



# ***Cardiovascular Center Onze Lieve Vrouwziekenhuis, Aalst, Belgium***

***To share the clinical expertise  
To provide the teaching across all professional levels  
To collaborate in cutting edge and clinically oriented research***

***Marc Vanderheyden***

# Cardiovascular Center

## MISSION and VISION

$$E = mc^2$$

### ***Patients Care (c)***

- *Excellence is a standard*
- *Personal interaction between the patient and “his” doctor*
- *Expertise in all fields of modern cardiology*

### ***Teaching***

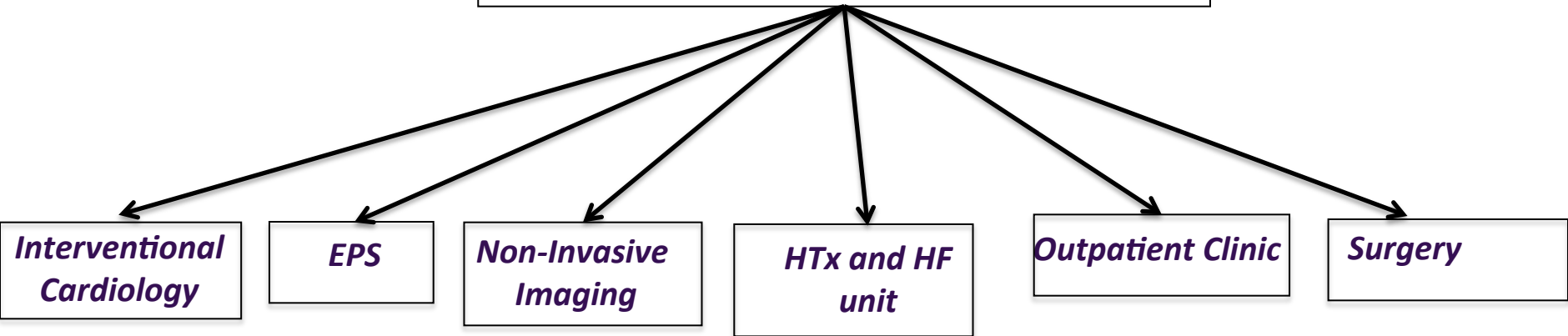
- *Students, nurses, referring physicians, patients*
- *Trainees in cardiology*
- *International clinical research fellows*
- *National and international workshops and courses*

### ***Research (m)***

- *Equally important as patient care*
- *Direct application for the benefit of our patients*

***Academic, non-university, supra-regional “center of excellence”***

# ***Clinical Care and Research PLATFORM***



## **Coronary/vascular:**

- Coronary physiology (FFR)
- Platelet biology/function
- Early CAD detection
- Translational program (biomarkers: ischemia, vulnerability)

## **Structural/myocardial:**

- Translational program in HF and hypertrophy
- HF reversibility
- Cardiac resynchronization
- Valvular heart disease (FMR, AS)
- Stem cell program
- Telemonitoring

## **Arrhythmias:**

- Atrial fibrillation/arrhythmia surgery
- Registries
- Telemonitoring

# ***Networking: Academia Belgica***

***First Joint Meeting October 2010***  
***Second Joint Meeting June 2012***  
***Third Joint Meeting September 2014***



# Contagious Enthusiasm Commitment

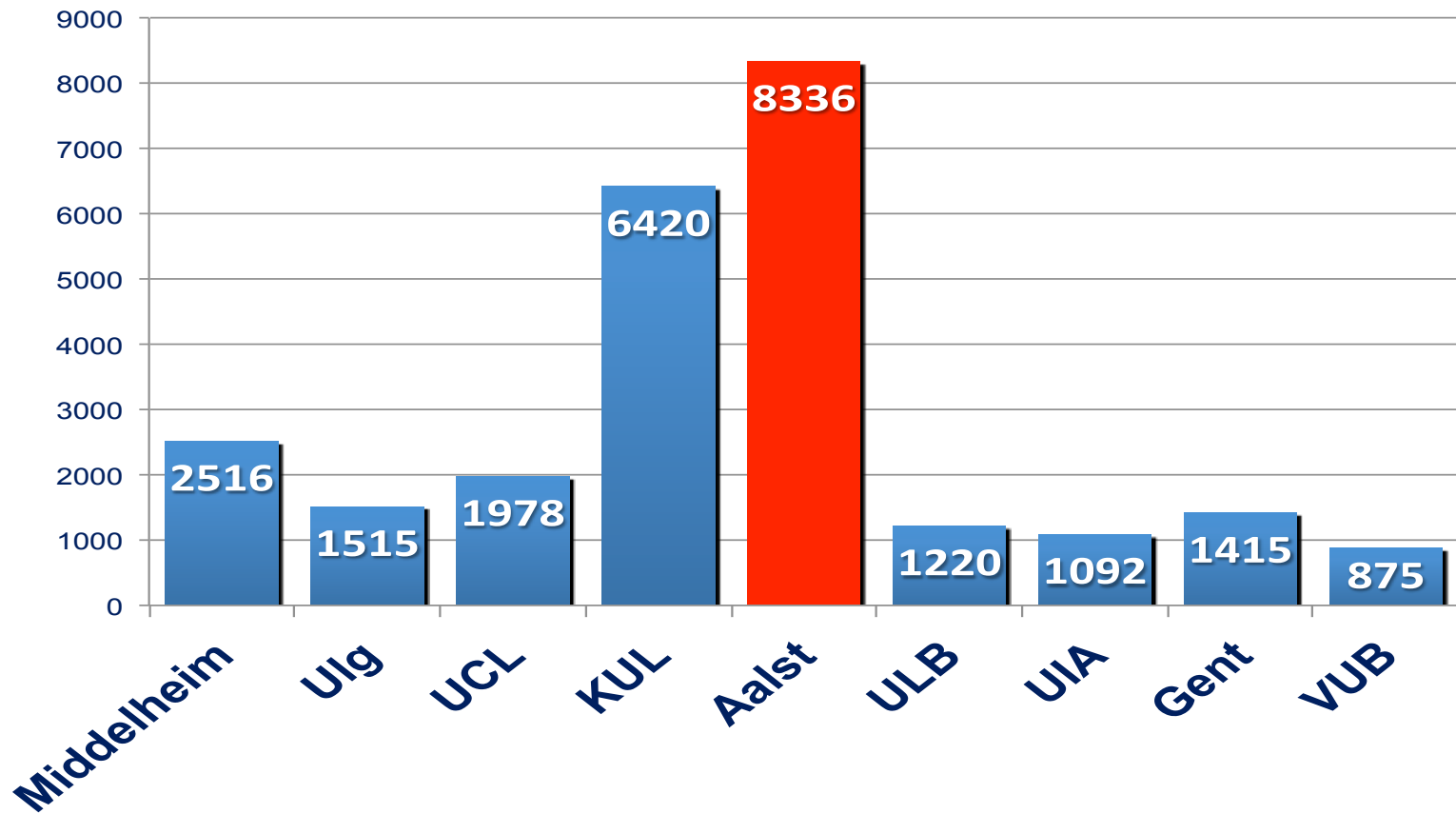
## Former Fellows of the CVC Aalst

Juan Escudier Villa	Spain
Giovanna Sarno	Italy
Narbeh Melikian	United Kingdom
Sergio Richter	Germany
Jean-Baptiste Chierchia	Italy
Andrea Sarkozy	Hungary
Giorgos Kourgiannides	Greece
Juraj Madaric	Slovakia
Samer Mansour	Canada
Giedrius Davidavicius	Lithuania
Ganesh Manoharan	United Kingdom
Philip McCarthy	United Kingdom
Martin Penicka	Czech Republic
Alexander Berger	Switzerland
Dionysios Kalpakos	Greece
Raquel Fuentes Manso	Spain
Maximo Rivero Ayerza	Argentina
Ibrahim El Zoubi	Syrian Arab Republic
Emanuele Barbato	Italy
Jorge Toquero Ramos	Spain
Valeria Ferrero	Italy
Constantinos Klebetsanis	Greece
Mireille Portegies	Belgium
Jean Champagne	Canada
Frank Provenier	Belgium
Filippo Ottani	Italy
Ignaci Anguera	Spain
Michel Roba	Belgium
Sleiman El-Khoury	Belgium
Peter Goethals	Belgium
Herbert Felice	Malta

Flavio Ribichini	Italy
Leonardo De Martino	Italy
Lenesis de Paula	Brazil
Huarez Neuhaus Barbisan	Brazil
AntonGuilio Maione	Italy
Joao Primo	Portugal
Emmanouil Manios	Greece
Adalberto Lorga Filho	Brazil
Roland Stroobandt	Belgium
Karekezy Nzayinambaho	Belgium
Hemant Ramchurn	Belgium
Luc Declerck	Belgium
Erdem Diker	Turkey
Tibor Malacky	Slovakia
Guilherme Fenelon Costa	Brazil
André D'Avila	Brazil
Ana Clara Rodrigues	Brazil
Alpay Celiker	Turkey
Kallinikos Tsakonas	Greece
Luis Elvas	Portugal
Eduardo Antunes	Portugal
Vassilis Skeberis	Greece
Olga Souza	Brazil
Jozef Bartunek	Slovakia
Josep Brugada	Spain
Jacob Atie	Brazil
Frank H.M.M. Simonis	The Netherlands
Gunter Steuer	Austria
Wlodzimierz Mojkowski	Poland
Samira Nasr Kaissar	Brazil
Lluís Mont	Spain
Sinan Gursoy	Turkey

# Competition to the Excellence

- *In-house clinical and translational research and innovation: leadership in research on coronary physiology, heart failure, cardiac regeneration and valvular disease*
- *Citation index*



# *Why Research?*

“On the sixth day God created man...”

