Veterinary Bioscience 1: Cardiovascular System

VETS 90124/VETS30014

THE UNIVERSITY OF MELBOURNE

FACULTY OF VETERINARY SCIENCE

Lecture Nine:
Determinants of Cardiac Output
Week Two
Semester 2, 2023

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Checkpoints for learning: Lecture Six

1. End diastolic volume is defined as _____ .
2. Ejection fraction is defined as _____.
3. End diastolic volume is likely to increase if ___.
4. Ejection fraction is likely to decrease if _____.
5. During isovolumetric contraction of the ventricle the AV valve is / open /closed and the outlet valve is open/ closed.
6. Mean pressure in the vena cava of a dog is approximately ___ mm Hg.
7. Cardiac output is the product of _____ & _____ .

Determinants of Cardiac Output: The Mechanics of Systole and Diastole

- Determinants of cardiac output
- Preload and afterload- what do they mean?
- Length/tension relationships: the Frank Starling law of the Heart
- Modulators of cardiac contractility: inotropy

Learning outcomes

- Describe the relationship between cardiac output, heart rate and stroke volume.
- Identify the major determinants of stroke volume, and explain the effect of altered pre-load and after-load on stroke volume.
- Define the terms preload and afterload in the context of cardiac function
- Describe the relationship of altered preload and afterload to length-tension relationships in the heart
- Define the terms “contractility” and “inotropy”
- Describe the effect of altered sympathetic neural activity on cardiac inotropic state.

Measures of the Heart's Performance

Some key measures of performance

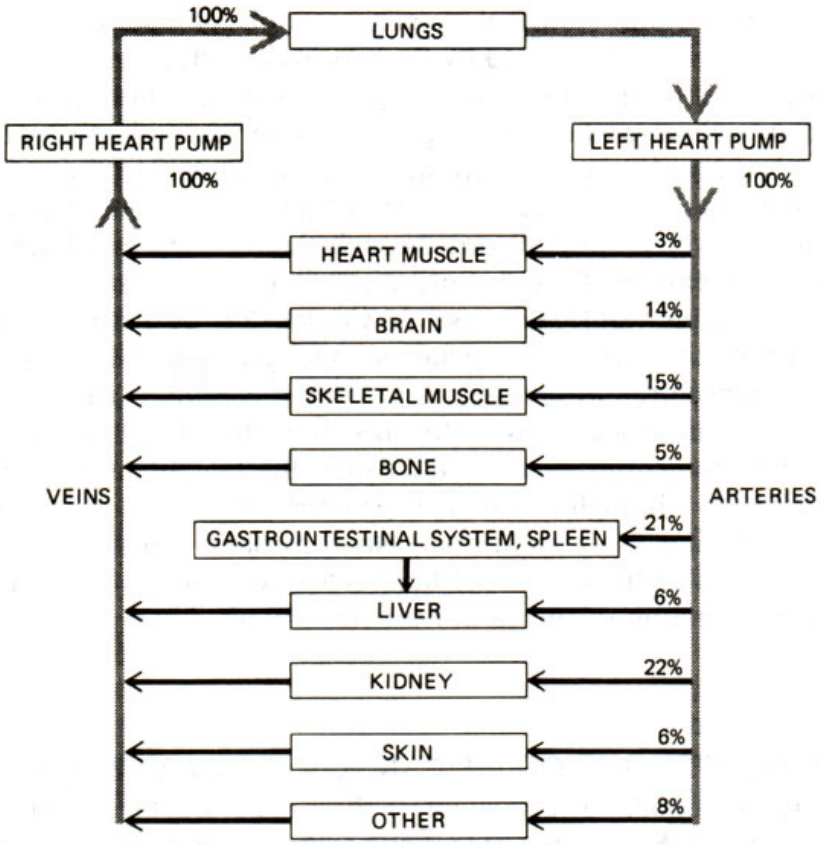
- Stroke volume (mLs)
- Heart rate (beats/minute)
- Cardiac output:

  CO = HR X SV (litres/minute)

- Stroke volume:

