CVS
PHYSIOLOGY

Modified NO: 10

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تدقيق: ميس العتيق

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Cardiovascular Physiology

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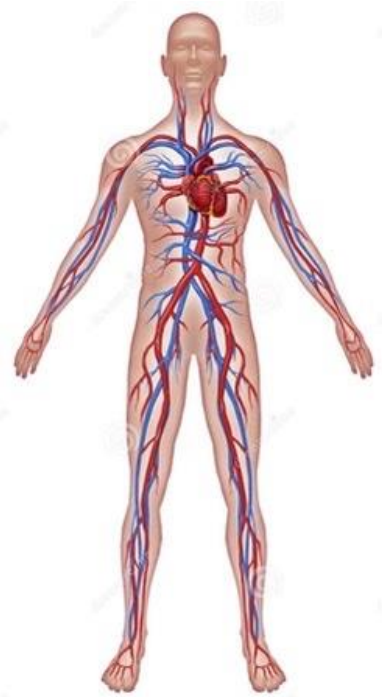

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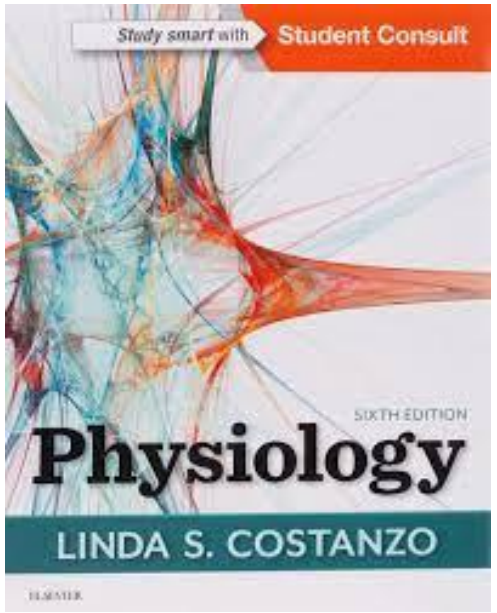
