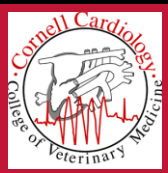# Cardiovascular physiology review
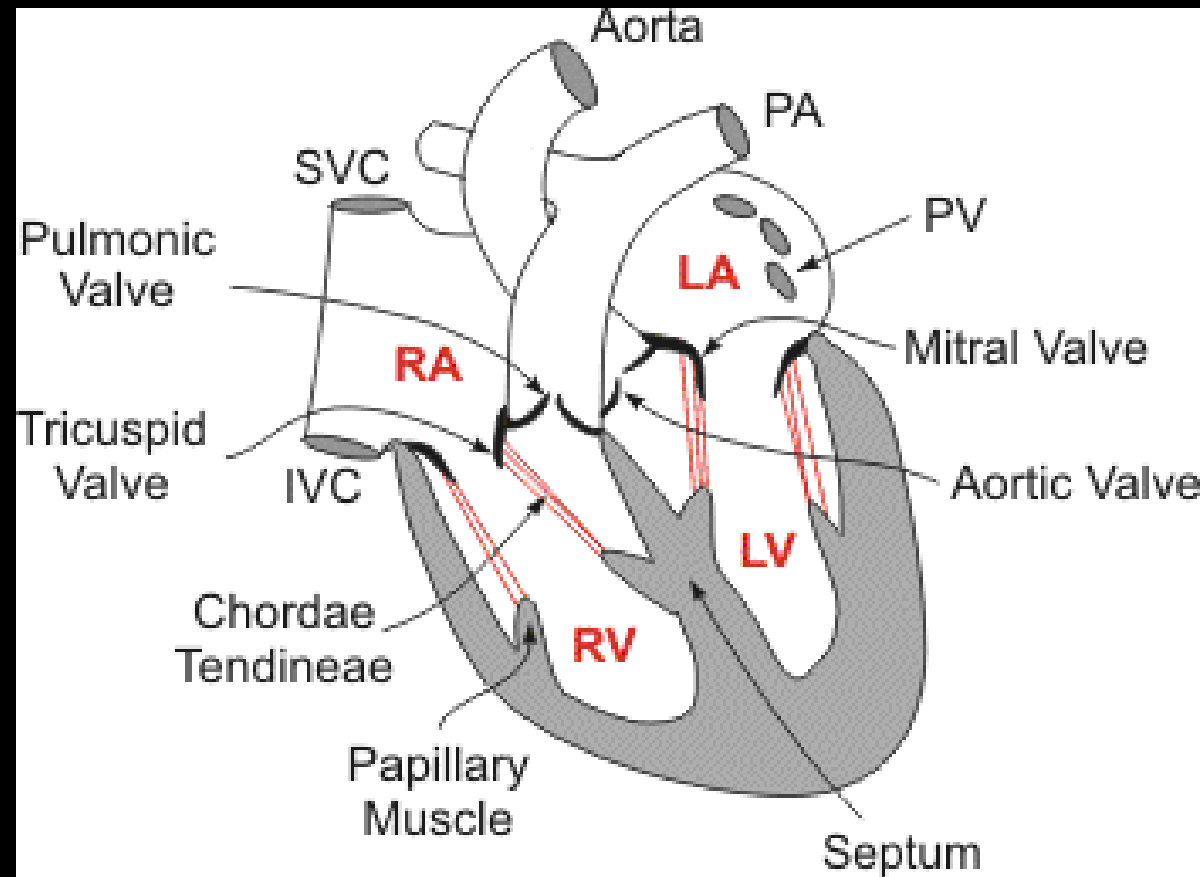
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Anatomy and intracardiac pressures

Pressures (mmHg)

LA: 6/4

LV: 120/0

Aorta: 120/80

RA: 5/3

RV: 25/0

PA: 25/15

PWP: 6

Cardiac performance

- The heart pumps to circulate blood to bring oxygen and nutrients and remove CO_2 from the metabolizing tissues

- Adequate cardiac output (CO) is determined by several factors
  - Preload
  - Afterload } SV
  - Contractility
  - Heart rate

- Cardiac output = stroke volume *x* heart rate
  - SV = EDV - ESV

- Blood pressure: CO *x* peripheral vascular resistance
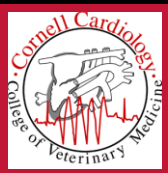
Peripheral vascular resistance

- TPR is represented mathematically by the formula

  TPR = ΔP/Q

  - ΔP is the change in pressure across the systemic circulation from its beginning to its end.
  - Q is the flow through the vasculature (=CO)

  Or:

TPR = (Mean Arterial Pressure - Mean Venous Pressure) / Cardiac Output

  - Mean Arterial Pressure (MAP) = 2/3 DP+ 1/3 SP
 - Mean Venous pressure (=CVP) (0-4 mmHg) .