  = End diastolic volume- End systolic volume

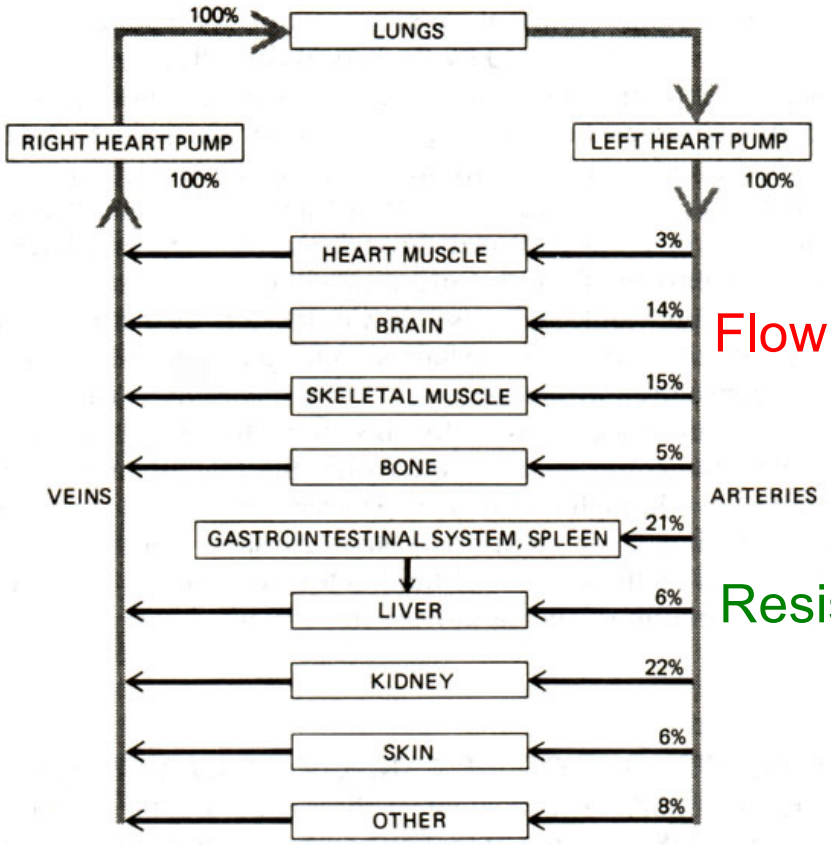
Measures of **cardiovascular** performance



Flow α pressure gradient
resistance

Measures of cardiovascular performance

0 mm Hg



100 mm Hg

Flow α pressure gradient
resistance

Resistance

Relating the flow equation to cardiovascular performance

- The basic flow equation:

$$\text{flow } (Q) = \frac{\text{pressure difference } (\Delta P)}{\text{resistance}}$$

- Q = Cardiac Output (litres /minute)
- Δ P = pressure gradient (equivalent to MAP)
- Resistance = resistance to flow throughout the vascular tree- mainly determined by resistance in the arterioles

Measures of Cardiovascular Performance

…The maintenance of a pressure gradient is critical to maintaining flow and perfusion of tissues

According to the basic flow equation:

$$\text{Flow (cardiac output)} = \frac{\text{pressure gradient}}{\text{Resistance}}$$

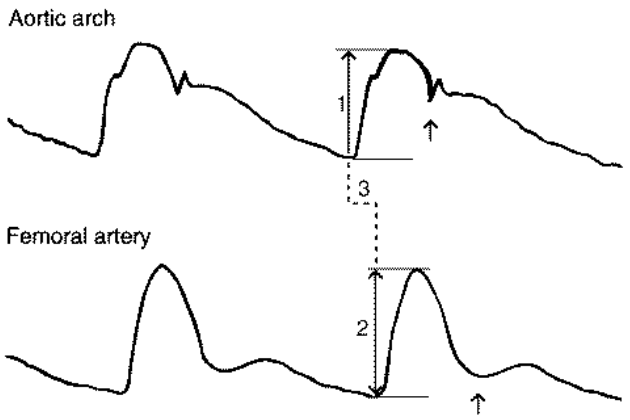
OR

Mean arterial pressure = Cardiac output X resistance

Pressure (mean arterial pressure) is maintained by modulating cardiac output and arteriolar resistance

Understanding flow and pressure…….

- MAP : Mean arterial pressure
  = Diastolic pressure + pulse pressure/3
- Systolic pressure: peak pressure as blood is ejected
- Diastolic pressure: pressure when aortic valve is closed



Understanding flow and pressure…….

- Cardiac output = HR X SV

  cardiac output is amount of blood pumped per minute
- Stroke volume = EDV - ESV

  volume of blood ejected with each heart beat
- Total peripheral resistance (TPR)

  overall resistance to flow through entire circulation

Understanding flow and pressure…….