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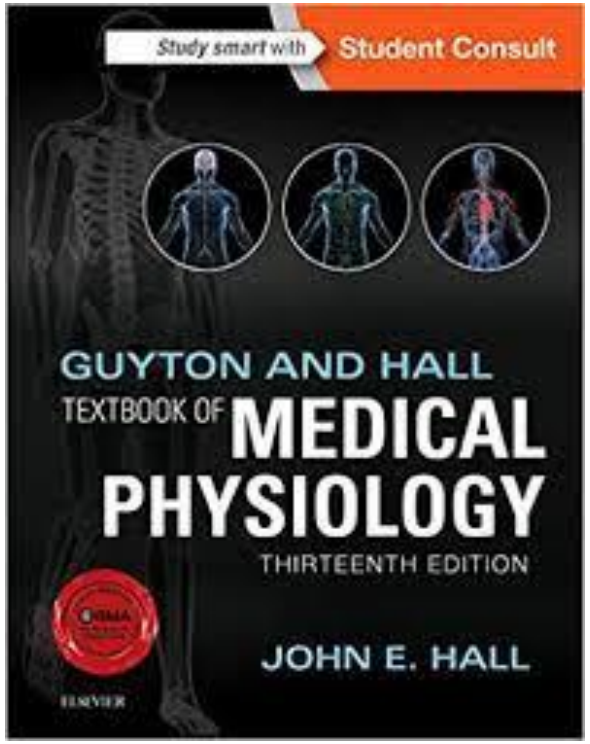
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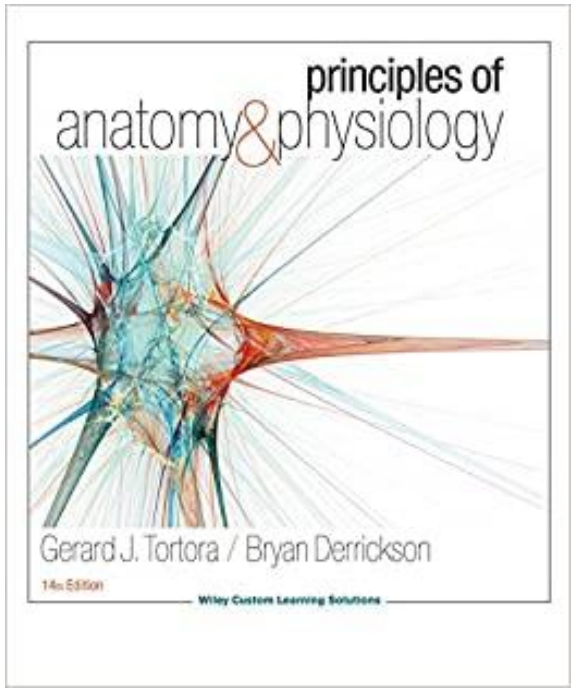
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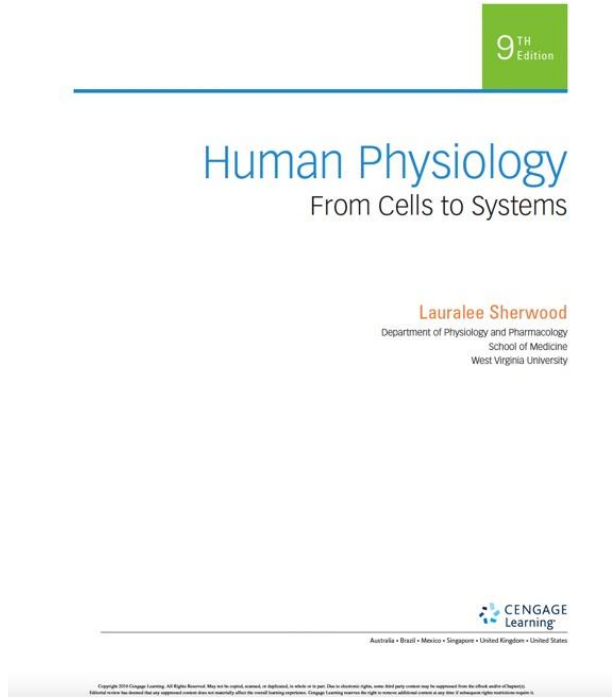
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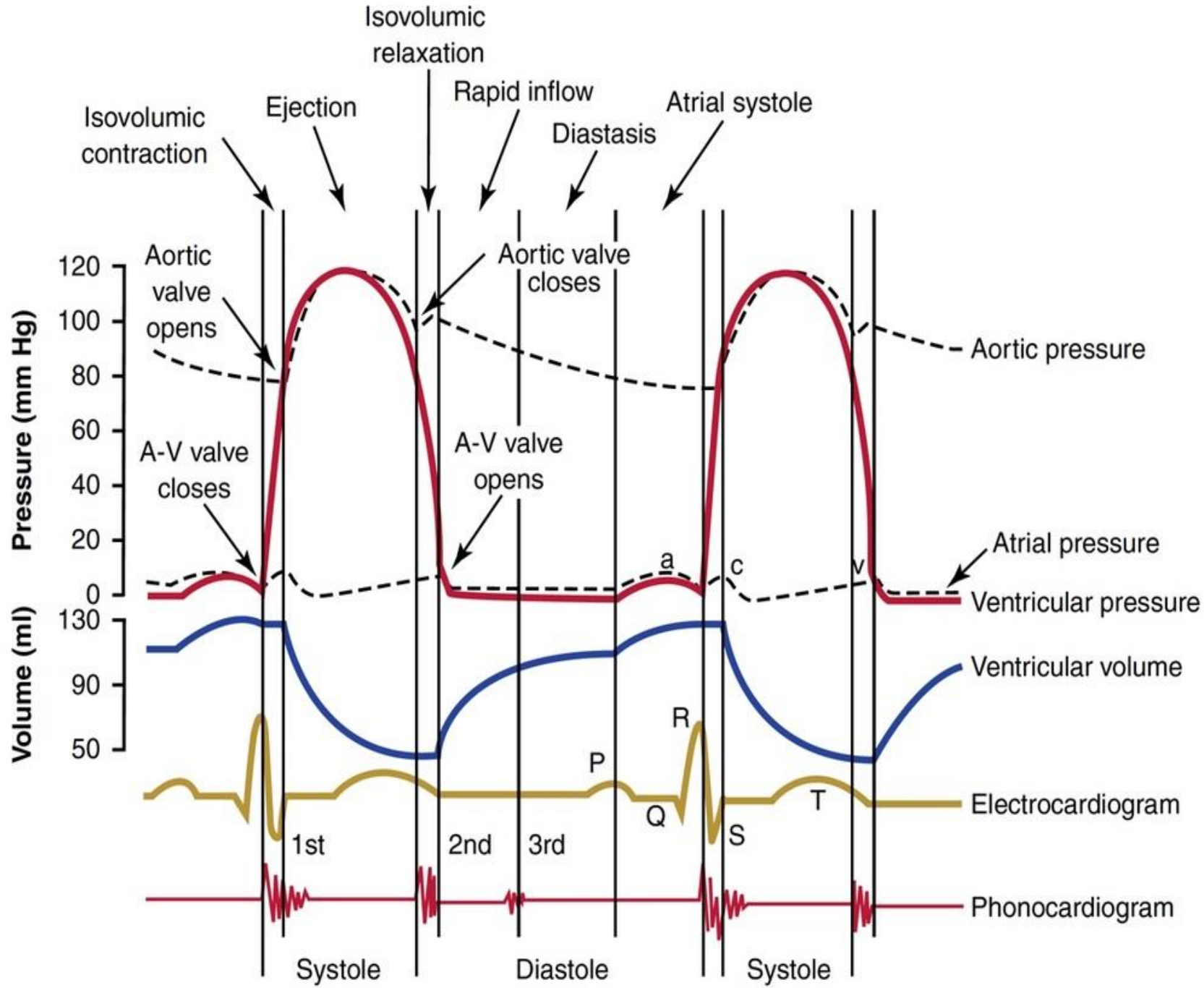
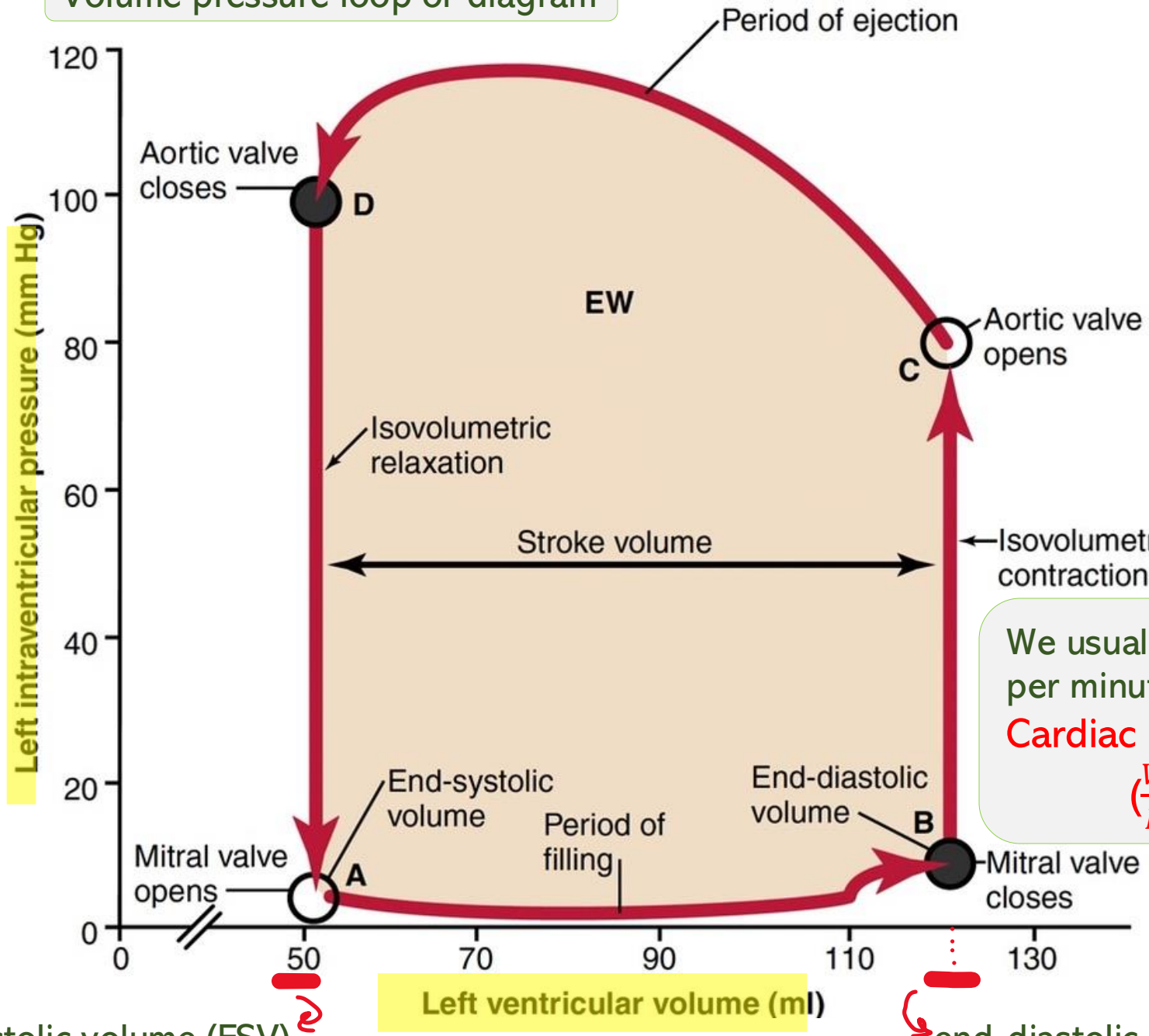
Mechanical events of the cardiac cycle


