinman B, *et al*, *NEJM* 2015

SGLT2 Inhibitors and Heart Disease

- Some data is inconclusive

- In the DECLARE-TIMI 58 study, did not improve overall heart outcomes in 17,000+ patients
  - However, rate of HF hospitalization appeared to be lower with SLGT2 inhibitor
  - But the trial was not specifically designed to prove this hypothesis

Wiviott SD, *et al*, *NEJM* 2019

SGLT2 Inhibitors and Heart Failure

- May improve HF outcomes by providing better fluid balance
  - May work equally well for HFrEF and HFpEF?
- May improve the heart's efficiency and energy use

Hallow KM, et al, *Diabetes, Obesity, and Therapeutics* 2017
Marten P, *et al*, *Current Treat Option in Cardiovasc Med* 2017

SGLT2 Inhibitors and Heart Failure

Summary of Current Data

- Early studies suggest a benefit in HF patients
  - Primarily by reducing risk of hospitalization
- Hypothetical additional HF benefits have been proposed
- May benefit both HFrEF and HFpEF patients
- No definitive proof exists
  - But is being studied currently

SGLT Inhibitors

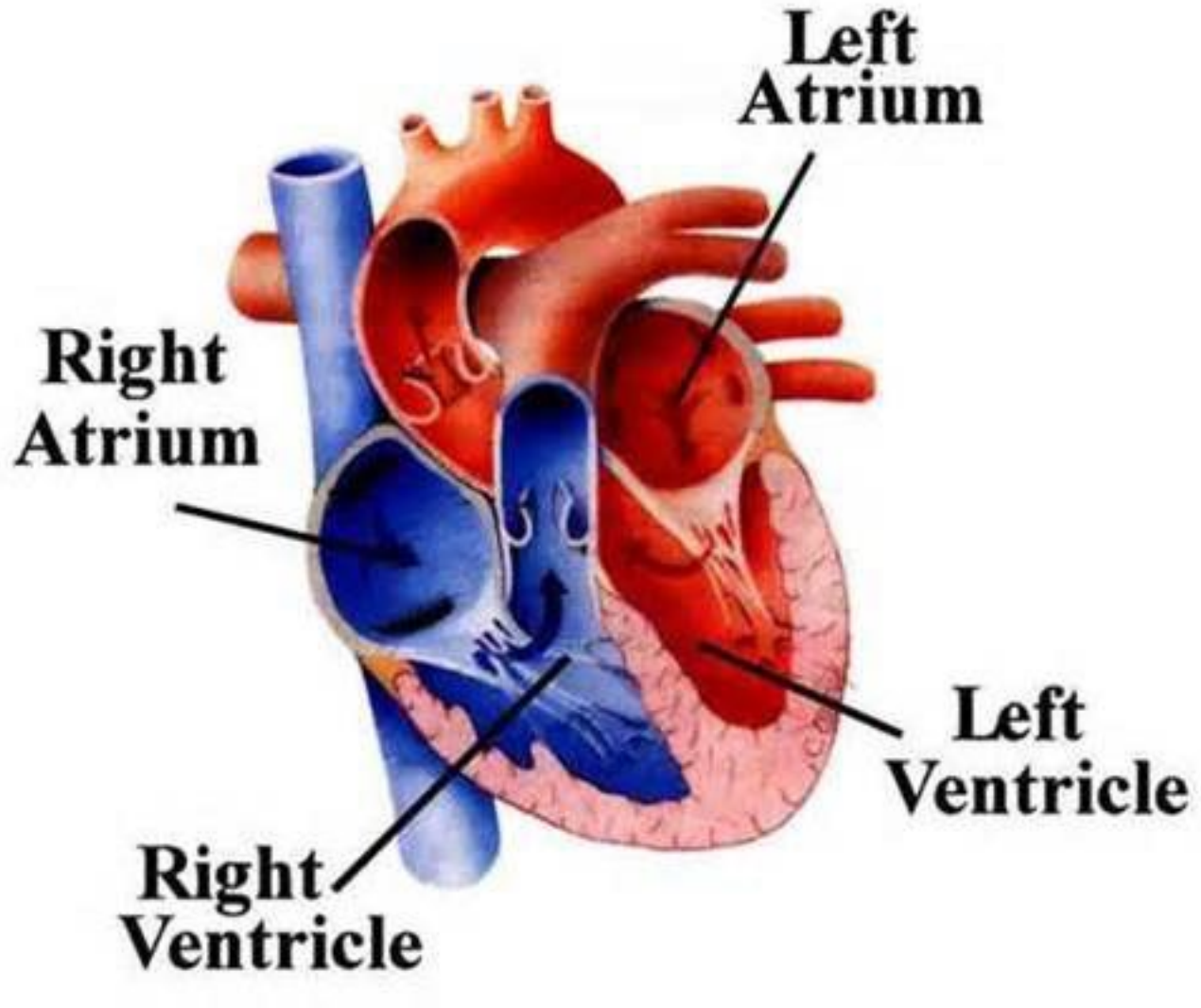
Final Thoughts

- Multiple agents are FDA approved
- At present, may be appropriate for patients with T2DM
- SGLT2 inhibitors are associate with increased genital infection risk