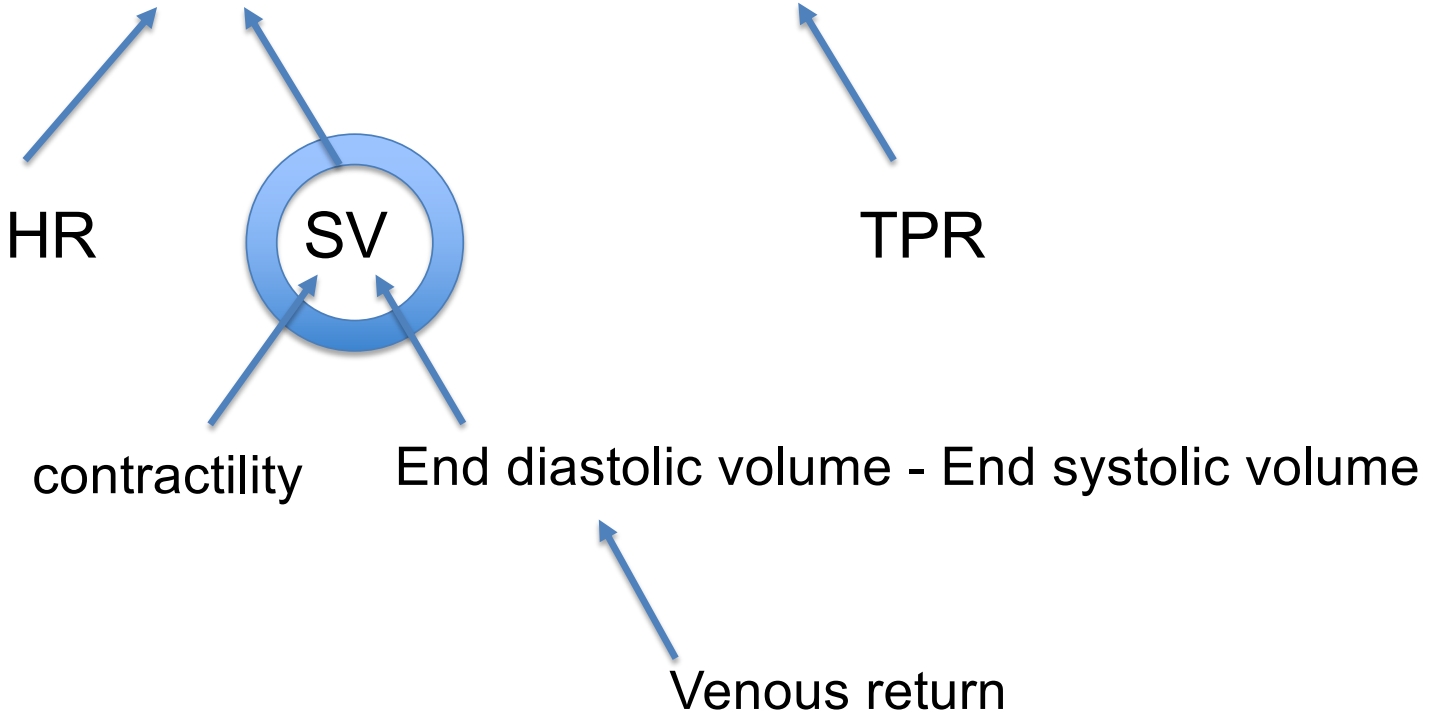
- Mean arterial pressure =

  cardiac output X total peripheral resistance

Factors that affect stroke volume…

- Mean arterial pressure =

  cardiac output X total peripheral resistance



The concepts of preload and afterload

- PRELOAD:

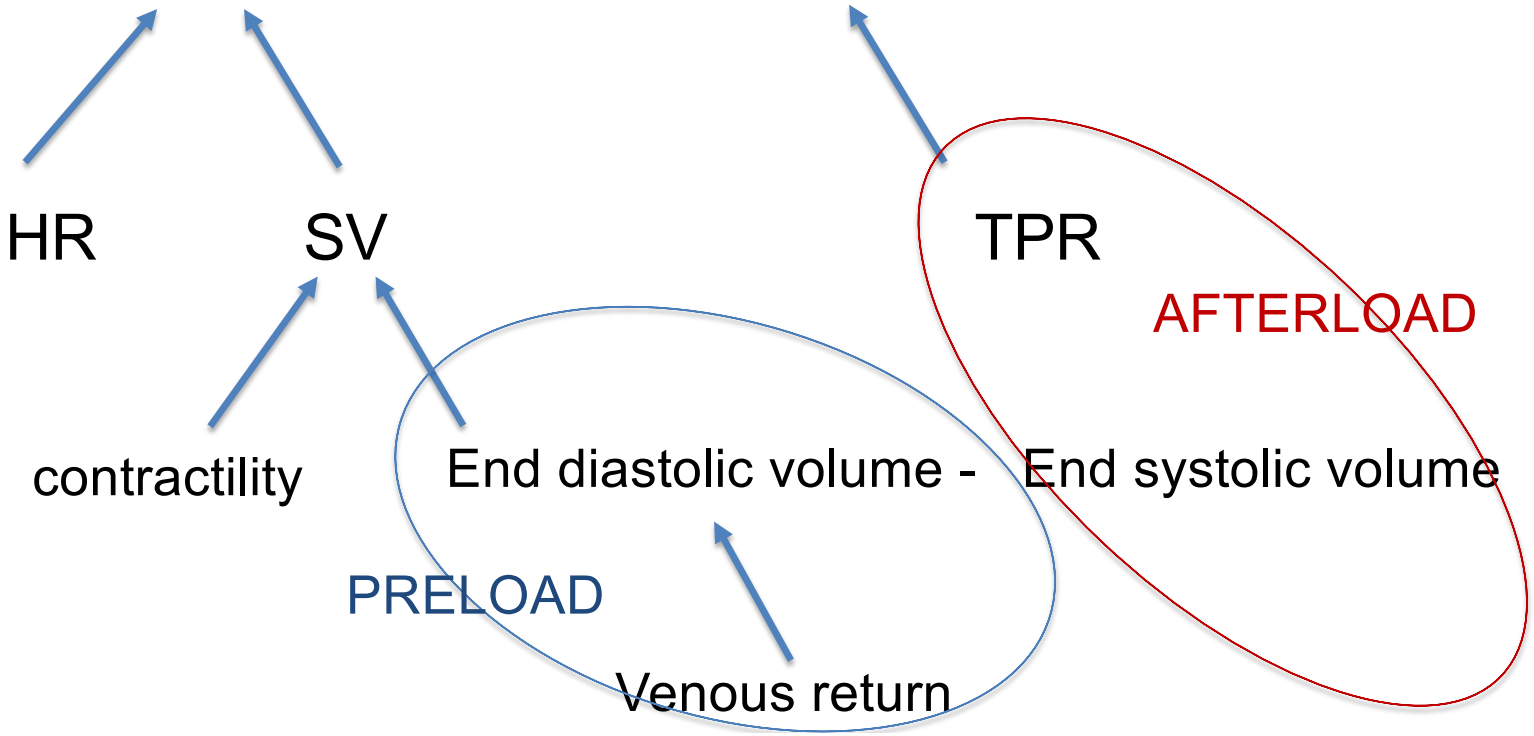
force stretching a relaxed myocardium

- AFTERLOAD:

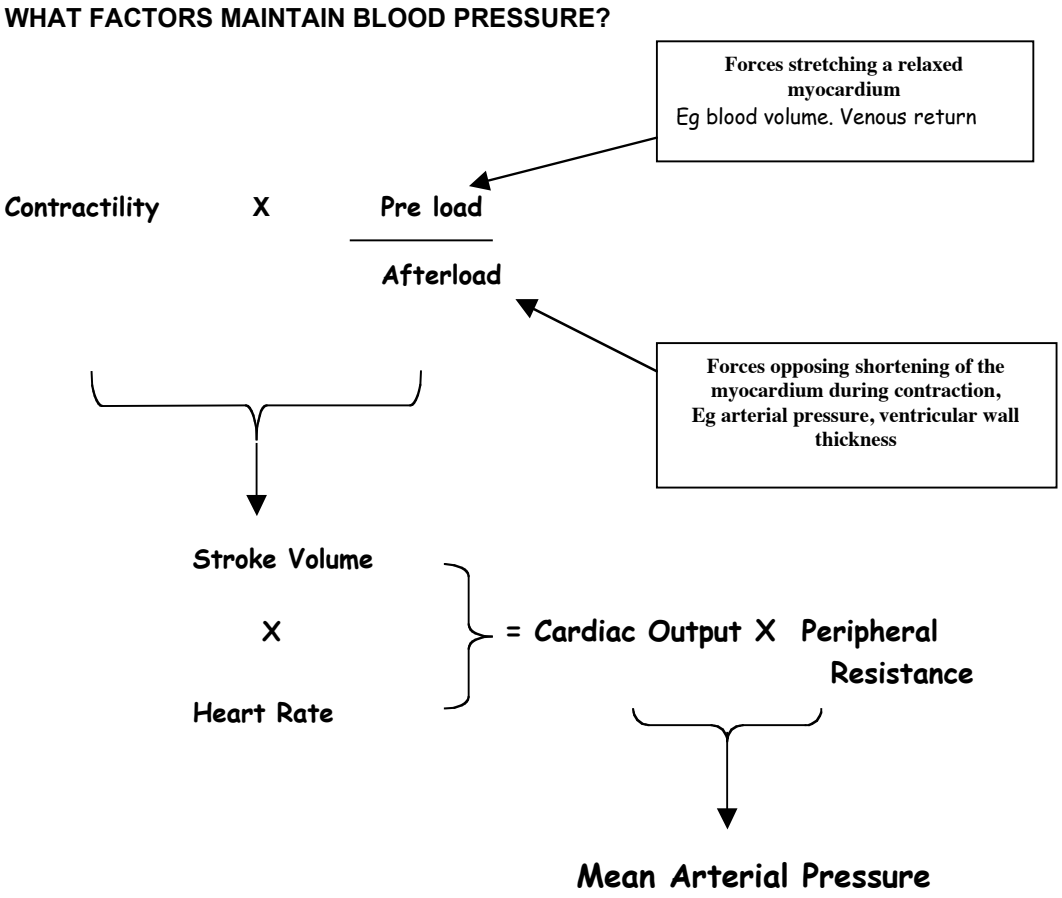
force opposing shortening of myocardium during contraction