Isovolumic relaxation
Isovolumic contraction
Ejection
Rapid inflow
Diastasis
Atrial systole
Aortic valve opens
Aortic valve closes
A-V valve closes
A-V valve opens
Pressure (mm Hg)
120
100
80
60
40
20
0
Volume (ml)
130
90
50
a
c
v
Aortic pressure
Atrial pressure
Ventricular pressure
Ventricular volume
R
P
Q
S
T
Electrocardiogram
1st
2nd
3rd
Phonocardiogram
Systole
Diastole
Systole

Volume pressure loop or diagram



Stroke volume is the blood volume ejected by the left ventricle per cardiac cycle

Stroke volume :
EDV – ESV
120 - 50 = 70ml

We usually measure the parameter related to heart per minute, so the stroke volume per minute is?

Cardiac output = Stroke volume X heart rate

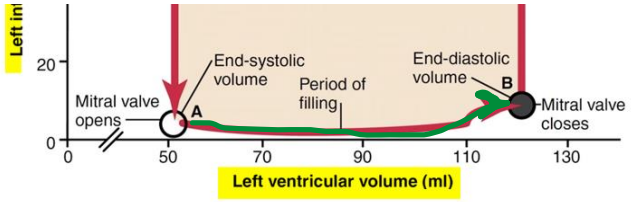
$$\left(\frac{Volume}{Minute}\right) = \left(\frac{volume}{Beat}\right) \quad X \quad \left(\frac{Beat}{Minute}\right)$$

end-systolic volume (ESV)

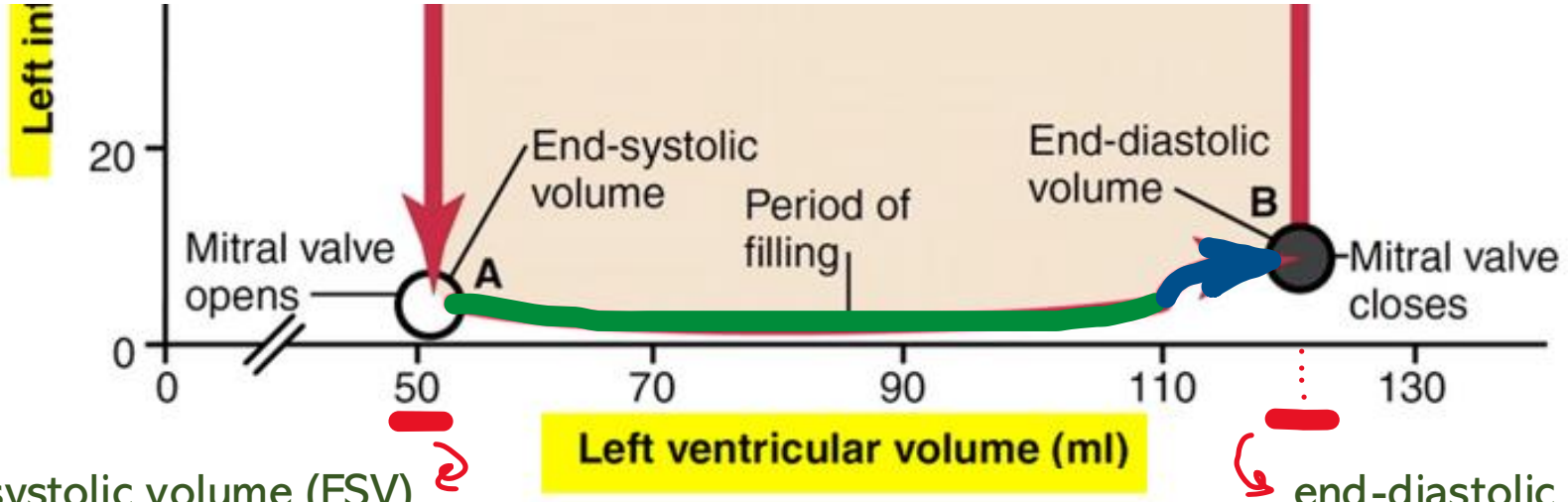
end-diastolic volume (EDV)

Volume pressure diagram (loop)

- Phase I: Period of Filling. (ventricular diastole)



- Start with AV valve opening and end at closure of AV valve.
- begins at a ventricular volume of about 50 ml (end-systolic volume ESV) and a diastolic pressure of 2 to 3 mm Hg (end-diastolic volume EDV).
- The amount of blood that remains in the ventricle after the previous heartbeat, 50 ml, is called the end-systolic volume. (The minimum amount of blood in left ventricle.)
- After systole, ventricular pressure fall rapidly, become less than atrial pressure open the AV valve allowing blood flow.
- As venous blood flows into the ventricle from the left atrium, the ventricular volume normally increases to about 120 ml, called the end-diastolic volume, an increase of 70 ml.
- After that, the ventricular pressure increase slowly (passively) to become higher than atrial pressure so the AV valve close.



end-systolic volume (ESV)

end-diastolic volume (EDV)

In the green arrow →, it's the period of the passive filling in atrial diastole.
In the blue arrow →, the atrial contraction start, atrial systole.

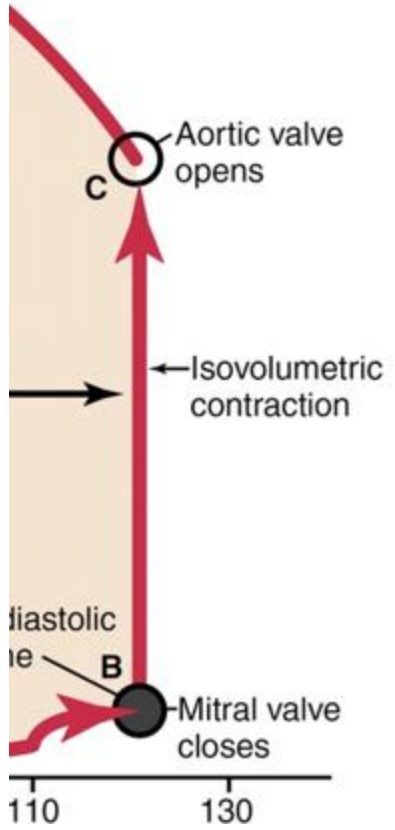
Volume pressure diagram (loop)

- Phase II: Period of Isovolumic Contraction.

- During isovolumic contraction, the volume of the ventricle does not change because all valves are closed.