Preload

- Quantity of venous return that fills the ventricles during diastole: end-diastolic volume

- Determines the resting length of sarcomeres (stretch) = end-diastolic wall-stress

- State of systemic venous dilation or constriction determines preload
  – Venous dilation: preload is reduced
 – Venous constriction: preload is increased

Frank Starling: role of PRELOAD
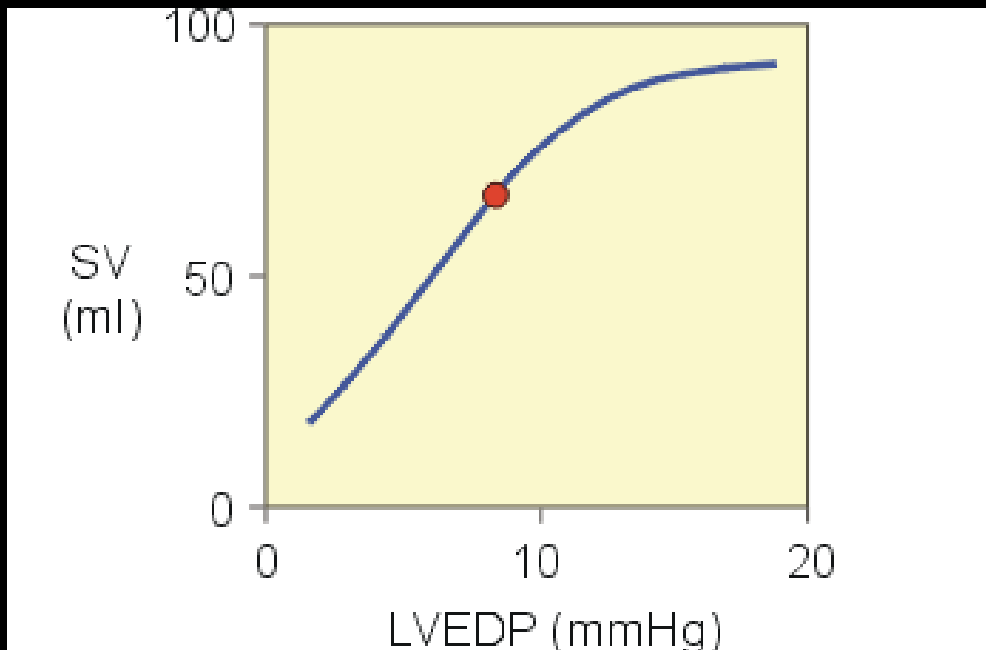
Increased venous return
= ↑ preload

– increased LV end-diastolic volume

– end-diastolic pressures

– ↑ stroke volume

Starling described dependence of contractility on the state of stretch that the myocytes are in just prior to contracting (number of contractile units that are cycling and amount of Ca available)

Afterload

- Is the force that impedes contraction
- Or: force required to achieve a certain intraventricular pressure = Systolic wall-stress
- Arterial blood pressure (systemic vascular resistance) can be used as an index of afterload
- Also determined by aortic compliance
- High afterload may result in reduced CO
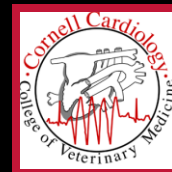
Wall stress- Law of LaPlace

- Ventricular wall stress (σ):

$$\sigma = P*r/ h$$

  P=ventricular pressure; r=ventricular radius; h=wall thickness

  – the pressure (P) that the ventricle generates during systolic ejection is close to aortic pressure

- Wall stress is wall tension divided by wall thickness

  – wall tension (T) is proportionate to the pressure (P) times radius (r)