Devices for HFpEF

- Some HFpEF patients can have significant symptoms
  - Especially with activity
  - But do not improve significantly with standards medications
- For HFrEF patients, we have been able to use devices
- But relatively few devices exist for HFpEF

Exercise Symptoms in HFpEF

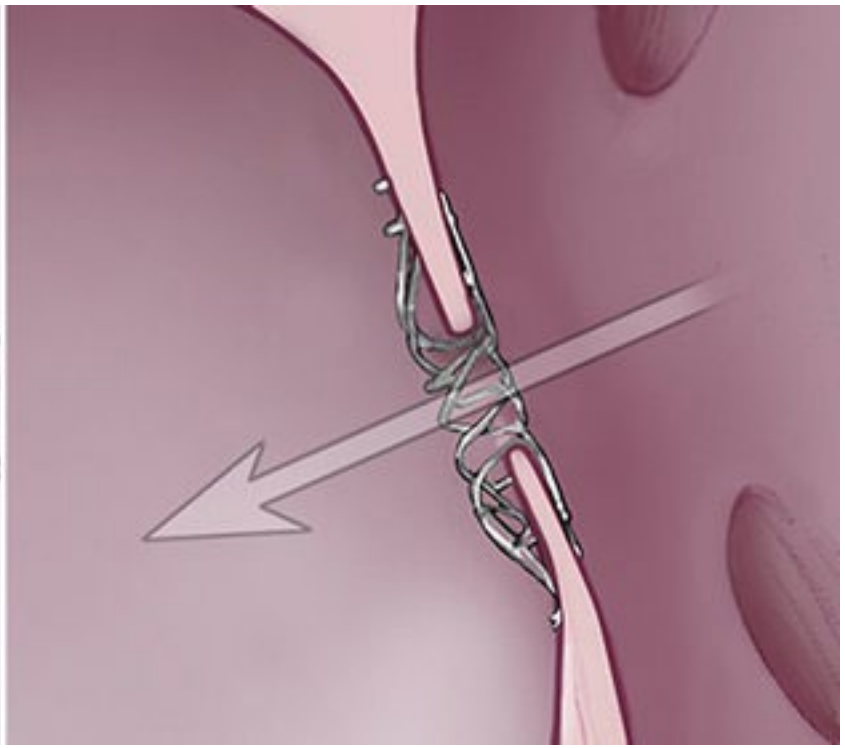


Help May Be On the Way

Can we create a pressure release valve to improve symptoms?

Intra-atrial Shunt Devices (IASDs)

- Strategically placed hole in the heart to prevent excessive pressure build up
- Minimally invasive procedure
- Device placed in the wall between the right and left atria