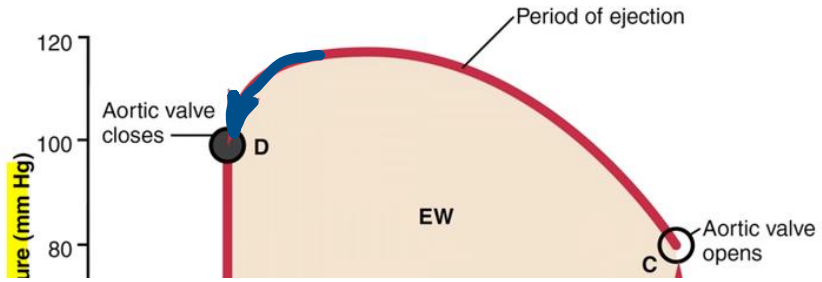
- However, the pressure inside the ventricle increases to equal the pressure in the aorta, at a pressure value of about 80 mm Hg.

- isometric contraction in ventricles increasing the pressure.
- Only the pressure increase in this phase, volume is fixed.
- Start after the end of atrial diastole, ventricular diastole and the closure of mitral valve.
- End with the opening of aortic valve (ventricular pressure higher than the aortic pressure).



Volume pressure diagram (loop)

- Phase III: Period of Ejection. (Ventricular systole)
  - Start with aortic valve opening and end with aortic valve closure.
- During ejection, the systolic pressure rises even higher because of still more contraction of the ventricle.
  - Then the repolarization start (in blue arrow) causing relaxation and decrease the pressure lower than the aortic pressure causing the aortic valve closure.



- At the same time, the volume of the ventricle decreases because the aortic valve has now opened, and blood flows out of the ventricle into the aorta.

Volume pressure diagram (loop)

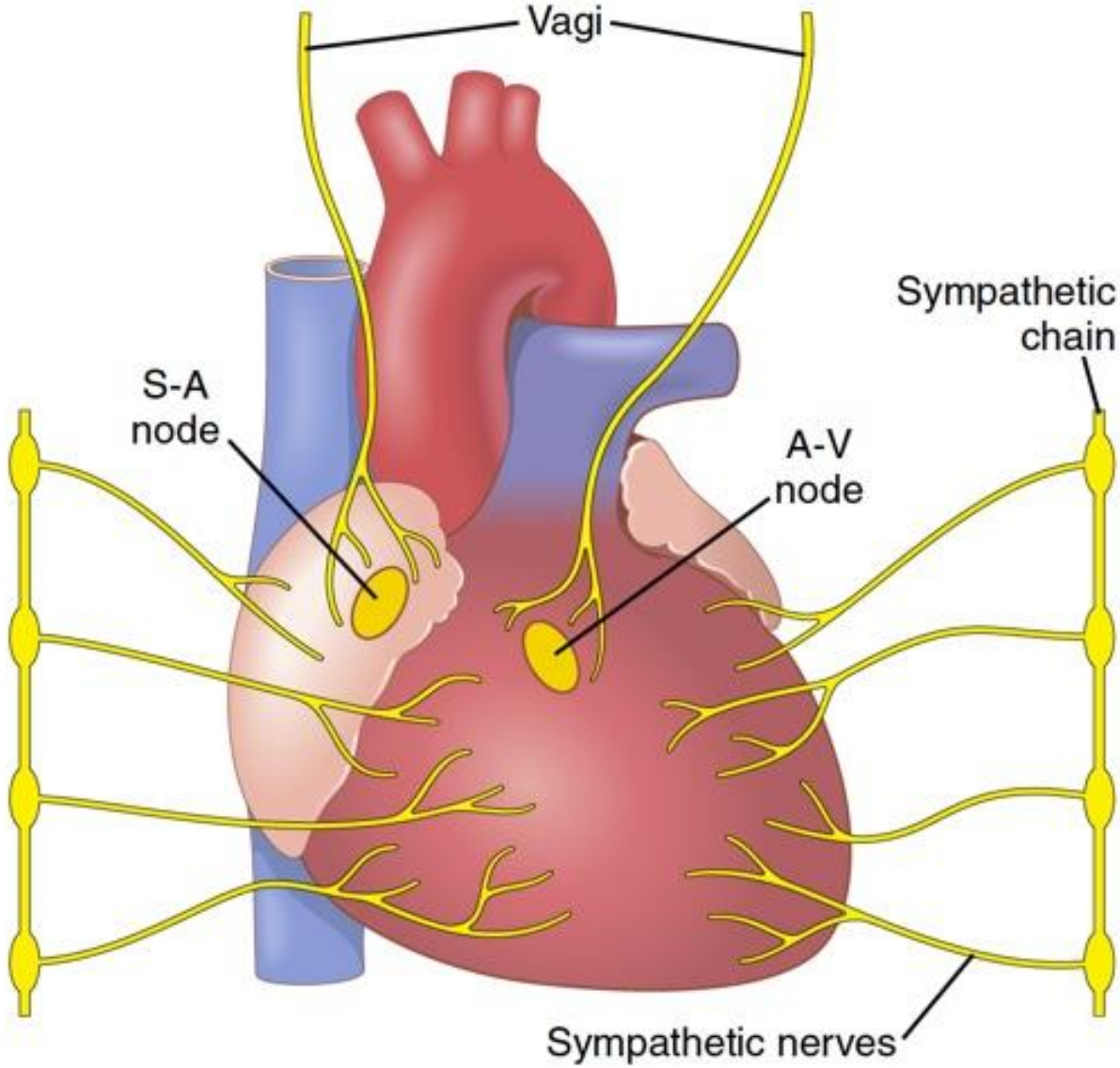
- Phase IV: Period of Isovolumic Relaxation.
- AV valve and aortic valve is closed.
- Only pressure change in this phase, volume is fixed.
- At the end of the period of ejection, the aortic valve closes, and the ventricular pressure falls back to the diastolic pressure level, without any change in volume.
- Ventricular pressure less than atrial pressure causing the AV valve opening.

- Thus, the ventricle returns to its starting point. And the cycle start again (that's why it's also called loop).

Regulation of heart pumping

- The basic mechanisms for regulating heart pumping are as follows:
- (1) intrinsic cardiac pumping regulation (inside the heart) in response to changes in volume of blood flowing into the heart.
- (2) control of heart rate and heart strength by the autonomic nervous system. Extrinsic (outside the heart).
- When we talk about heart pumping, we mainly change two parameters :

1. strength of the contraction (contractility)
2. speed of frequency of the contraction (heart rate)


Vagi
Sympathetic chain
S-A node
A-V node
Sympathetic nerves

1) Regulation: autonomic nervous system

- The pumping effectiveness of the heart is controlled by the sympathetic and parasympathetic (vagus) nerves, which abundantly supply the heart.