- At a given pressure, wall stress and therefore afterload are increased by an increase in ventricular inside radius (ventricular dilation). A hypertrophied ventricle (smaller lumen or radius) reduces wall stress and afterload
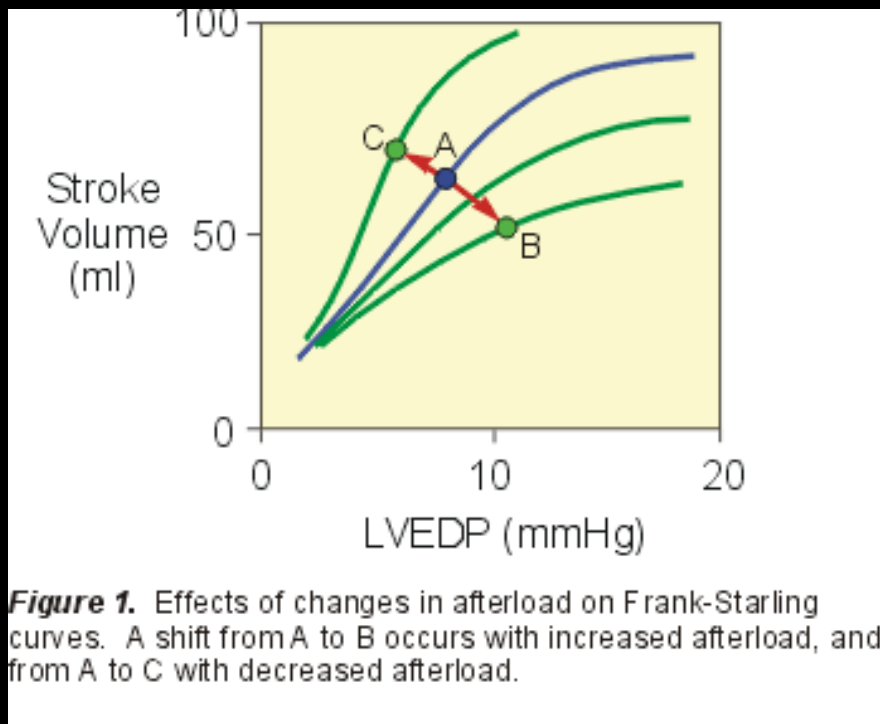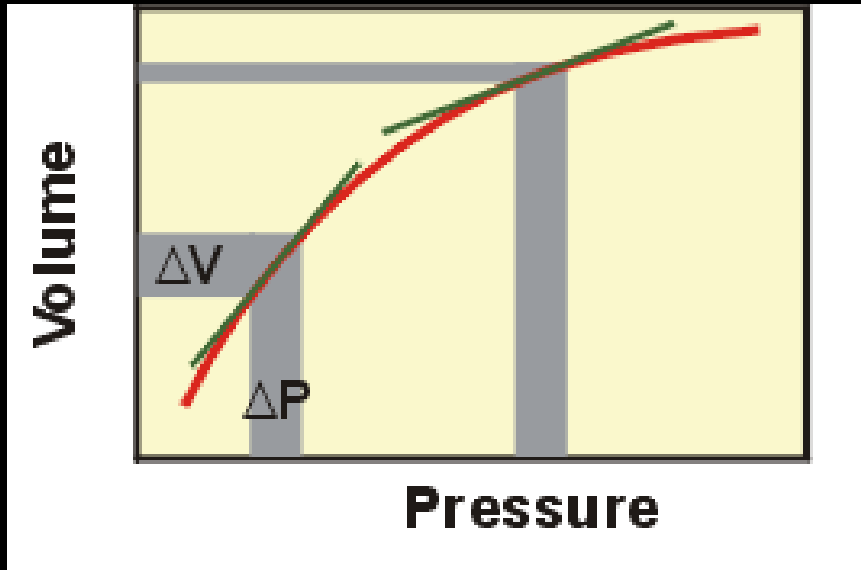
Afterload

Afterload goes up when:

– Increased systemic/ aortic pressure

– Increased peripheral vascular resistance

– Subaortic stenosis

– Ventricular dilation

When afterload goes up (A to B), the end-systolic volume increases causing a decrease in stroke volume

Figure 1. Effects of changes in afterload on Frank-Starling curves. A shift from A to B occurs with increased afterload, and from A to C with decreased afterload.
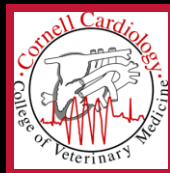
Compliance- filling curves