But omitted to provide a repair manual. Hence, medical history reflects the writing of this repair manual by the succeeding generations of physicians.”

C. de Duve, Nobel Prize for Medicine 1994

**“Medical practice should be based on clinical evidence,  
Yet, clinical evidence should be based on clinical research”**



**CardioPaTh**

Cardiovascular Pathophysiology & Therapeutics

# **Novel therapeutic strategies for the treatment of heart failure**

***Cardiovascular Center  
Onze Lieve Vrouwziekenhuis,  
Aalst, Belgium***

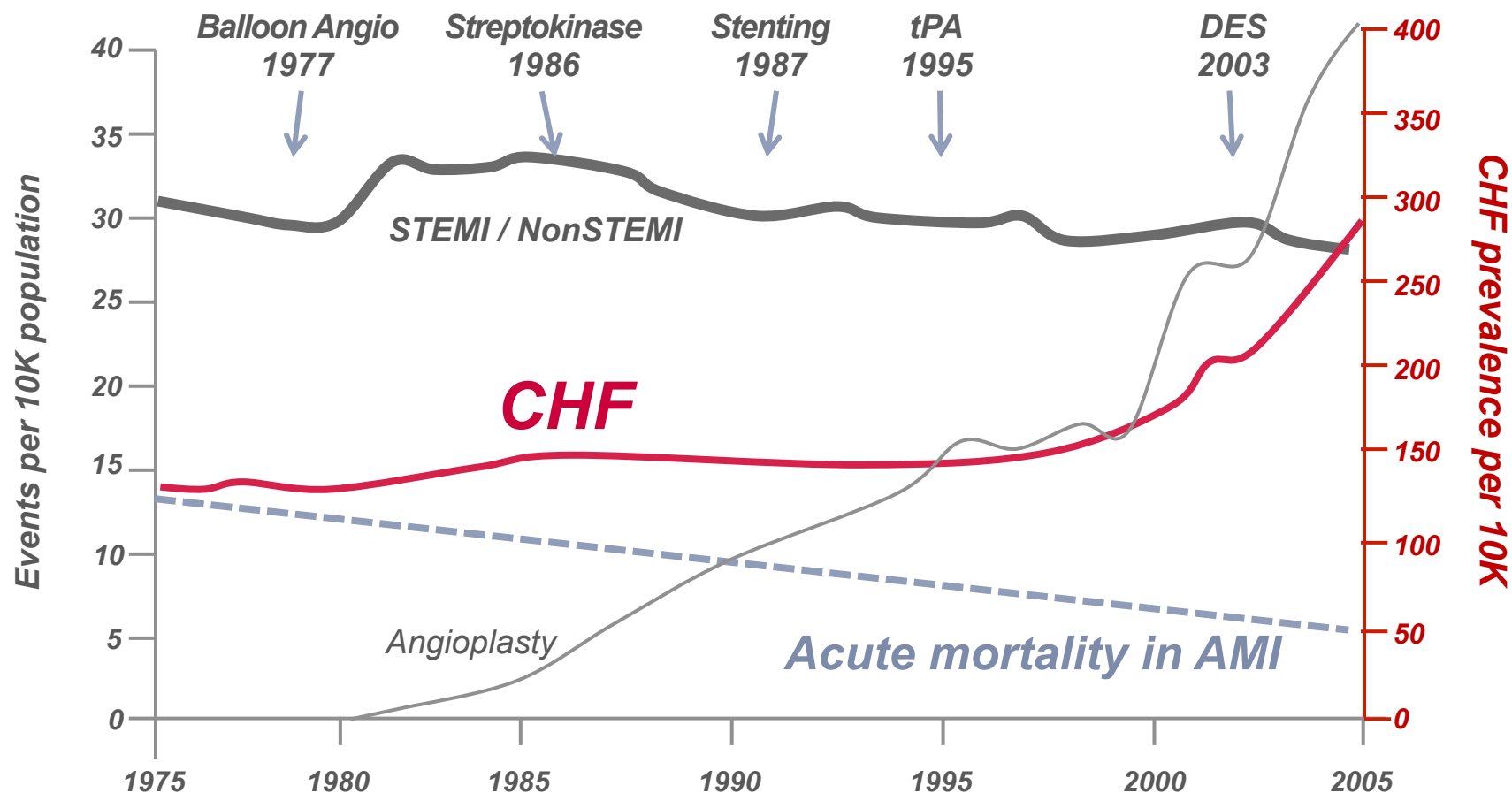
***CardioPaTh, Naples***

***Marc Vanderheyden***





## Increasing Incidence of Heart Failure Despite Reperfusion Therapies

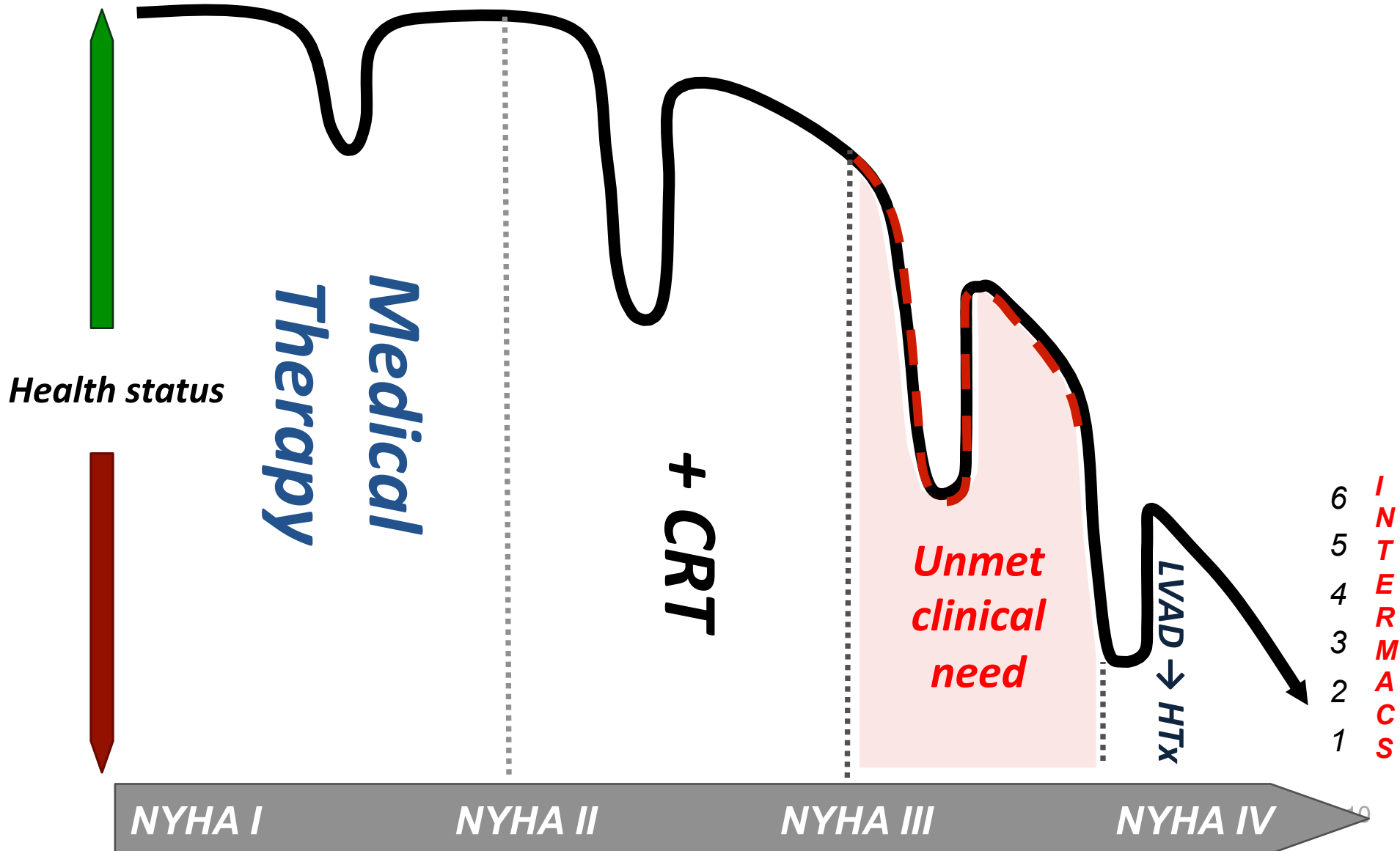


Courtesy of A. Behfar & A. Terzic, Mayo Clinic

Modified from Heart Disease and Stroke Statistics:2015 Update, Circulation 2015



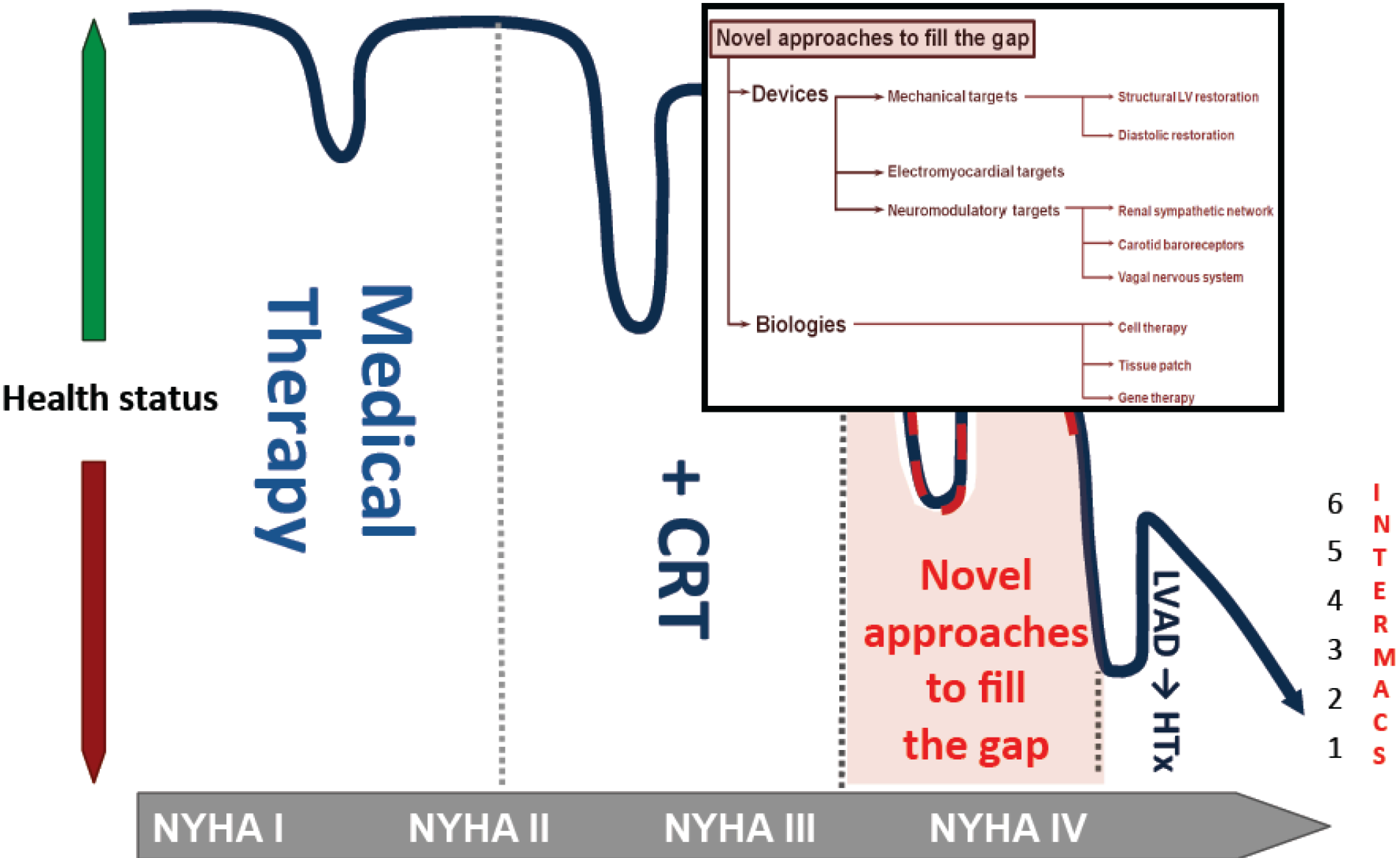
# Why Devices for Heart Failure Unmet Clinical Need