Sympathetic stimulation effects

- The overall effect of sympathetic stimulation on the heart is to improve its effectiveness as a pump by:

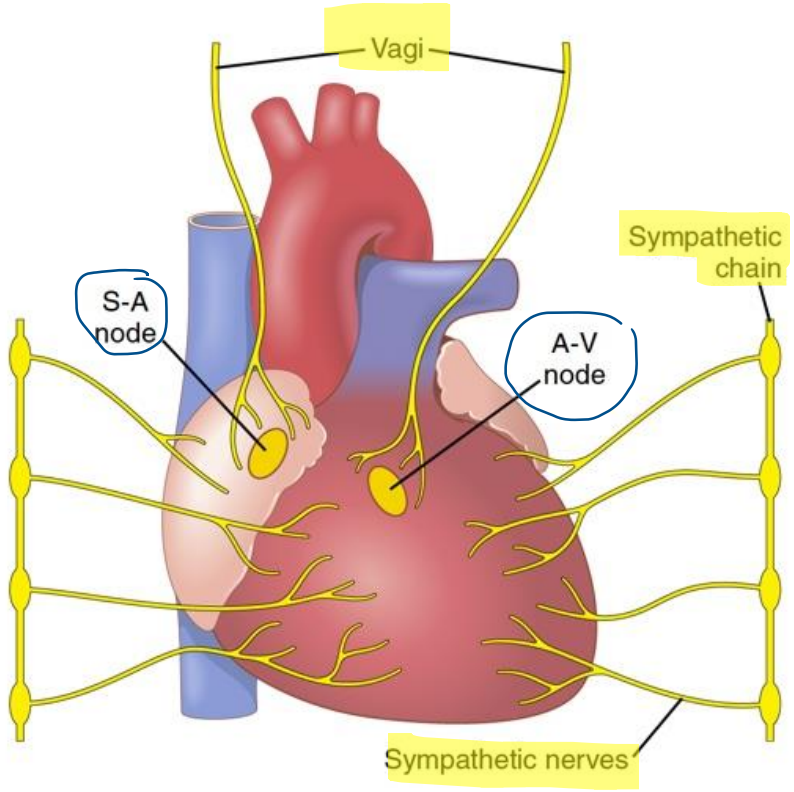
1. ↑ increasing HR (heart rate)
2. decreasing the delay between atrial and ventricular contraction, decreasing conduction time throughout the heart → ↑ increase the speed of conduction.
3. ↑ increasing the force of contraction (contractility).
4. and ↑ speeding up the relaxation process.

Parasympathetic stimulation

- The vagal fibers are distributed mainly to the atria and not much to the ventricles, where the power contraction of the heart occurs.
- This distribution explains why the effect of vagal stimulation is mainly to decrease the heart rate rather than to decrease greatly the strength of heart contraction.
- Nevertheless, the great decrease in heart rate, combined with a slight decrease in heart contraction strength, can decrease ventricular pumping by 50% or more.

Autonomic :

- **Parasympathetic** (vagus nerve): mainly distributed to <u>atria</u>, it will affect:
  1. ↓ Decrease the Heart rate (supply the SA node)
  2. ↓ Delay and decrease the speed of conduction between the atria and ventricle prolong this period (affect the AV node)
  3. ↓ Decrease the atrial contraction (the effect here is not obvious)
  4. No direct effect on the ventricle contraction
  5. Indirect effect on ventricle contraction→ ↓ Heart rate → ↓ overall contractility
- **Sympathetic** : extinctive supply (most of the heart)



Other factors that can affect the heart pump:

- **Chemicals like:**

A. Sympathetic:

1. Epinephrine (from adrenal medulla) → ↑ increase the heart rate, increase the contractility
2. Norepinephrine (from the sympathetic neurotransmitter, its receptor is Beta 1)

B. Parasympathetic (vagus):

1. Acetylcholine (its receptor is muscarinic receptor)

- **Electrolyte**
  - If you inject potassium or the patient have hyperkalemia → ↓ Decrease the Heart rate increase the repolarization, increase the relaxation → possibly flaccidity and heart arrest
  - If the calcium increase → ↑ the contractility will increase
- **Temperature** : can also affect the heart function

Now let's talk about intrinsic regulation

2) Intrinsic regulation: Frank-Starling law

Heart's ability to Adapt to changes around it

- The intrinsic ability of the heart to adapt to increasing volumes of inflowing blood is called the Frank-Starling mechanism of the heart.

Exercise or effort --> venous constriction --> higher venous return

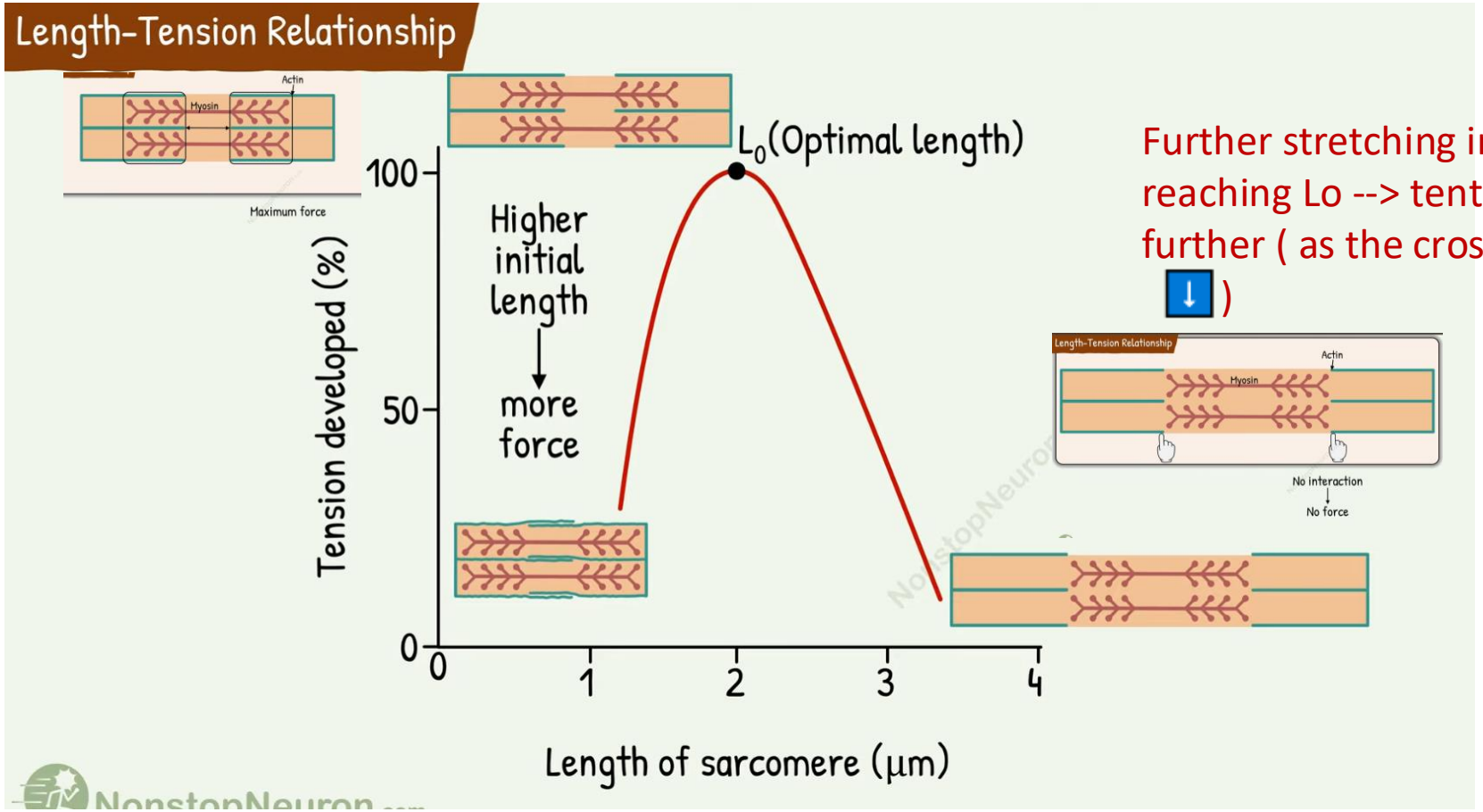
- The more the heart muscle is stretched during filling, the greater is the force of contraction, and the greater is the quantity of blood pumped into the aorta.