Factors that affect stroke volume…

- Mean arterial pressure =
  cardiac output X total peripheral resistance

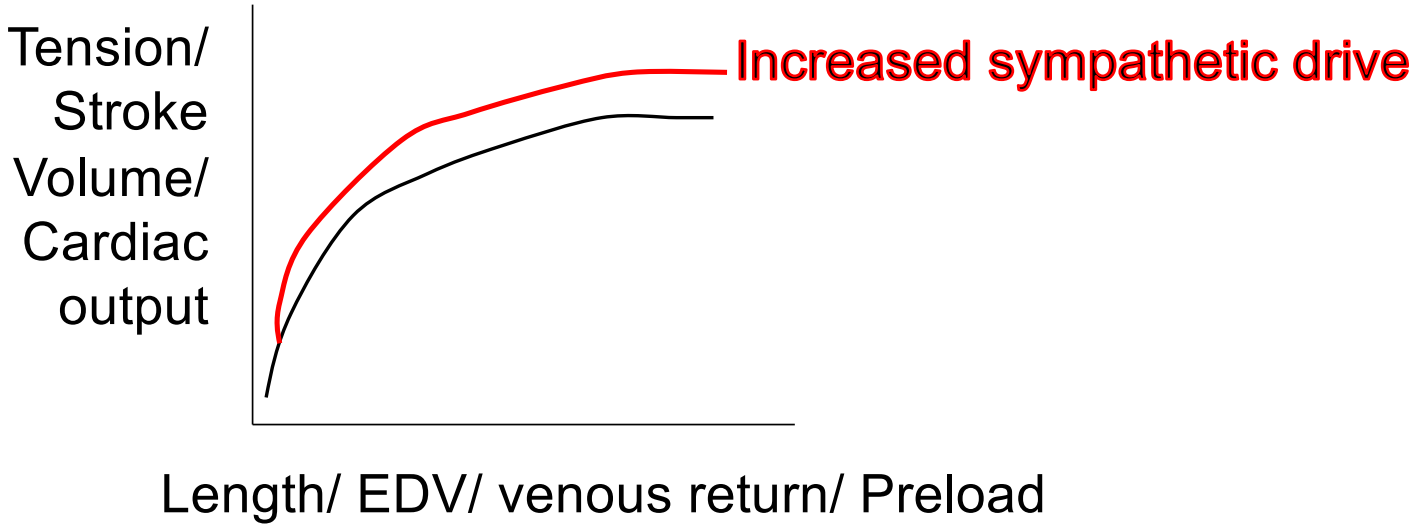


Forces maintaining pressure



Determinants of stroke volume- Frank's back!

- Venous return determines end diastolic volume
- Sympathetic drive modifies contractility



Increased stroke volume

Can be achieved by:

- Increasing muscle length (venous return)..
  - The Frank Starling principle
- Increasing contractility (force generated for any given length) ..
  - By increasing intracellular Ca during contraction

The Frank Starling principle and increasing contractility: two mechanisms to increase stroke volume