Compliance (green slopes) is greater at low pressures. I.e. Allowing more volume for a given change in pressures
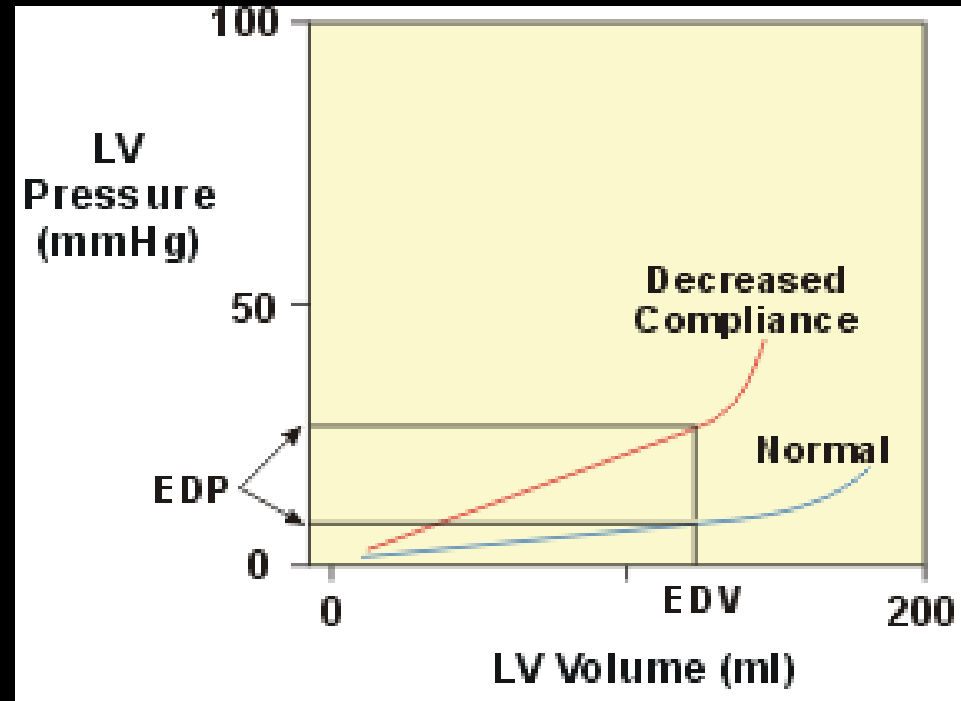
Steeper slope of passive pressure-volume curve due to decreased compliance (ie hypertrophy)
Increased EDP for any given EDV

Contractility

- Extent to which the sarcomere contracts *independent* of load

- Inherent myocardial cellular property:
    - = Inotropic state
    - – Actin-myosin interaction
    - – Dependent on intracellular calcium levels
    - – Cellular ATP production

- Inotropic state is increased:
    - – When increased sympathetic tone: ↑ Norepinephrine: can lead to increased CO

- Inotropic state is decreased:
    - – Increased vagal tone: ↑ Ach: decreased CO

Ventricular performance
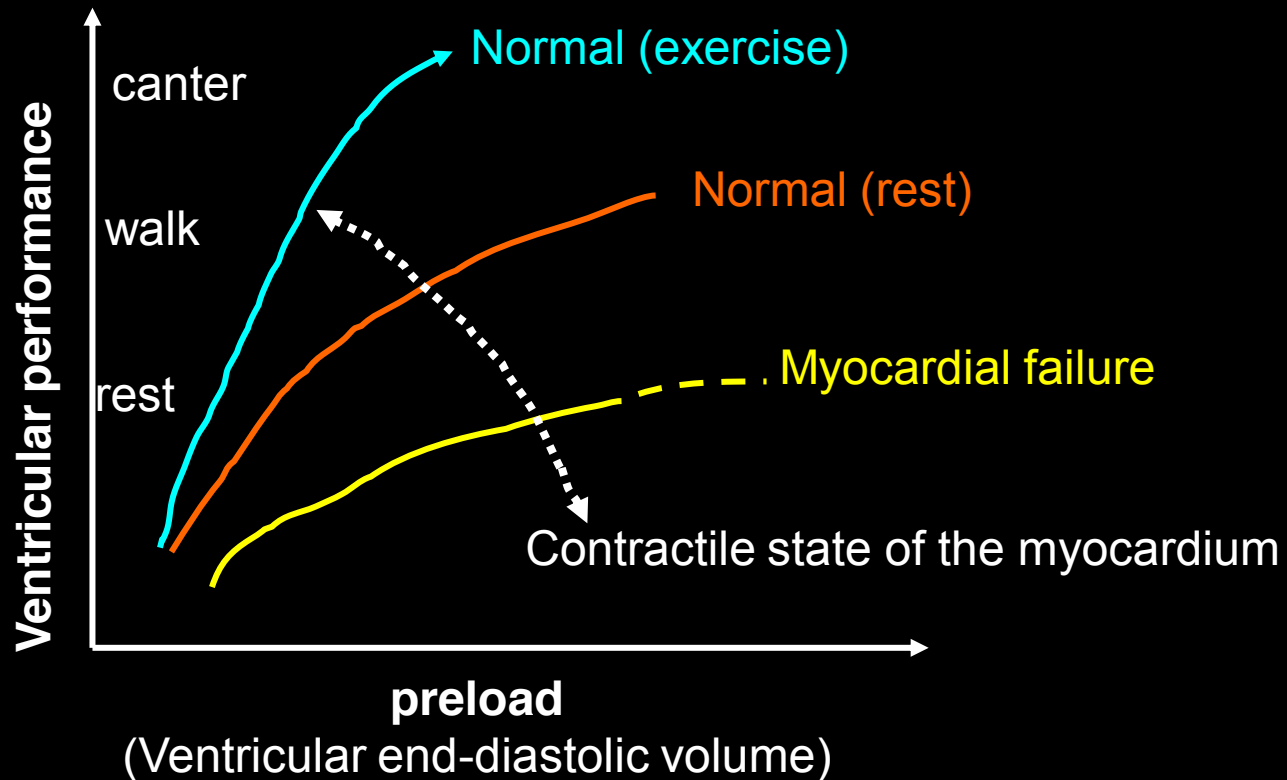
Family of **Starling curves:**