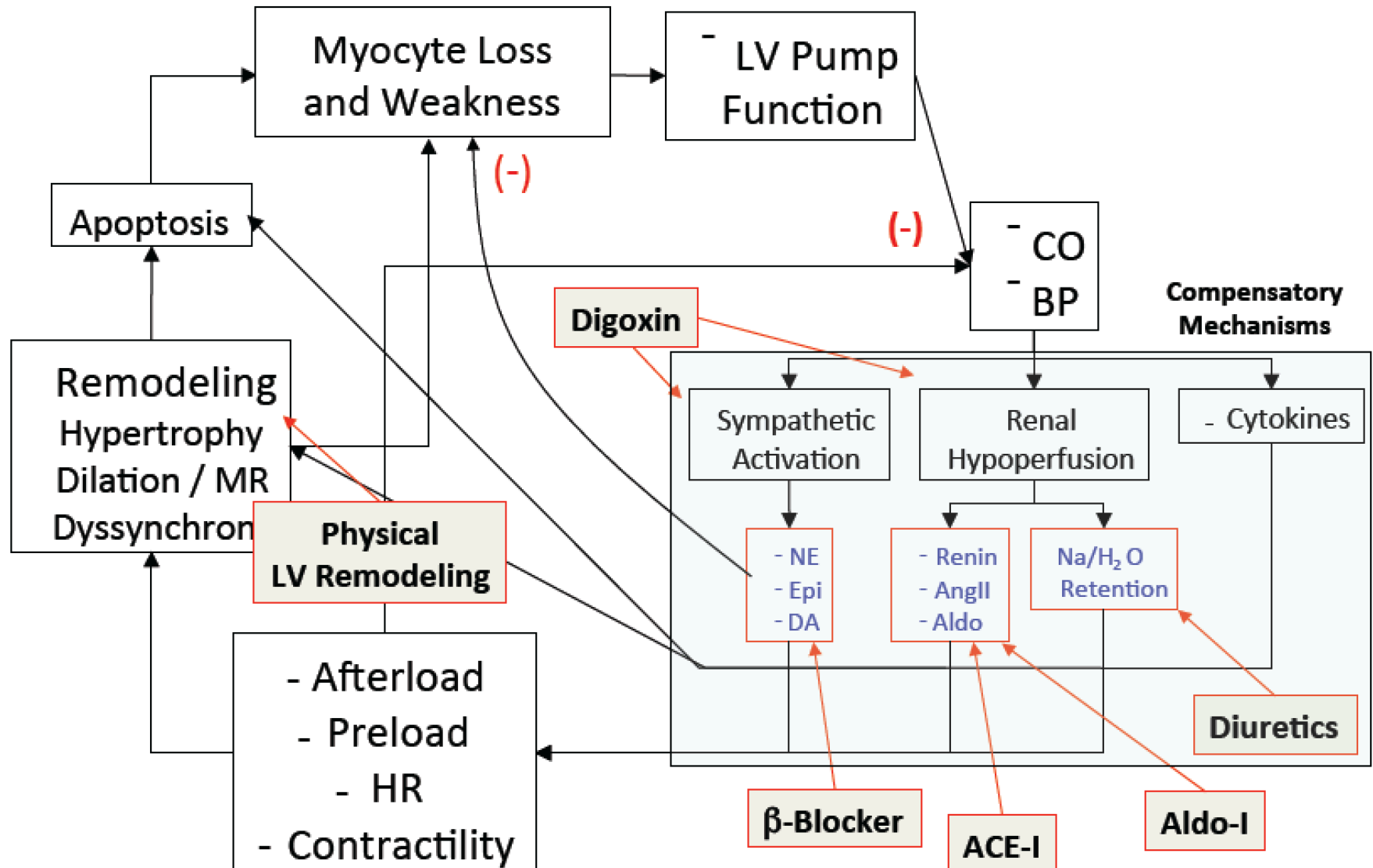


## Congestive Heart Failure

### Progression and Therapeutic Approaches



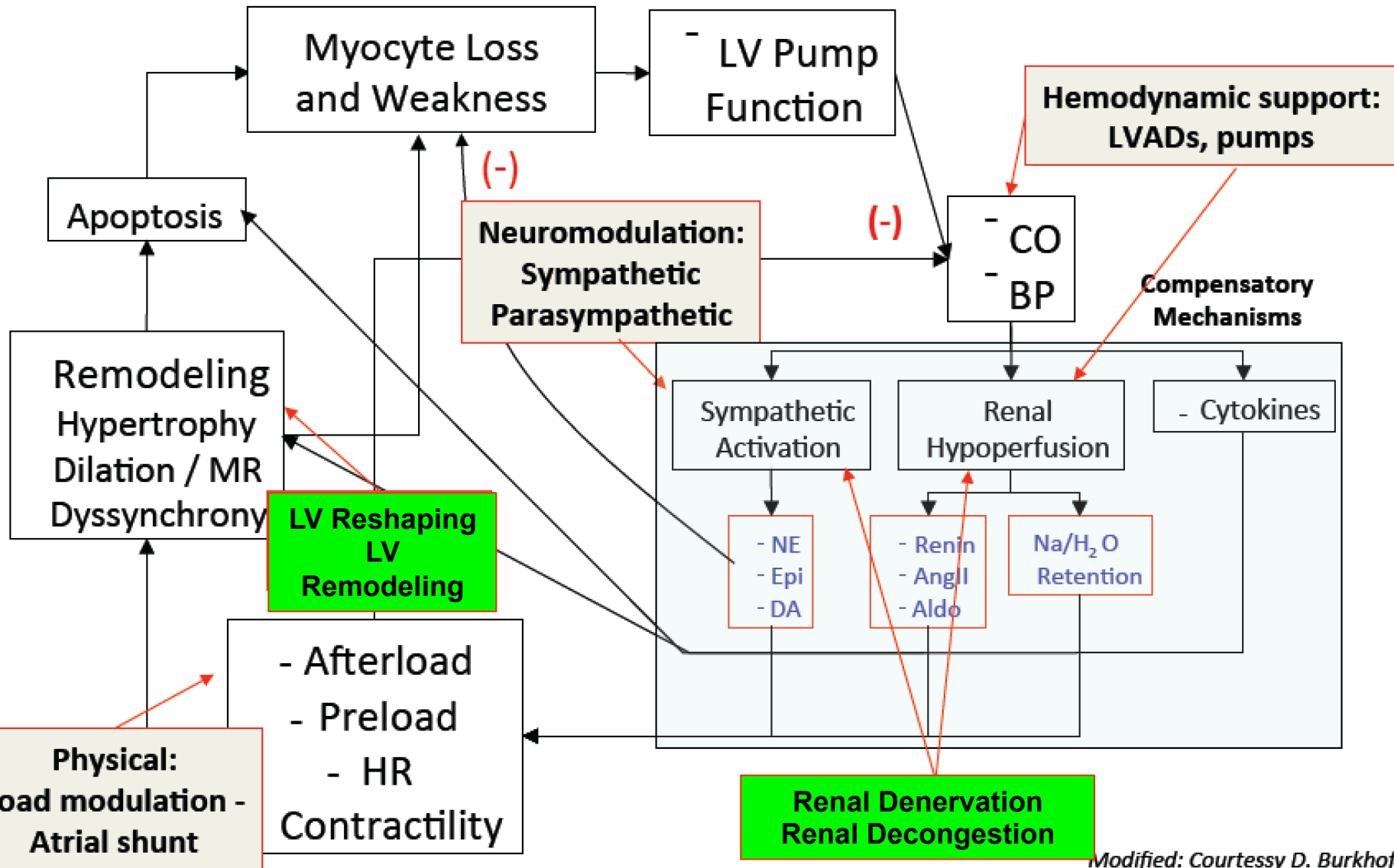
## *Pharmacologic vs Device-based Interventions*



*Courtesy, D. Burkhoff*



## Pharmacologic vs Device-based Interventions





## ***Two main epidemiologic facts about kidney function in Heart Failure patients***

- *Renal dysfunction\* is observed in about 40% of HF patients*
- *Worsening of renal function complicates about 30% of admitted HF patients, increases risk for in-hospital death 7-fold, and length of stay 3-fold*

*McAlister et al. Circulation 2004*

*Forman et al. JACC 2004*

*Hillege et al. Circulation 2006*

*Smith et al. J Am Coll Cardiol 2006. .*

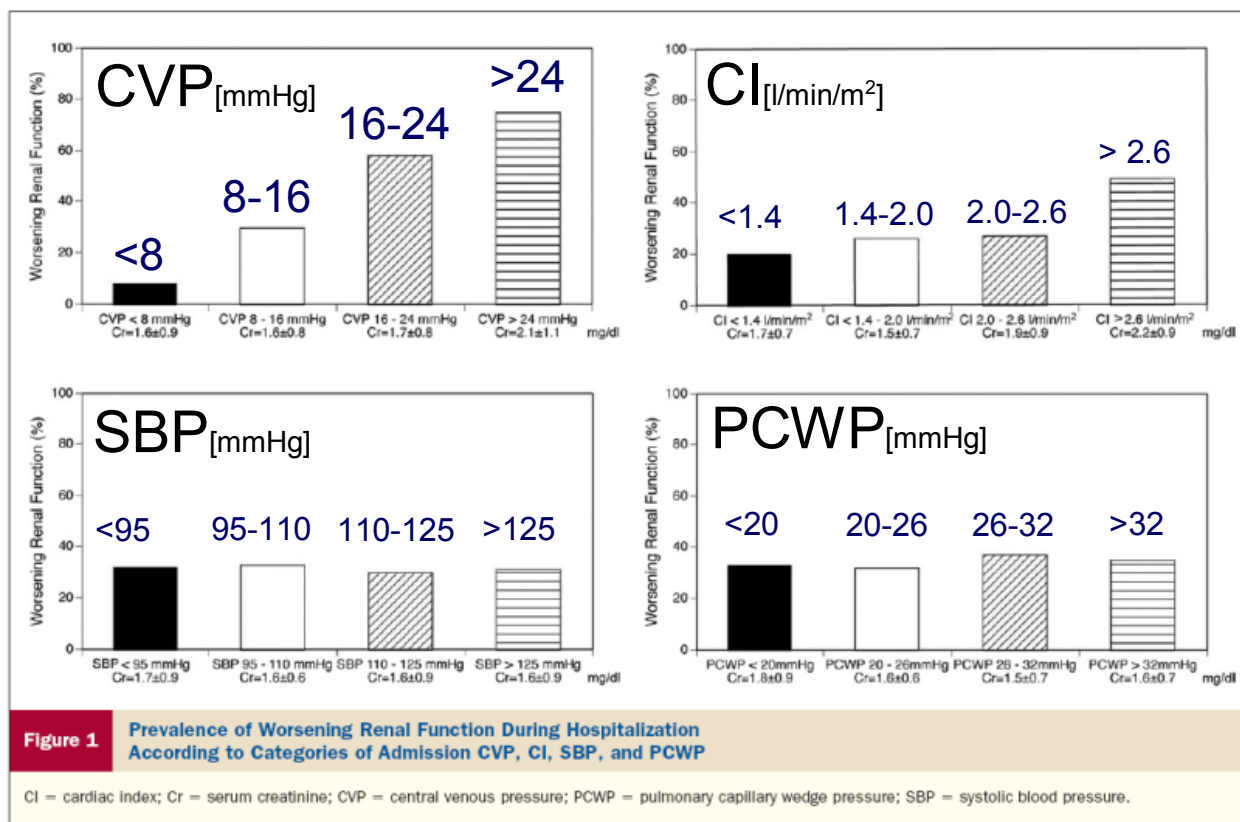
*Heywood et al J Card Failure 2007*

*Damman et al. Progr in Cardiovas Dis 2011*

*\*defined as  $GFR < 60 \text{ ml/min/1.73m}^2$*

# Importance of Venous Congestion for Worsening of Renal Function in Advanced Decompensated Heart Failure

***Venous Pressure, but not Art. BP or Cardiac Output predicts worsening renal function in advanced decompensated HF***



Cardiac index (CI) not associated with renal function in HF (percentage of worsening renal function highest in pts with normal CI). Systolic blood pressure (SBP), and pulmonary capillary wedge pressure (PCWP) were also not associated