Nijenhuis V, *et al Netherlands Heart J* 2017

IASDs

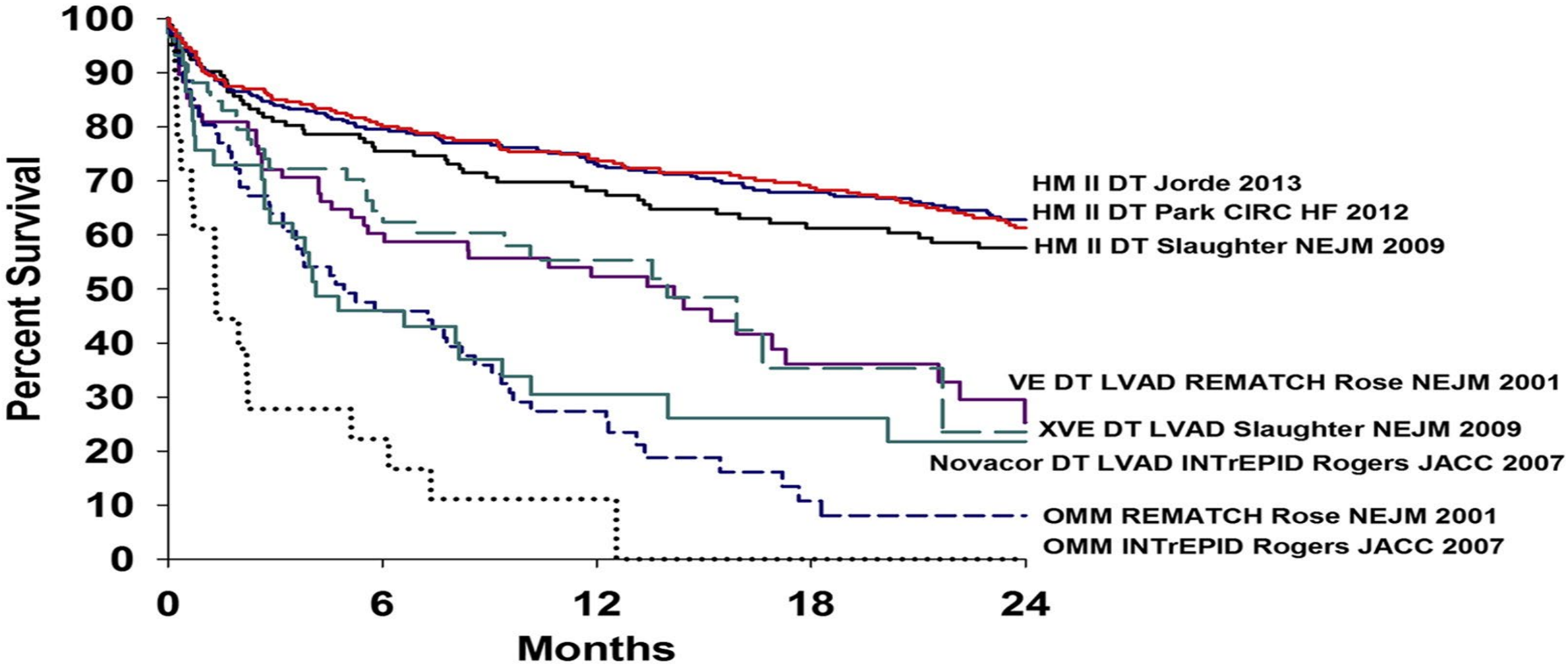
- Very 1st patient in the US enrolled at Ohio State
- In an early trial, IASD resulted in better heart pressures with exercise
- Follow up studies are being done to prove benefit
- Additional designs of IASD devices are being evaluated

Feldman T, *et al*, *Circ* 2017

Advanced Heart Failure

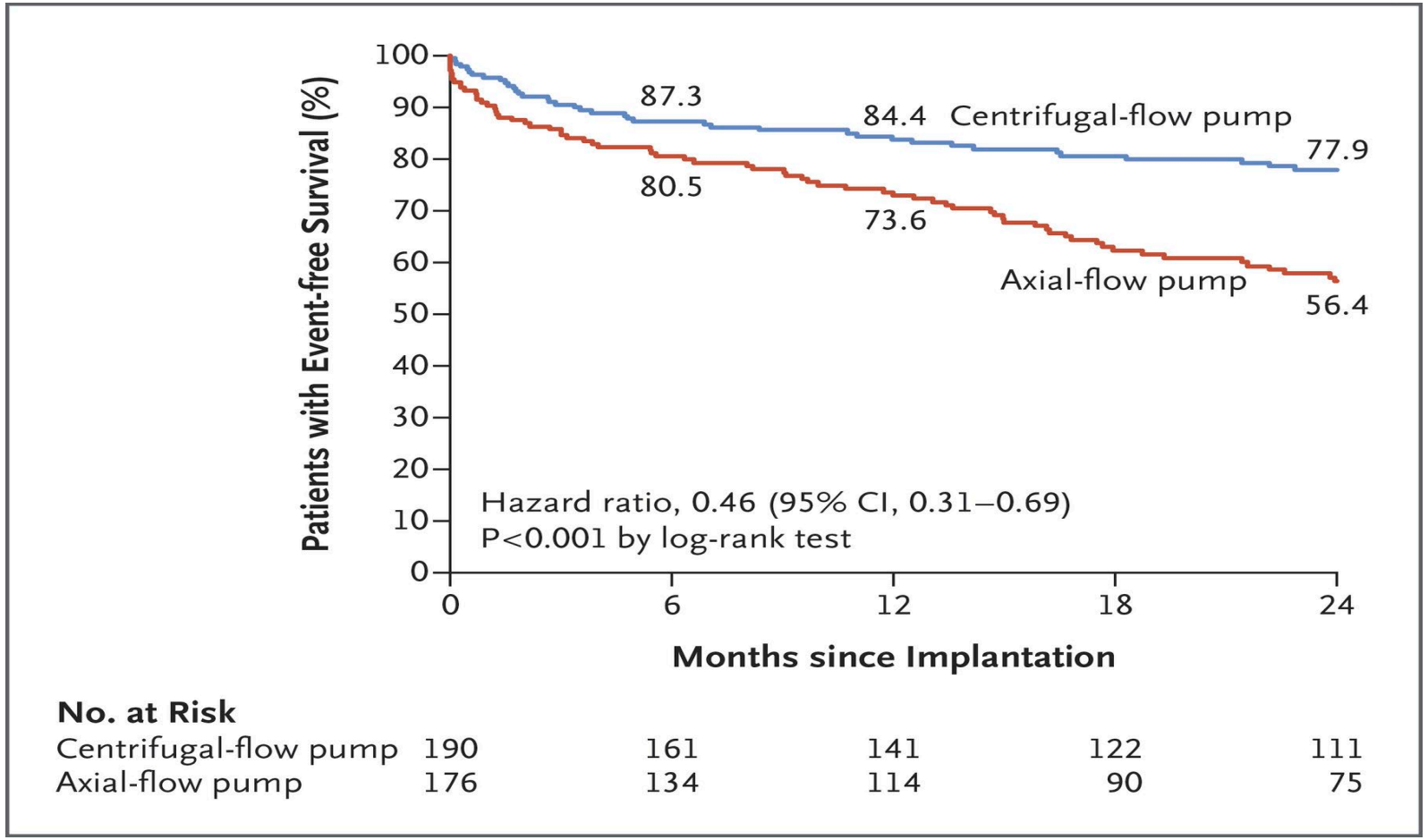
- Left Ventricular Assist Devices (LVADs) can treat advanced heart failure
- First pump created in the 1960s
- First “modern” pump available in 2001
- Several generations of pumps since then
- Each generation of pump results in better outcomes