Increased end-diastolic volume (stretch of myocardial fibers) → greater ventricular performance

Myocardial failure is defined as a true decrease in myocardial contractility

Influence of heart rate on CO

- Heart rate is determined by the rate of spontaneous discharge from the sinus node
  - Depends on autonomic tone
- Increase in heart rate is a response to a need for increased cardiac output
  - Excitement, exercise
  - Fever, thyrotoxicosis
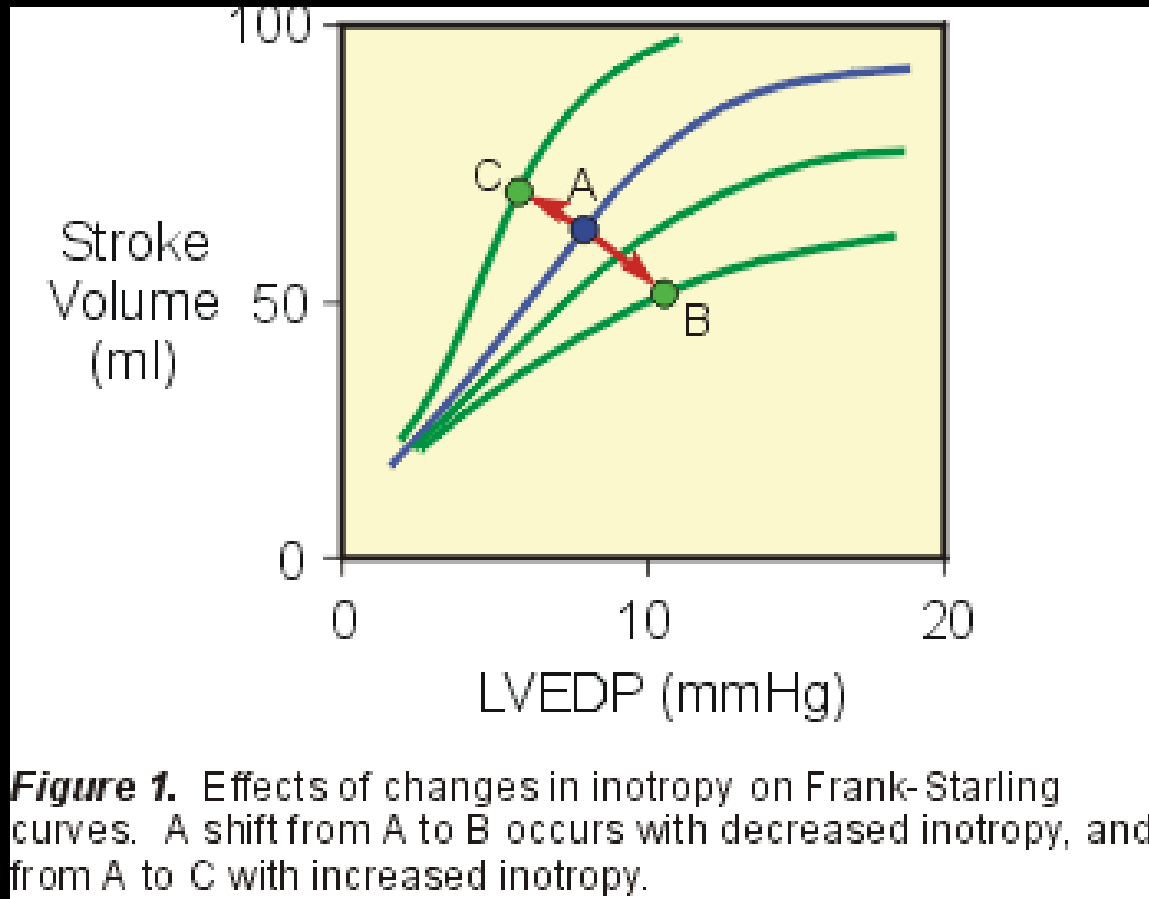 - Heart failure