## Failing Heart with Full Cardiorenal Syndrome

Central Venous Pressure  
30 mm Hg

Arterial Blood Pressure  
110/80 mm Hg

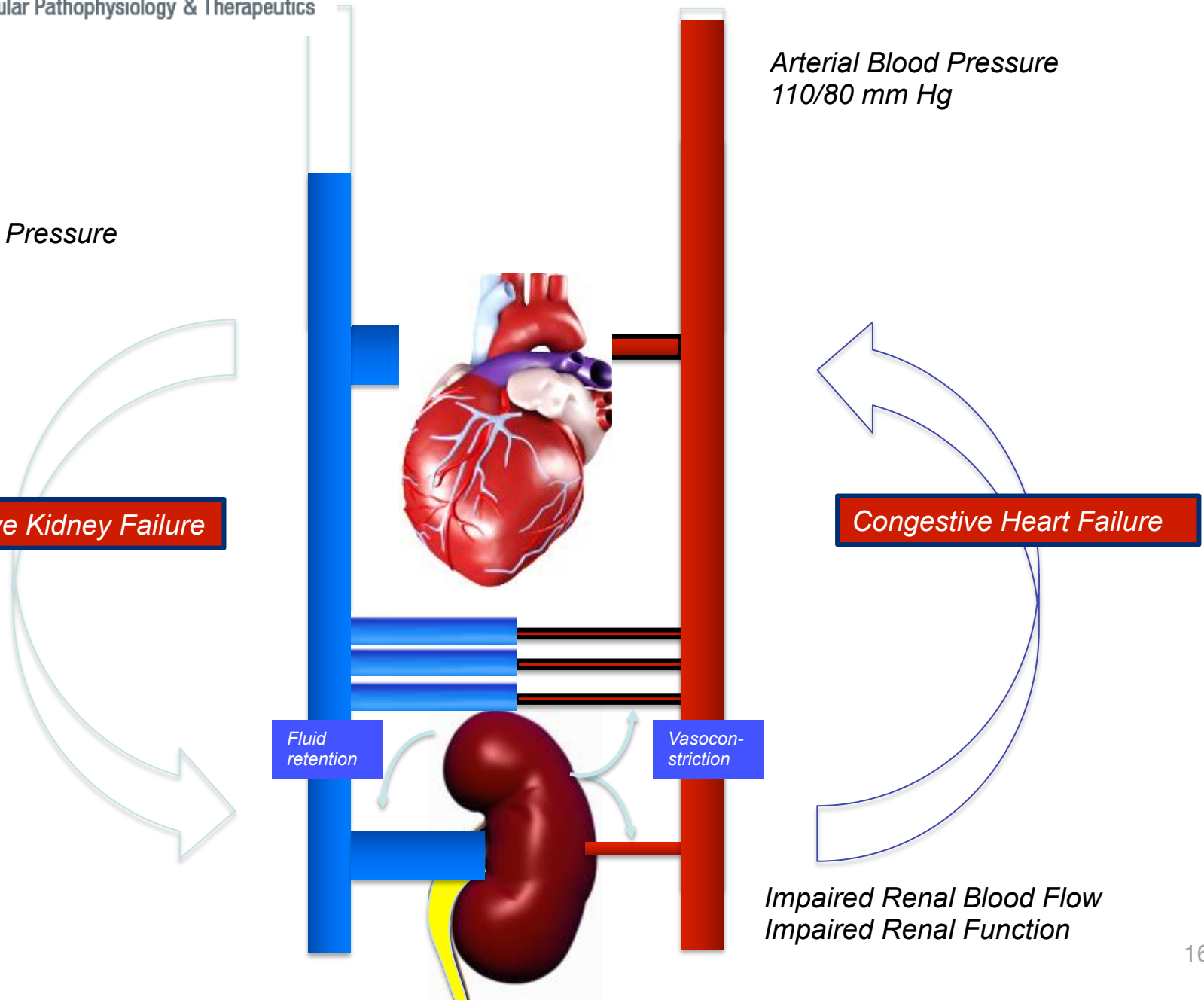
**Congestive Kidney Failure**

**Congestive Heart Failure**

Fluid  
retention

Vasocon-  
striction

Impaired Renal Blood Flow  
Impaired Renal Function







## ***Current Therapy Consists of Diuretics***

*(Can't live with them, can't live without them, don't always work)*

- *Remove water, but...*
- *Cause electrolyte imbalance (loss of  $K^+$ ,  $Mg^{++}$ , insuff.  $Na^+$  excr.)*
- *Activate neurohormonal vasoconstrictor systems (RAAS, SNS)*
- *Diminish renal blood flow*
- *Progressively deteriorate renal function*
- *Side effects (hearing loss, bone loss, photosensitivity, skin rash)*
- *Diuretic resistance (25-30% of patients, mainly d/t high RVP)*



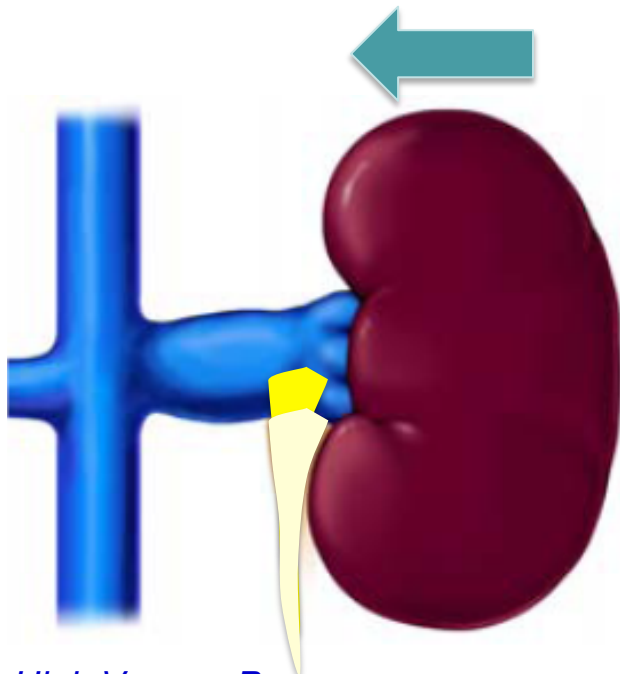
## *How to improve outcomes in acute heart failure?*

*By relieving kidney congestion - which results from heart failure, complicates it, and aggravates it - employing a safe, simple, and elegant transcatheter approach*



## *Transcatheter Renal Venous Decongestion (TRVD) for Congestive Heart Failure*

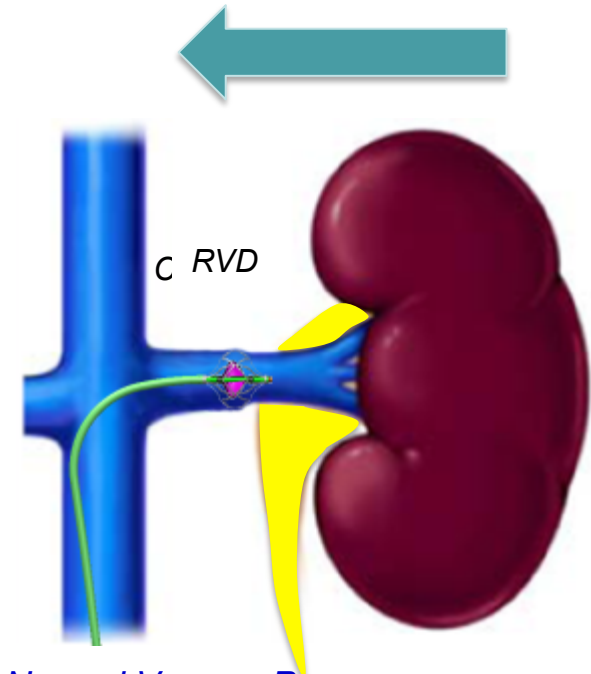
*Severely congested kidney in  
heart failure*