VAD Survival Through Eras



Jorde *et al*, *JACC* 2014

Current Generation Results



Mehra MR, *et al*, *NEJM* 2017

Thetis and Achilles (A. Borel, 18th Century) – Galleria Nazionale, Parma, Italy

Achilles' Heel of VADs?

FILVAS

Fully

Implantable

Left

Ventricular

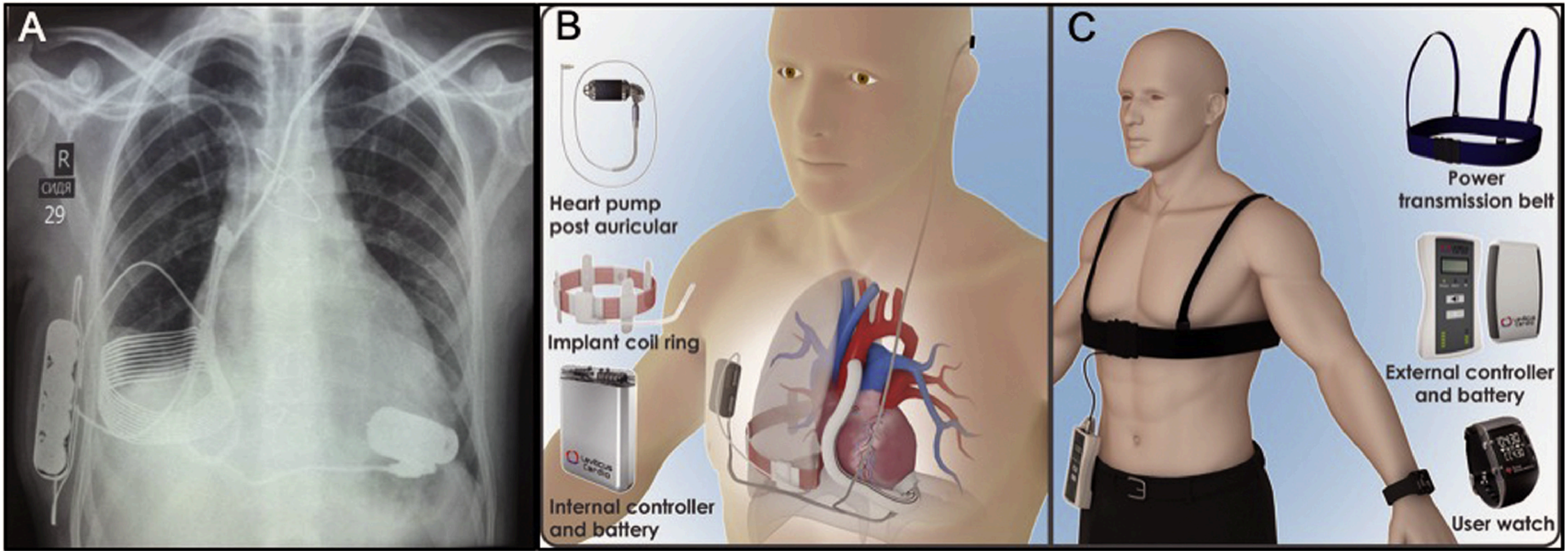
Assist

System

Challenges with FILVAS

- Miniaturizing the controller
- Balancing battery size with battery charge length
- Maximizing battery life cycles
- Minimize energy use of VAD
- Using biologically compatible materials/protection

First FILVAS Use



Pya U, *et al*, *JHLT* 2019

FILVAS

First 2 patients implanted in Astana, Khazakhstan in 2018

HF has many new and exciting developments coming!

Thank You