Myocardial oxygen Consumption

MVO_2 primarily determined by myocyte contraction

MVO_2 goes up if:

- HR↑: the number of tension generating cycles per unit time
  - doubling heart rate approximately doubles MVO_2 because myocytes generate twice the number of tension cycles/ min
- Increasing inotropy
  - Increase magnitude of tension development by myocytes
  - the rate of tension development
    - both result in increased ATP hydrolysis and oxygen consumption
- Increasing afterload
  - because it increases tension development
- Increasing preload (e.g., ventricular end-diastolic volume)
  - however, the increase is less than what afterload or inotropy

Contractility

Figure 1. Effects of changes in inotropy on Frank-Starling curves. A shift from A to B occurs with decreased inotropy, and from A to C with increased inotropy.
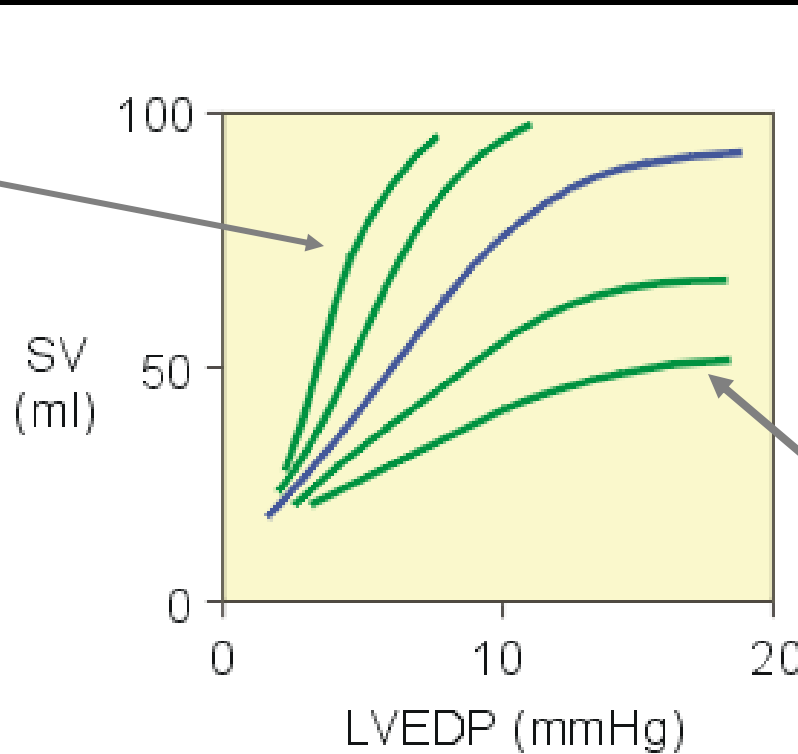
SV: role of afterload and contractility

decreased
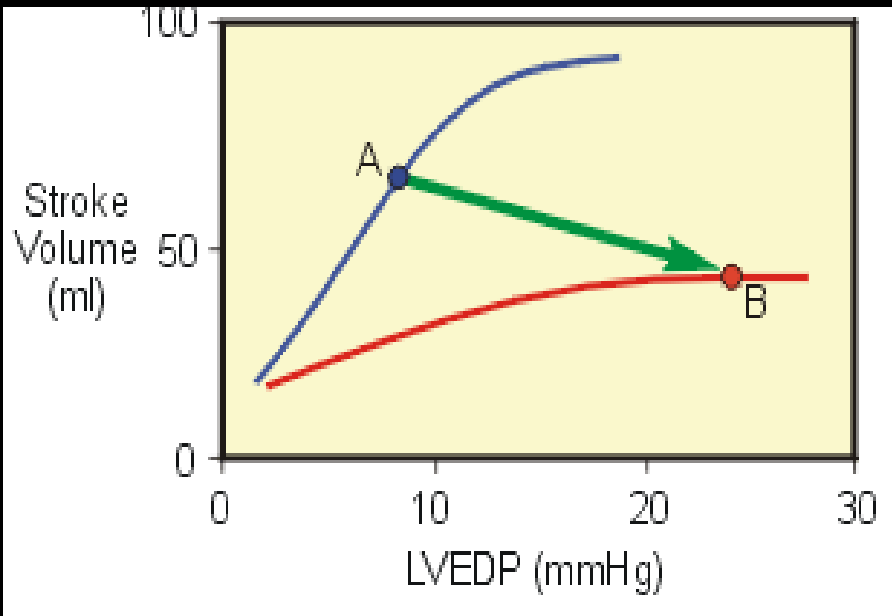afterload
or increased
contractility