*High Venous Pressure*

- Poor renal perfusion
- Poor renal function
- Fluid retention

*Decompressed kidney with  
flow pump*



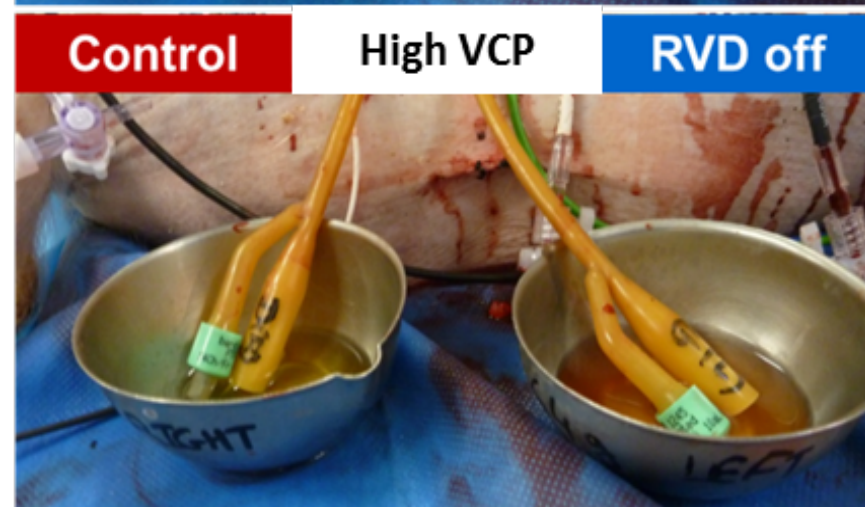
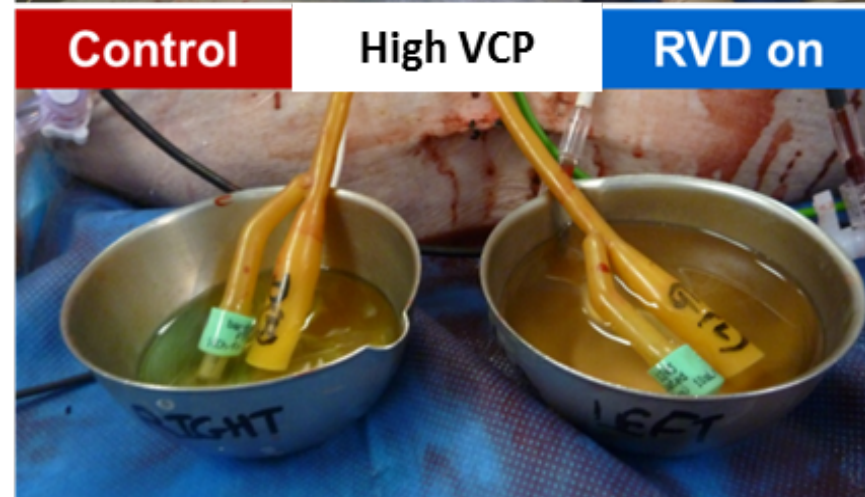
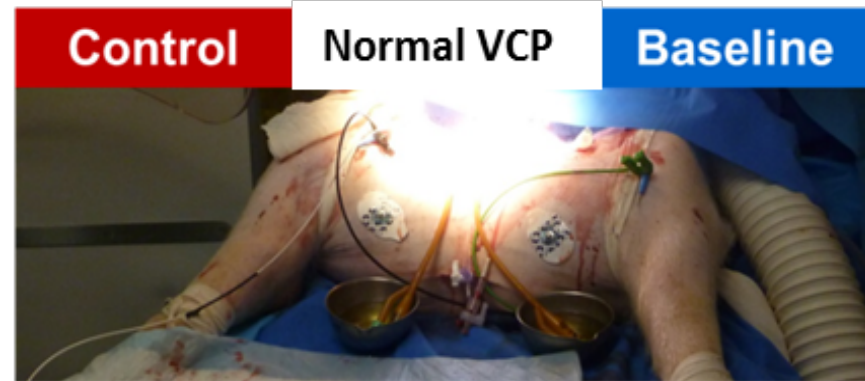
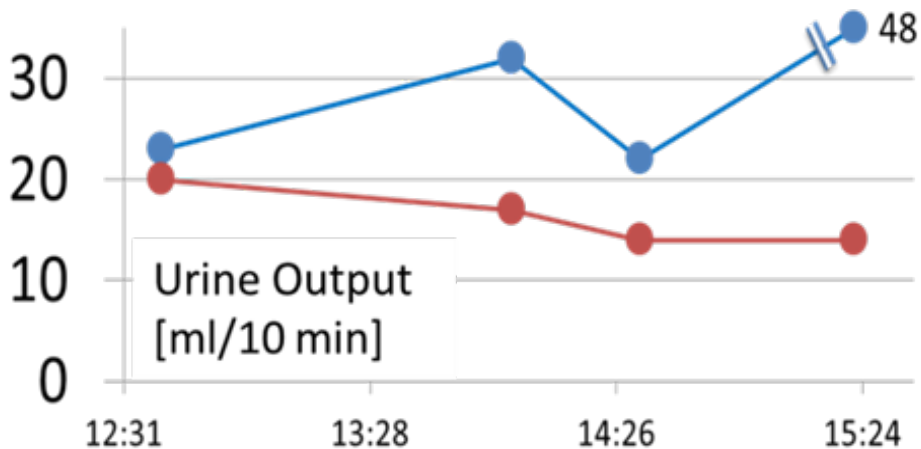
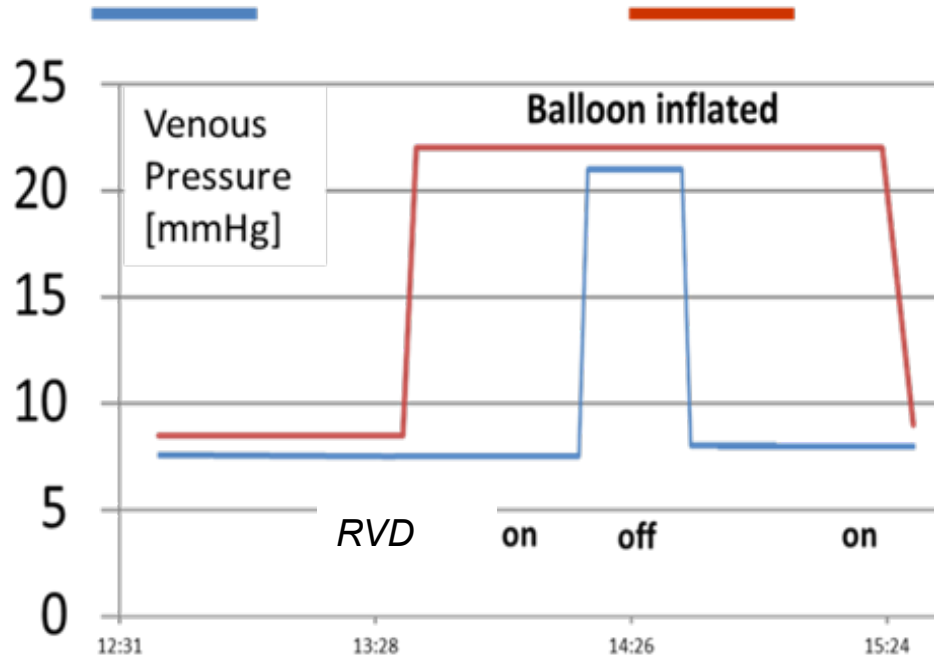
*Normal Venous Pressure*