- Within physiological limits, the heart pumps all the blood that returns to it by way of the veins.

Let's talk more specifically:
Remember we have one way blood flow (for example talking about left side): vein –atria—ventricle- arteries
#The amount of blood that accumulate in the left ventricle varies :
-at the end of the diastole we got the max volume (EDV) that may vary at different situations
Note: **venous return** : the amount of volume that returns from venous circulation -to-> atrium
VR will determine the volume at the end of the diastole so--> **the source of EDV is venous return**

Ex: (all # here are only for you to understand the concept)
resting EDV = 100 --> stroke volume(amount of blood ejected from the EDV) = 70
Exercise EDV = 150 --> volume ↑ -so-> SV Must also ↑ … How? by ↑ force of contraction (increase the contractility) … How will the heart do that without the use of extrinsic pathway (symp & parasymp) ?
Ans: simply ventricular myo-cardiocyte when it face an amount of volume --> it will expand (same as ballon example : ballon filled with 5ml of water will expand (stretch) < ballon filled with 50 ml of water)
Result : if VR ↑ --> ↑ EDV (as a result) --> more pressure on ventricular myocyte --> more stretching (lengthening of these muscles) --> more tension ability –to-> contract more forcefully

As stretching -> ↑ chance to make cross-bridging between actin & myosin.) ↑ until reach th optimal length (Lo) when almost all the actin are cross –bridging with the myosin)



Further stretching in skeletal muscle after reaching Lo --> tention won't increase further (as the cross –bridging # will ↓)

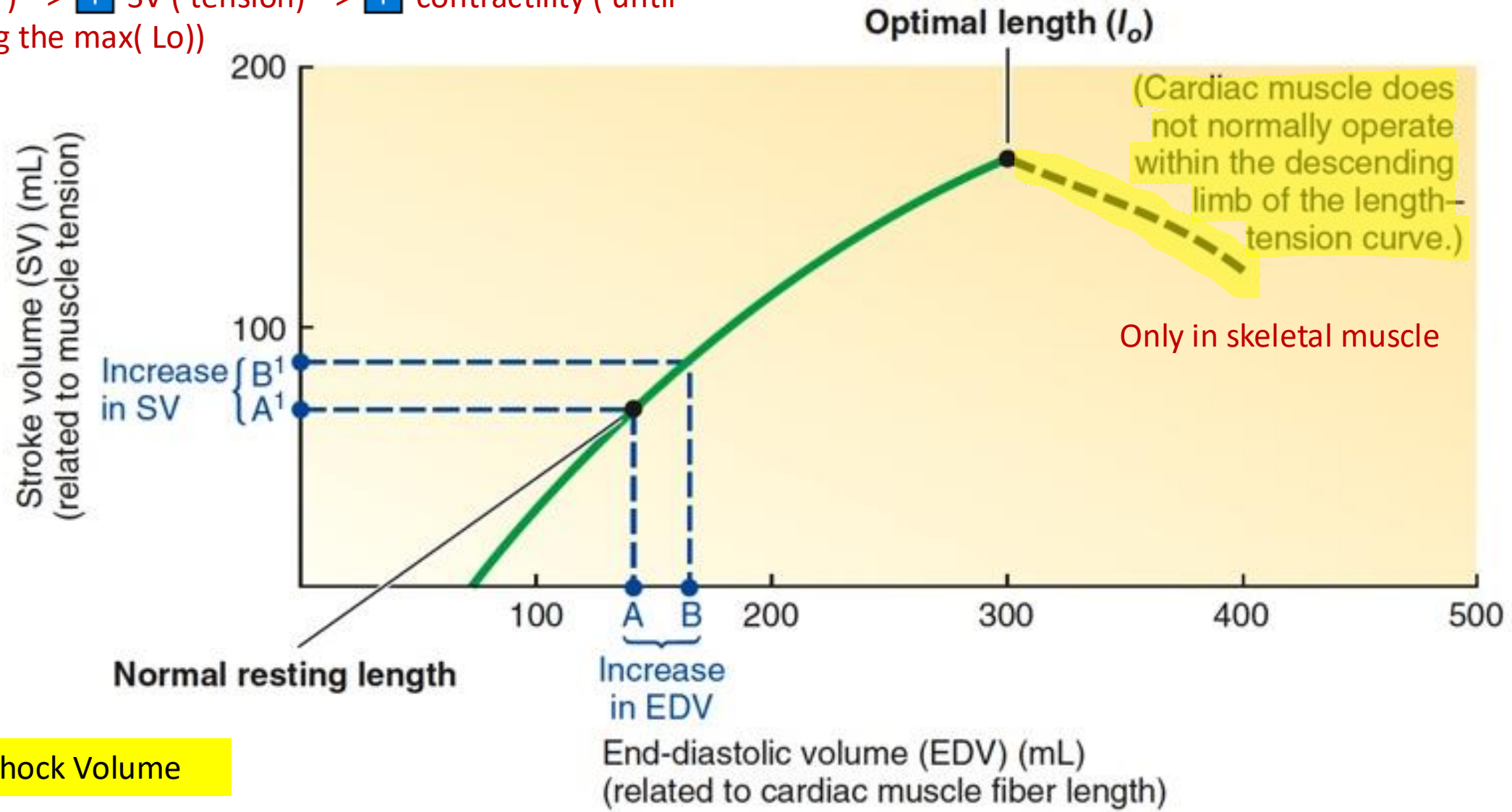
Same concept for cardiac muscle : as cardiac muscle at certain length (optimal length = max length) which is the last point I can stretch the cardiac myocytes