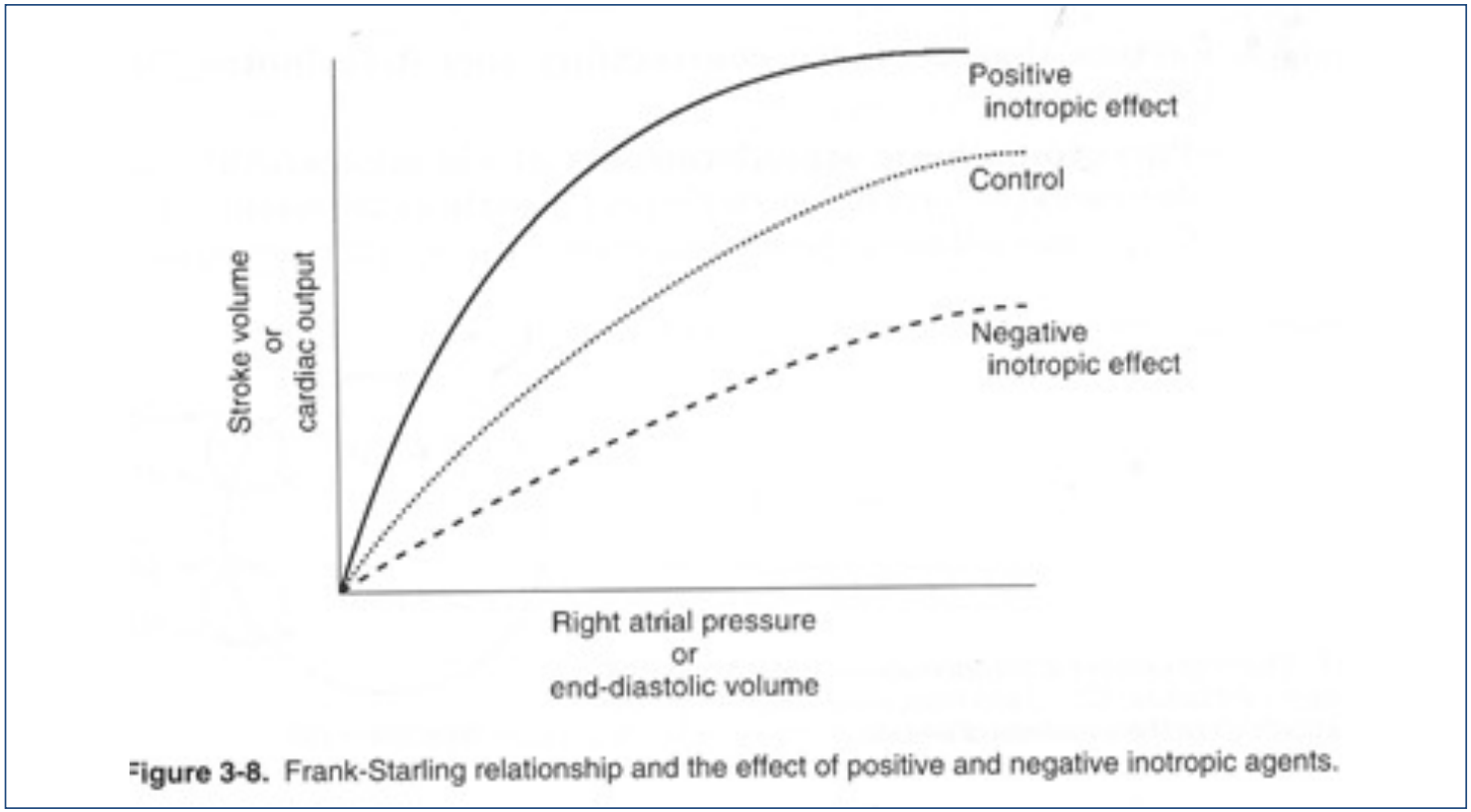
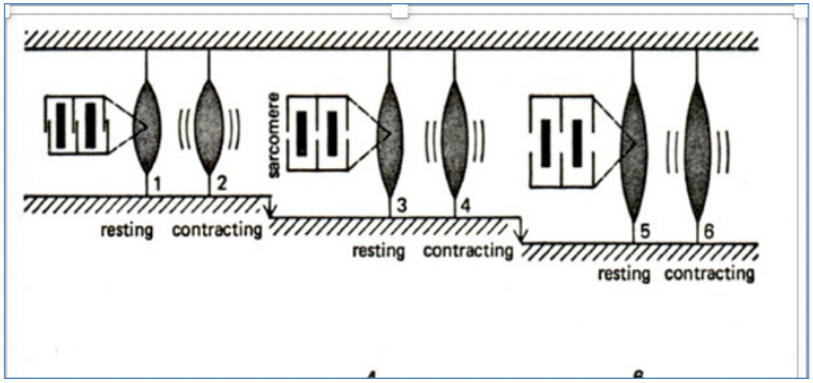


Figure 3-8. Frank-Starling relationship and the effect of positive and negative inotropic agents.

Effect of cell length (end diastolic volume)

- Cell length determines overlap of thick and thin filaments
- Length of relaxed cells is determined by amount of blood in the ventricle



- At a certain length overlap between thick and thin filaments is optimal and for a given rise in Ca will result in maximal tension

- Normal cell length is less that maximal

Physiological Significance of the Frank- Starling relationship

- The length-tension relationship of heart muscle allows for equalization of output from left and right sides of the heart.