- Improved renal perfusion
- Improved renal function
- Fluid removal

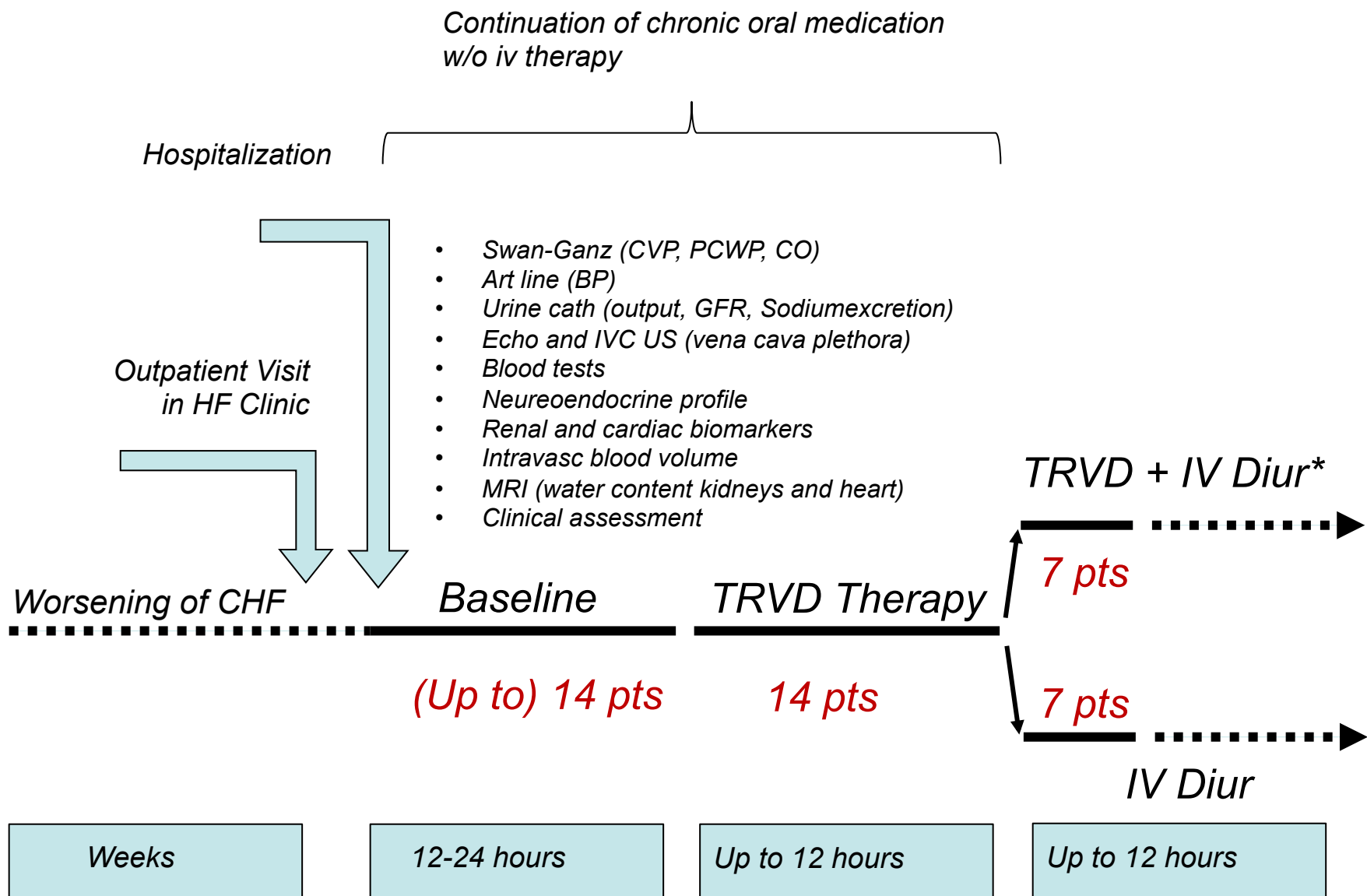


## Urine Production:

**Treated vs Untreated Kidney**

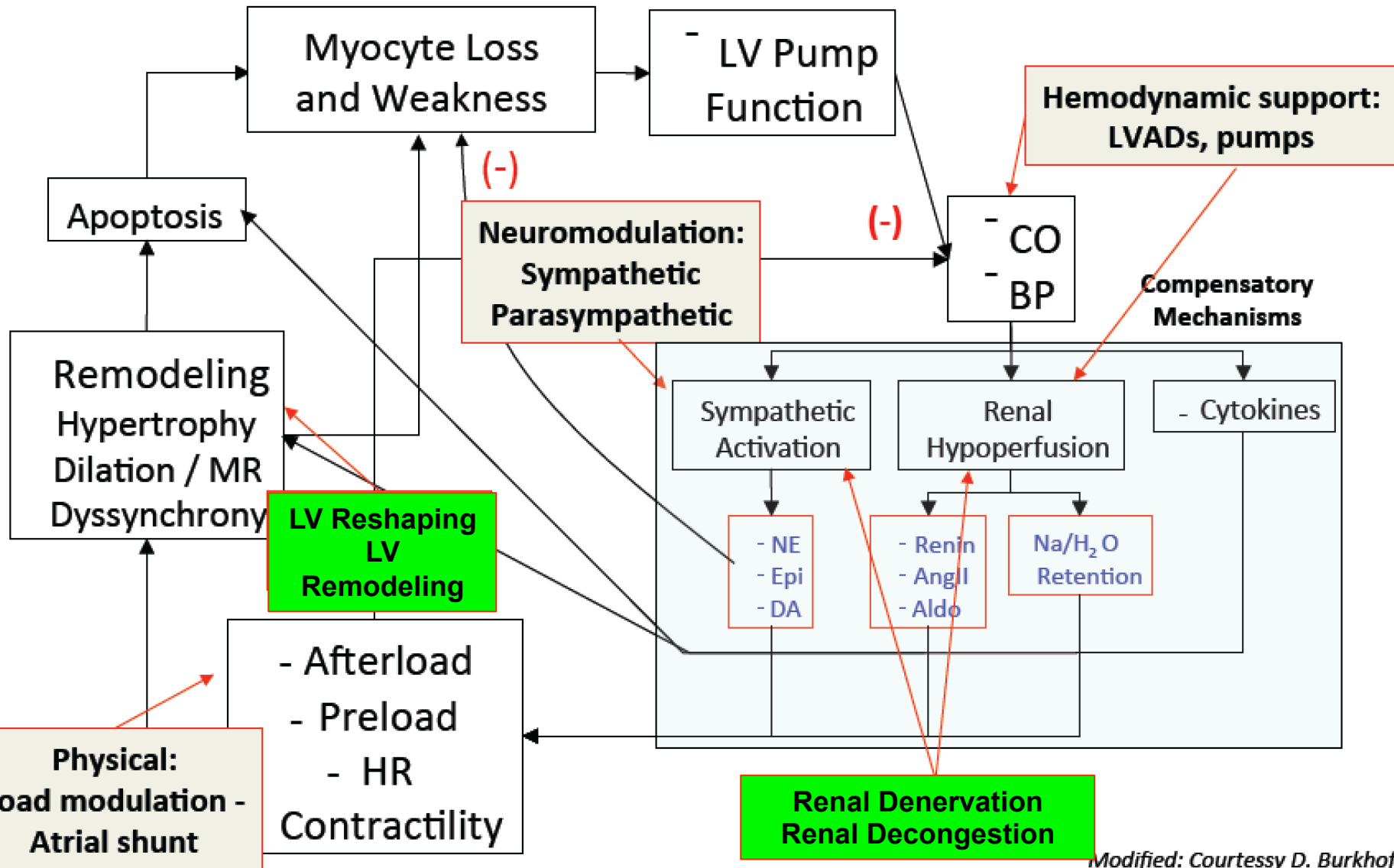


# First-in-Man Study Belgium





## Pharmacologic vs Device-based Interventions





# ***Why is Reverse Remodeling Important?***

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- 1. Reverse remodeling signifies a return of the CHF phenotype (abnormalities in molecular, biochemical, cellular, extracellular, structural pathways) towards normal*
- 2. Every therapy that induces reverse remodeling has been associated with reduction in mortality*



# *How Much Remodeling Occurs?*

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**$\Delta$ EDV**

***ACE-Inhibitors***

***~15 ml***

***$\beta$ -Blockers***

***~20 ml***

***CRT***

***~30 ml***

***LVAD***

***>100 ml***

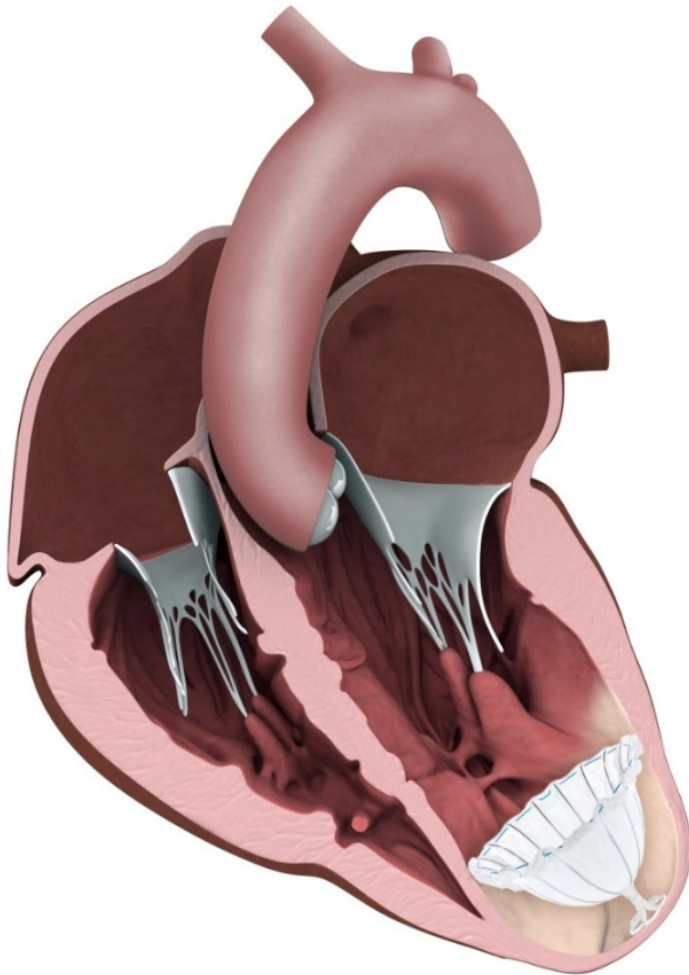




***Can the same benefits  
achieved by Rx/LVAD  
strategies also be  
achieved by “physically”  
reconstructing the LV?***