Result : ⚡

💪Skeletal muscle : ⬆ stretching --> ⬆ muscle fiber length --> ⬆ tension they contain

❓Cardiac muscle: ⬆ EDV --> ⬆ EDP (pressure as a result for sure) --> ⬆ SV (tension) --> ⬆ contractility (until reaching the max(Lo))

Length – tension curve (Frank–Starling law of the heart)



SV = Shock Volume

Intrinsic regulation

- Intrinsic control of stroke volume, which refers to the heart's inherent ability to vary SV, depends on the direct correlation between end-diastolic volume (EDV) and SV.
- As more blood returns to the heart, the heart pumps out more blood, but the relationship is not as simple as it might seem because the heart does not eject all the blood it contains.
- This intrinsic control depends on the length–tension relationship of cardiac muscle, which is similar to that of skeletal muscle.
- 1)For skeletal muscle, the resting muscle length is approximately the optimal length at which maximal tension can be developed during a subsequent contraction. When the skeletal muscle is longer or shorter, the subsequent contraction is weaker.

Intrinsic regulation

- For cardiac muscle, the resting cardiac muscle fiber length is less than optimal length. Therefore, the length of cardiac muscle fibers normally varies along the ascending limb of the length–tension curve.
- An increase in cardiac muscle fiber length, by moving closer to optimal length, increases the contractile tension of the heart on the following systole.
- Unlike in skeletal muscle, the length–tension curve of cardiac muscle normally does not operate at lengths that fall within the region of the descending limb. That is, within physiologic limits, cardiac muscle does not get stretched beyond its optimal length to the point that contractile strength diminishes with further stretching.

Intrinsic regulation

- This intrinsic relationship between EDV and SV is known as the Frank–Starling law of the heart. Stated simply, the law says that the heart normally pumps out during systole the volume of blood returned to it during diastole; increased venous return results in increased SV.

As we have pre --> we have after-load

- The extent of filling is referred to as the **preload** because it is the workload imposed on the heart before contraction begins.

- The ventricle wants to contract to eject blood,
before this contraction there is a load on the ventricle cells (the blood volume it contain – the EDV (from venous return) - before the contraction (precontraction)) --> we call it **preload** and it reflects the venous return ✨(more about venous load & preload relation in the vascular system)
    - slides about preload, afterload and venous return are at the end of this lecture 🔥

Length-tension relationship

So cardiac muscle tension will increase with the length due to 2 factors :

1) ↑ In cross – bridging between actin & myosin (same as skeletal)
2) ↑ Ca sensitivity …. (as cardiac muscle length ↑ --> Ca sensitivity ↑ as well)

Similar in

- Although the length–tension relationship in cardiac muscle fibers depends to a degree on the extent of overlap of thick and thin filaments, similar to the length–tension relationship in skeletal muscle, the key factor relating cardiac muscle fiber length to tension development is the dependence of myofilament Ca sensitivity on the fiber's length.

Cardiac differ in

The mechanism :

- Specifically, as a cardiac muscle fiber is stretched as a result of greater ventricular filling, its myofilaments are pulled closer together side by side.
- As a result of this reduction in distance between the thick and thin filaments, more cross-bridge interactions between myosin and actin can take place when Ca pulls the troponin– tropomyosin complex away from actin's cross-bridge binding sites—that is, myofilament Ca sensitivity increases.
- Thus, the length–tension relationship in cardiac muscle depends not on muscle fiber length per se but on the resultant variations in the lateral spacing between the myosin and actin filaments.

Intrinsic regulation

- What causes cardiac muscle fibers to vary in length before contraction? (in left ventricle)

Mainly: varying amount of EDV …. (↑ volume → ↑ stretching ---until ----> optimal length)

- The main determinant of cardiac muscle fiber length is the degree of diastolic filling.
- The greater the diastolic filling (more volume) , the larger the EDV, and the more the heart is stretched. The more the heart is stretched, the longer the cardiac fibers before contraction. The increased length results in a greater force on the subsequent cardiac contraction and thus in a greater SV.

Intrinsic regulation

- Advantages of the Cardiac Length–Tension Relationship

- The built-in relationship matching SV with venous return has two important advantages. (the purpose of the length-tension Relationship)

- **First**, this intrinsic mechanism **equalizes output between** both sides ; **the right and the left sides of the heart** so that blood pumped out by the heart is equally distributed between the pulmonary and systemic circulations (that will go to the pulmonary veins--> lungs)

  . -remember that heart is 2 separate pumps, but shouldn't be separated completely, a certain type of communication must be there as both outputs must be equal … And this is by the intrinsic mechanism.

Intrinsic regulation

- If, for example, the right side of the heart needs to eject a larger SV, more blood enters (the veinous circulation) the pulmonary circulation, so venous return to the left side (left atrium first) of the heart increases accordingly (more veinous return arrived)
  .
- The increased EDV of the left side of the heart causes it to **contract more forcefully**, so **it too pumps out a larger SV**. In this way, output of the two ventricular chambers is kept equal.
- If such equalization did not happen, too much blood would be dammed up in the venous system before the ventricle with the lower output.

Intrinsic regulation

The 2nd advantage of the cardiac length-tension Relationship

- **Second**, when a larger CO is needed, as during exercise (change in homeostasis)--> more need of blood flow to the skeletal muscles , venous return is increased by the sympathetic nervous system constricting the veins(as the veins are capacitates – store blood until needed-) to drive blood forward and by the contracting muscles compressing the veins, which squeezes more blood toward the heart(**increasing venous return**)
- Induce intrinsic mechanism (length- tension relationship) The resulting increase in EDV automatically increases SV correspondingly. (this cardiac output is very important to supply the tissues with more needs of blood)
- Because exercise also increases HR, these two factors act together to increase CO so that more blood can be delivered to the exercising muscles.

What happens if there is sympathetic stimulation on top of this intrinsic mechanism?