- eg increased output from right side of heart leads to increased filling of left ventricle (increased EDV), hence increased stretch of cardiac muscle fibres, increased force development in left ventricle, and increased left ventricular output.

Physiological Significance of the Frank- Starling relationship

- Increased arterial blood pressure leads to higher afterload, and a reduction in volume of blood ejected from the heart with each beat. (ejection fraction)

- The resultant increase in end systolic volume and end diastolic volume increases cardiac muscle stretch, thereby increasing force of contraction and stroke volume.

Increasing contractility: another way to increase stroke volume

- A positive inotrope is any agent that increases peak isometric tension at a fixed length.

- Inotropes act by modulating Ca levels in cardiac muscle cells.

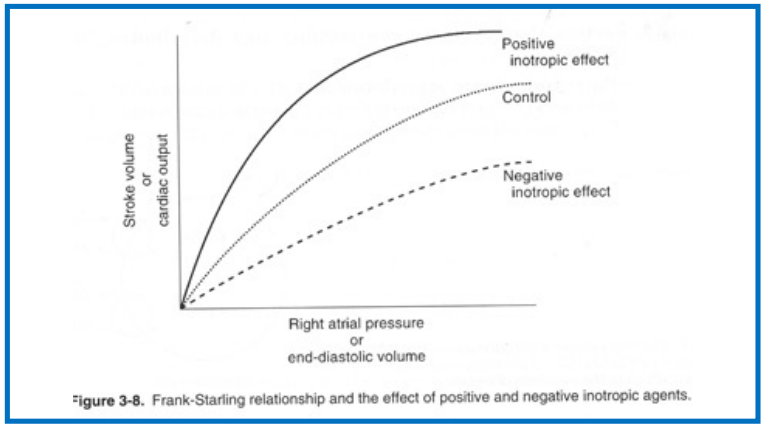


Figure 3-8. Frank-Starling relationship and the effect of positive and negative inotropic agents.

Increasing the force of contraction in cardiac muscle

(compared with skeletal muscle)

- In skeletal muscle – force is increased by increasing
  - Frequency of action potentials
  - Number of fibres stimulated (recruitment)
- In cardiac muscle:
  - Action potential frequency is determined by SA node→ beat
  - All fibres contract with each heart beat

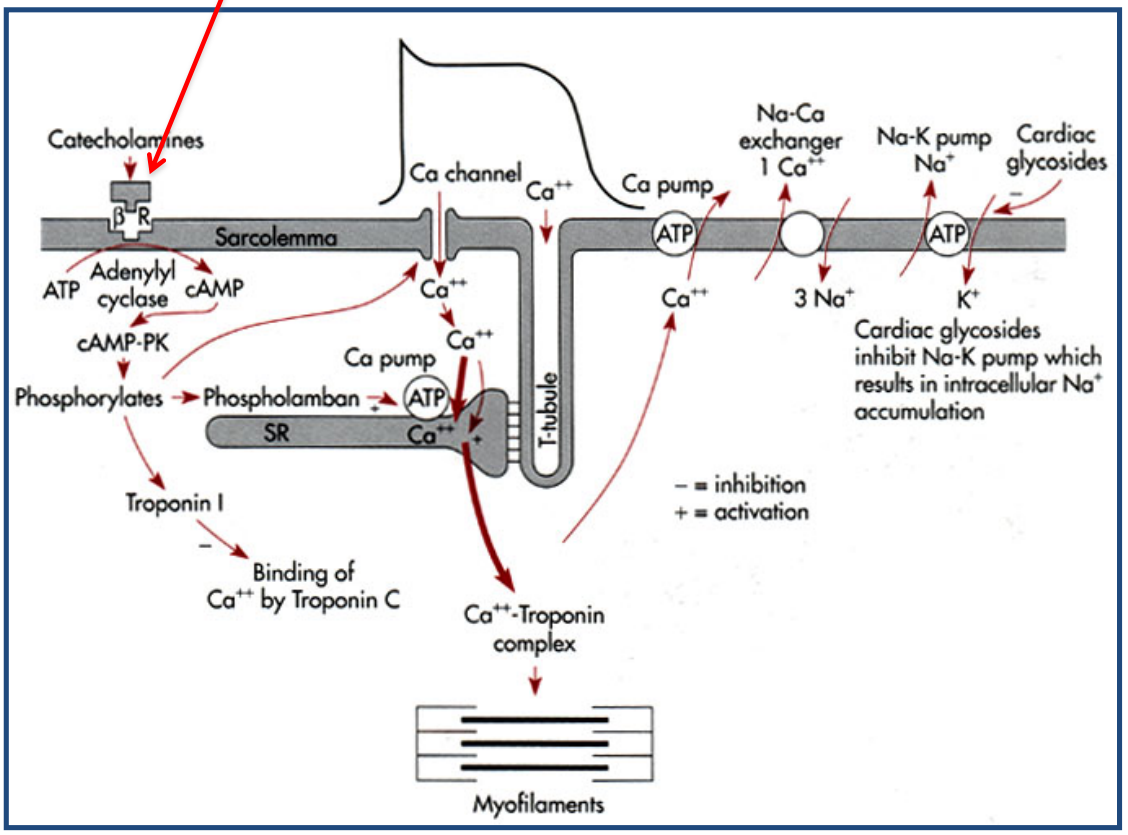
Increasing the force of contraction in cardiac muscle