## ***“Parachute” Catheter-based LV Reconstruction Goals and Mechanisms***



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### **(1) “RESTORING EFFECT”**

*Reduces wall stress in the upper chamber by changing LV geometry and reducing volume.*

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### **(2) “SYNCHRONIZING EFFECT”**

*Replaces the eccentric wall motion in the apical region with a more **compliant Parachute**. The benefits of **synchronized apical wall motion** throughout the cardiac cycle allows for improved cardiac output and reduced filling pressure.*

# Catheter-based LV Reconstruction

## Parachute Technology

### PARACHUTE IMPLANT

**Anchor (Laser Cut)** .....  
Engages LV Wall  
(2mm)

**Suture (Polypropylene)** .....  
Collapses

Device. Supports  
ePTFE at the  
Edge

**Membrane (ePTFE)** .....  
Dual layer occlusive  
membrane. Allows  
tissue growth.

**Frame (Nitinol)** .....  
16 Arms Laser  
Cut from a Single  
Tube

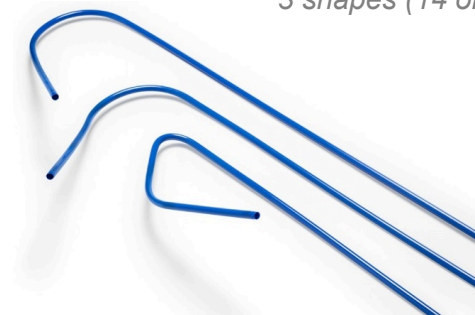
**Foot (Urethane)** .....  
Radiopaque.  
Shock Absorber



	65mm	75mm	85mm	95mm
Standard (+3mm)	X	X	X	X
Short	X	X	X	X

### GUIDE CATHETER

3 shapes (14 or 16Fr)



### DELIVERY SYSTEM

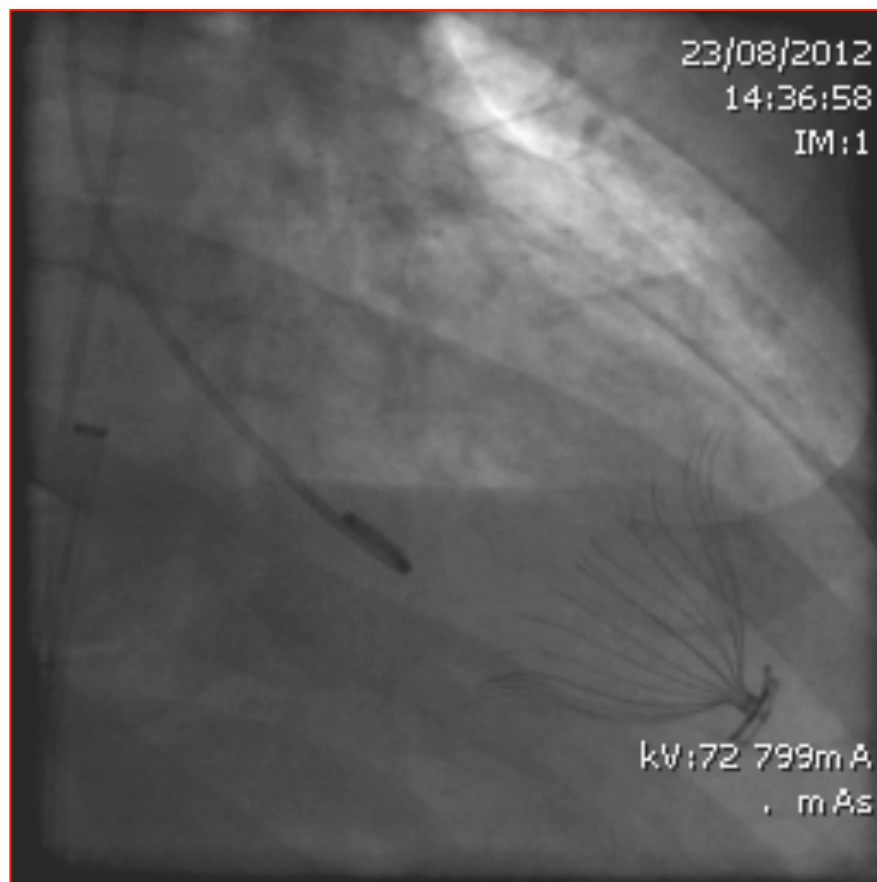
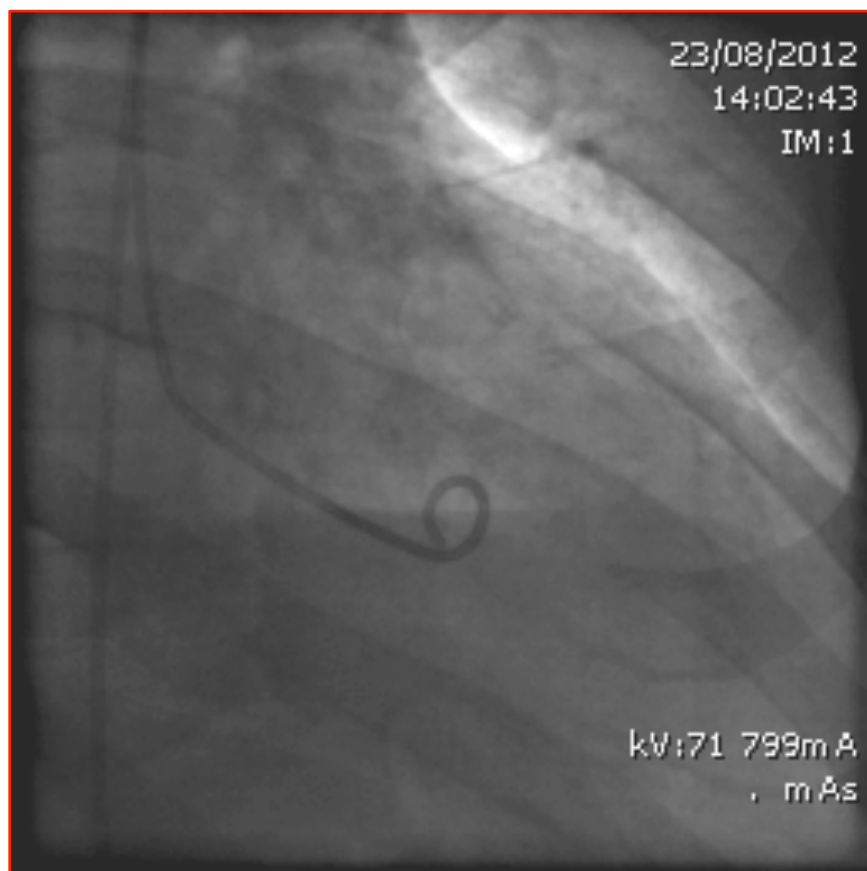
20cc balloon is inflated to anchor device





## *Example: first case*

*Male, 69 yo, NYHA 3, 10 years after anterior STEMI*





## ***“Parachute” Clinical Program Summary***

- *High procedural feasibility with favorable safety profile*
- *Hemodynamic improvements observed in both systolic and diastolic function*
- *Functional improvement is shown by an increase in the 6MWT and reduction in NYHA class*
- *23.6% Mortality + HF hospitalization rate supports U.S. pivotal trial design*

# *Conclusions*

1. Device-based interventions expand the available armamentarium of the current multidisciplinary management of heart failure
2. They offer a tailored management of specific heart failure phenotypes by targeting specific substrates or deleterious pathophysiological mechanisms
3. The therapeutic potential as well as appropriate patient selection of those benefiting most from the device-based approaches needs to be addressed in the appropriately designed clinical trials