Sympathetic stimulation

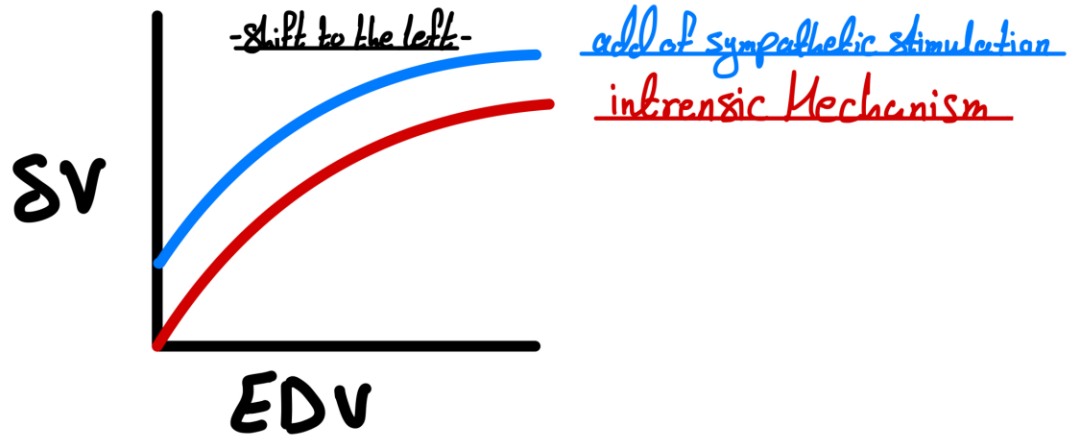
- Sympathetic stimulation and epinephrine enhance the heart's contractility, which is the strength of contraction at any given EDV.
- In other words, on sympathetic stimulation the heart contracts more forcefully and squeezes out a greater percentage of the blood it contains, leading to more complete ejection.
- This increased contractility results from the increased Ca influx triggered by norepinephrine and epinephrine.
- The extra cytosolic Ca lets the myocardial fibers generate more force through greater cross-bridges.

See the diagram in the next slide

With sympathetic stimulation: the same volume –will generate --> higher –force of - contraction (as there will be a doubling effect of the intrinsic mechanism) …. so left shift of the length-tension curve

Sympathetic stimulation

- In effect, sympathetic stimulation shifts the Frank–Starling curve to the left.
- Depending on the extent of sympathetic stimulation, the curve can be shifted to varying degrees, up to a maximal increase in contractile strength of about 100% greater than normal.



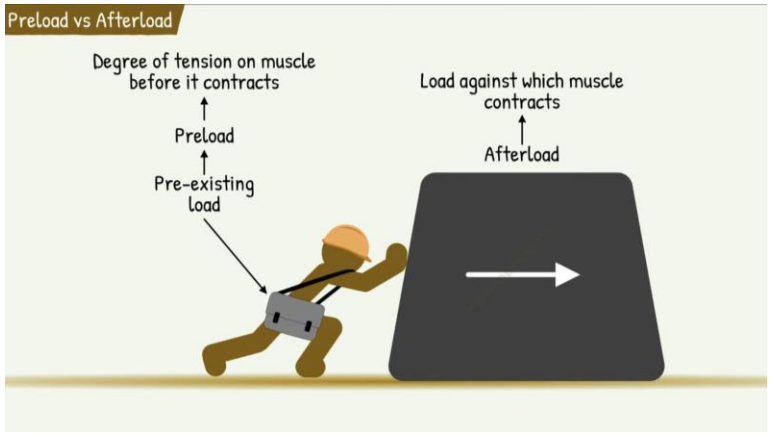
Other intrinsic mechanisms

less important than Frank-starling

- In addition to the important effect of lengthening the heart muscle, another factor increases heart pumping when its volume is increased.
- **Stretch** specifically **of the right atrial wall** (where we have SA node) directly increases the heart rate by 10% to 20%, which also helps increase the amount of blood pumped each minute, although its contribution is much less than that of the Frank-Starling mechanism.
- A stretch of the atrium also activates stretch receptors and a nervous reflex, the Bainbridge reflex, that is transmitted by the vagus nerve and may increase heart rate an additional 40% to 60%. will be further explained in vascular system.
- You must know that : When there is a stretch in atria --> will be reflected and activate certain reflexes.

Preload

Extra image:

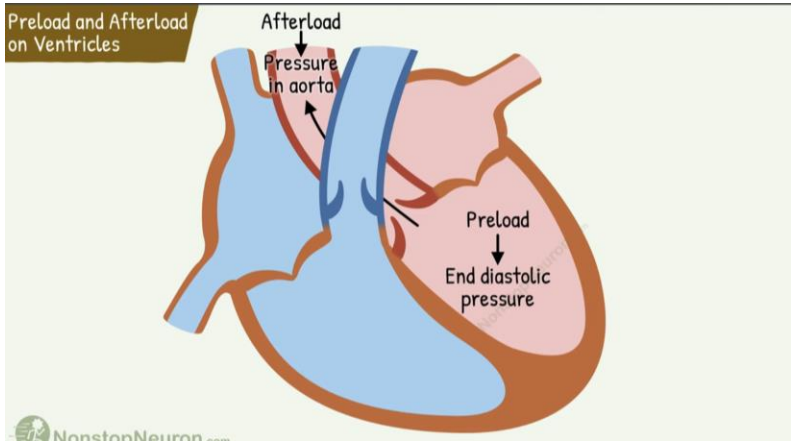


- Preload:
- the degree of tension on the muscle when it begins to contract.

- For cardiac contraction:
- Preload is usually considered to be the end-diastolic pressure when the ventricle has become filled.

Afterload

Extra image:



- Afterload:
- the load against which the muscle exerts its contractile force.

- For cardiac contraction:
- Afterload of the ventricle is the pressure in the aorta leading from the ventricle (or the resistance that oposing this ejection force).

Certain situations/ conditions will ↑ the Afterload –so--> will affect the pumping function of the heart

Venous return

(the source of EDV)

determine the volume at the end of the diastole

VR (opposite to cardiac output (CO)) .. more about this point in the next lec!

- Venous return is important because it is the quantity of blood flowing from the veins into the right atrium each minute.

- The venous return and the cardiac output must equal each other except for a few heartbeats when blood is temporarily stored in or removed from the heart and lungs.

The Exception:

- **For a few heartbeats, the balance may temporarily shift:**
  - **Blood may be stored in the heart or lungs (e.g., during diastole when the heart chambers fill).**
  - **Blood may also be removed from these areas briefly.**
- **These slight imbalances occur during activities like breathing or positional changes but are quickly corrected.**

Purpose:

This mechanism ensures smooth blood flow and stable circulation, adapting to short-term changes in body needs.

Thank you

Additional sources :
preload vs afterload

اللّهمّ إنّي أسألك النصر لأهل غزة الذي نصرت به رسولك وفرّقت به بين الحقّ والباطل حتّى أقمت به دينك وأفلجت به حجتك، يا من هو ولي ذلك والقادر عليه ، اللهم نستودعك أهالي غزّة وفلسطين فانصرهم واحفظهم بعينك التي لا تنام، واربط على قلوبهم وأمدهم بجُندك وأنزل عليهم سكينتك وسخر لهم الأرض ومن عليها.

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	21	Inverted sentence	As stretching -> ⬆ chance to make cross-bridging between actin & myosin.) ⬆ until reach th optimal length (Lo) when almost all the actin are cross –bridging with the myosin)
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا!!