- Increased force of contraction (at any given fibre length) depends on **intracellular Calcium concentration**

- Intracellular calcium concentration:
  - depends on entry of Ca through VOCC
  - release of Ca from sarcoplasmic reticulum
  - Both of these are modulated by **cell surface receptors**

Increasing the force of contraction in cardiac muscle

receptor operated calcium channel



Depends on stimulation of the sympathetic nervous system

Increasing the force of contraction in cardiac muscle

Binding of noradrenaline to the beta-adrenergic receptor on cardiac myocyte leads to

- Activation of adenyl cyclase
- Increased intracellualr cAMP
- Phosphorylation of VOCC
- Increased inward movement of Ca
- Increased Ca release from sarcoplasmic reticulum (SR) and over time more Ca stored in SR
- Increased actino-myosin cross bridging
- Increased force of contraction

Increasing the force of contraction in cardiac muscle

- Drugs can also be used to increase (or decrease) the force of contraction
- Positive and negative INOTROPES

- (Subject of later lecture)

Frank's back!

- Poor exercise tolerance
- Cough, particularly overnight and in the morning
- Pan systolic murmur

Can we explain Frank's problems?

Why does Frank have poor exercise tolerance…?

- Regurgitation through an incompetent valve leads to reduced stroke volume
- Leads to reduced cardiac output--> reduced exercise tolerance
- Because

Cardiac output (ml/min) =

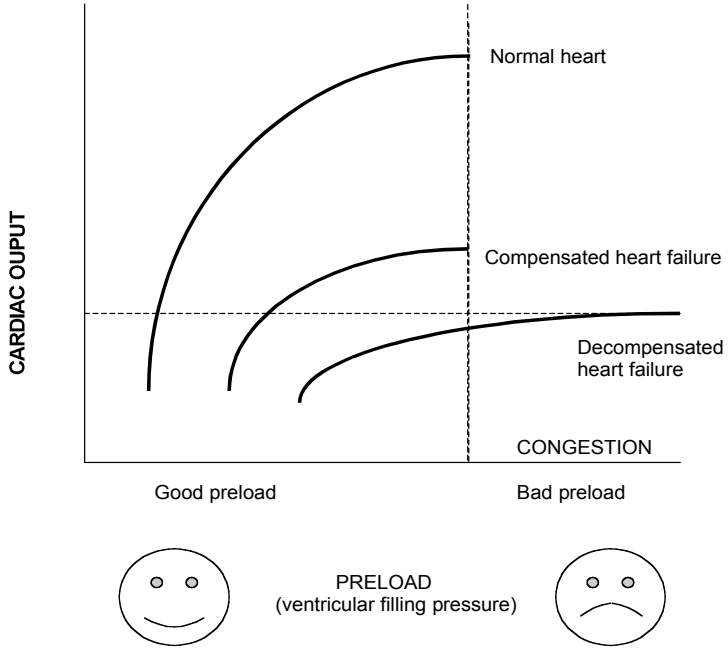
stroke volume (mL) X heart rate (beats/min)

Frank's back again!

- Poor exercise tolerance
- Increased respiratory rate at rest or when sleeping
- Pan systolic murmur

Can we explain Frank's problems?

Ventricular function curves and the Frank Starling principle: Frank's back again!



Bad preload

Increased EDV is not matched by Increased CO

Localising Frank's problem

- Where are the signs- systemic or pulmonary?
- Increased respiratory effort occurs as a result of congestion in the lungs, consistent with a left heart problem
- Mitral valve endocardiosis with regurgitation

IN SUMMARY: Determinants of Cardiac Output: The Mechanics of Systole and Diastole

- Determinants of cardiac output:
  - HR SV and venous return
- Preload and afterload
  - Can you explain what they are?
- Length/tension relationships: the Frank Starling law of the Heart
  - How does this relate to cardiac function?
- Modulators of cardiac contractility: inotropy
  - What is contractility and how is it increased?