normal

Increased
 afterload or
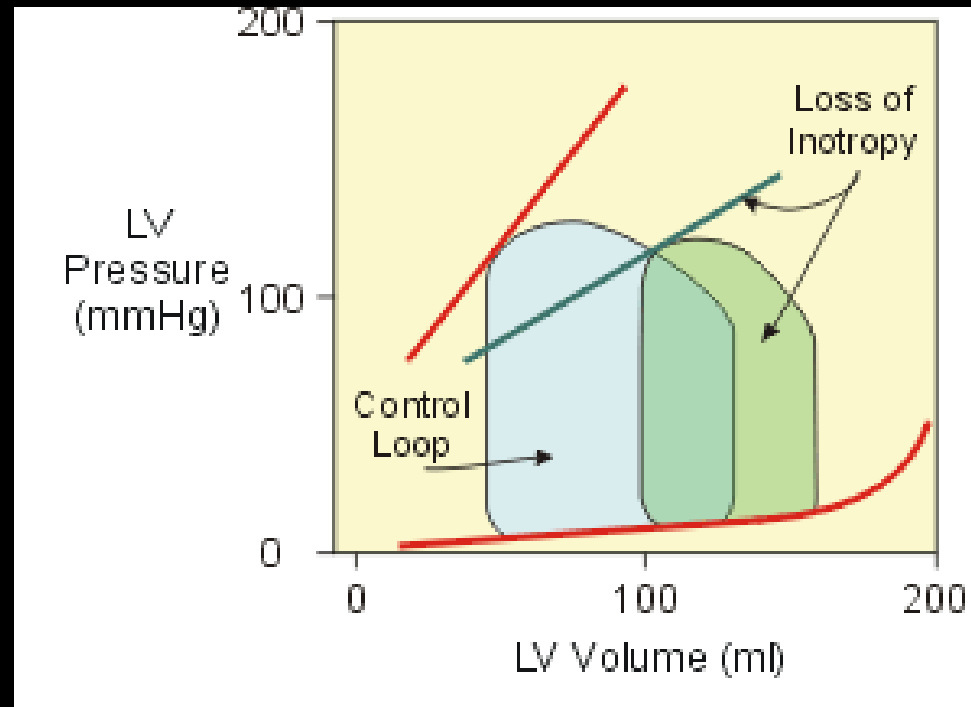decreased
contractility

Figure 2. Family of Frank-Starling curves. Changes in afterload and inotropy shift the Frank-Starling curve up or down.

Systolic dysfunction (heart failure)

Pressure-volume loops:

Heart failure (point B): Despite high LVEDP there is a reduced SV (=poor cardiac output)

How to measure systolic function?

- Problem 1:
  - Difficult to separate cellular mechanisms of contractility changes from effects of load
- Problem 2:
  - No ideal non-invasive index of contractility

- Indices of declining myocardial contractility:
  - Decreased rate of ventricular pressure development:
    - dp/dt: requires invasive measurement of left ventricular pressures by catheter
    - End-systolic elastance (PV catheters):
  - **Red**uced ejection-phase indices:
    - Fractional shortening, ejection fraction:
    - requires echocardiography

- Clinically we use echocardiography
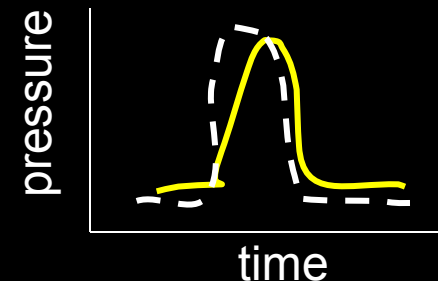
How do we quantify LV function by echo?

- M-Mode : FS
- E-point to septal separation
- Modified Simpson's Method
- Single plane area-length method
- Velocity of Circumferential Shortening
- Rate of rise of MR jet
- Index of myocardial performance

- Subjective assessment…

Echocardiographic indices of contractile state

- **End-systolic dimension:**
  - Impaired contractility: abnormally increased end-systolic volume because ventricle cannot eject as efficiently

- **End-diastolic dimension:**
  - Impaired contractility goes along with a degree of increased end-diastolic dimension

IVS

LV wall

- Both measurements are necessary to get :

   Percent fractional shortening (FS):

= % of change of the LV chamber in the short axis: amount of wall motion on the echo (measured from the M-mode)

The lower the contractility, the greater the end-systolic dimension, the lower the FS
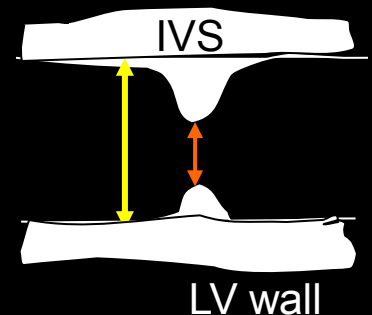
$$\frac{\text{End-diastolic dimension (mm)} - \text{end-systolic dimension (mm)}}{\text{End-diastolic dimension (mm)}}$$

LV Systolic Function Variables

$$FS = \frac{LVEDD - LVESD}{LVEDD} \times 100$$

Percent change in LV dimension with systolic contraction

FS approximates EF if there are no significant wall motion abnormalities

$$EF = \frac{EDV - ESV}{EDV} \times 100$$

Abnormal systolic function

- ## Myocardial failure
  - Primary myocardial disease:
    - Idiopathic dilated cardiomyopathy (DCM)
  - Secondary myocardial disease
    - Nutritional
    - Inflammatory- myocarditis
    - Drugs/Toxins
- ## Chronic volume-overload
  - AV valve insufficiency
    - I.e: Mitral or Tricuspid insufficiency
  - Arterio-venous shunts
    - I.e: Patent ductus arteriosus or Atrial septal defect

Dilated cardiomyopathy

- **Pathophysiology**
  - **Impaired systolic function:**
    - Increased end-systolic dimensions (Fractional shortening goes down)
  - **Some degree of diastolic dysfunction:**
    - Pathology of heart muscles leads to reduced ventricular compliance
  - **Backward failure:**
    - Elevated left-ventricular end-diastolic pressures
    - Elevated atrial pressures   **Congestive heart failure**
    - Elevated pulmonary venous pressures
  - **Forward failure:**
    - Reduced stroke volume   **Weakness exercise intolerance**
    - Systemic arterial hypotension

Primary myocardial disease
Dilated cardiomyopathy

- **Breed-specific subcategories**
  - Doberman Pinchers
  - Boxer
  - Portuguese Water Dogs
- **Other breeds commonly affected:**
  - Great Dane
  - German Shepherd
  - Irish Wolfhound
  - Any large/ giant-breed dog
- **Rare in dogs < 12 kg:**
  - Except American Cocker Spaniel

Dilated cardiomyopathy (DCM)

- **Etiology:**
  - **Familial / Genetic:**
    - Because of obvious breed predilections, most canine DCM is probably heritable
      - Boxer (ARVC), Great Dane, Newf, Portuguese Water dog
    - Duchennes muscular dystrophy: Golden Retrievers (X-linked)
  - **Onset of disease:**
    - Middle age to older: Doberman, Boxer, Great Dane
    - Juvenile (Portuguese Water dog)

ARVC

Histology:

– Scattered foci of degenerated myocardial cells (myocytolysis , myocardial necrosis, vacuolization of myocytes)

– Replacement with fibrous and fatty tissue

– In Boxers: Fatty infiltrates first detected in right ventricle

– Molecular dysfunction: Intercalated disk

– Mechanism triggering onset of the disease is still unknown!

Biochemical alterations Changes in myocyte energetics

- **Doberman**
  - **Impaired oxidative production of ATP**
  - **Morphologic changes in mitochondria:**
    - 50% reduction in mitochondrial electron transport
    - 90% reduction in myocardial myoglobin concentration
  - **Contraction and relaxation are energy-dependent**

DCM
Prevalence/ Demographics

- **Dobermans: DCM**
  - **~50 % of <u>all</u> Dobes are affected**
    - Vs 0.16% in mixed breeds!
  - **The risk of DCM increases with age**
    - Onset between 4 and 10 y of age
    - Predominantly male Dobes
    - Male dogs present with heart failure at a younger age than affected females

- **Boxers: Arrhythmogenic right ventricular dysplasia (ARVD) = Right ventricular cardiomyopathy**
  - **3.4% are affected**
  - **Inherited in autosomal-dominant trait**
    - No sex-predilection
  - **Onset between 6 and 12 y of age (mean: 8.5 years)**
    - May present with heart failure or just arrhythmias