PASSION ACADEMIC TEAM JU - MEDICINE

Cardiovascular System

Sheet#

Lec. Date :

Lec. Title : Cardiac Output

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Cardiac Output

Slide 2

- Cardiac output🩸 : the amount of blood ejected or pumping by each ventricle per minute.
- mathematically🎲: cardiac output =heart rate*stroke volume
- What is the stroke volume 🤔?
- Stroke Volume: the volume of blood ejected by each ventricle with each beat.(يعني حجم الدم المضخوخ بالنبضه الواحدة)
  and it's equal in adults =70

  طيب نرجع على ال—> cardiac output
  Normal Heart rate=70 and Stroke volume in adults =70
  So the cardiac output =70*70=4900ml =5L/min
  And this is the normal value of cardiac output in adults 👴 (5L- 6L /min)

  طيب نرجع للتعاريف الان🤓

- End diastolic volume: The volume of blood in each ventricle at the end of diastole .=130
- End systolic volume: The volume of blood remains in each ventricle at the End of systole and the value =50ml in adult.

  وبالتالي ال Stroke Volume and it's 130-50=80(يعني هذه النسبه بهاد الافرج بين 70-80)

  الفرق ما بين ال EDV and ESV؟
  (Stroke Volume)👑

  The percentage of end diastolic volume ejected with each beat(the ratio of stroke volume to EDV) it is what we called : Ejection Fractions
  تيجي نمثلها بصيغة معادلة...

  Ejection Fraction = (stroke Volume/EDV) *100%

  هي المعادلة بتعطيني ال (percentage of EDV that ejected with each beat).

وهي ال (percentage) إذا حصل فيها أي (change) حيكون عنا problems بال(contractility in the heart)أو(Heart failure)💔
(بعرف الجملة مستفزه بس يلا كمل🙄)

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Slide 3:

Factors that effect the cardiac output: 🎲من القانون🎲

- Stroke Volume
- Heart failure

-These two factors are the main determinant of cardiac output .
-These variables are interdependent(بيعتمدو على بعضهم البعض), they usually Changes together and in opposite direction .
As heart rate goes up and stroke volume goes down and vice versa.

طيب لو صار عندي

- **Reduction in Heart Rate to below 70 beat /min what will happen for cardiac output?**
  As heart rate decrease below 70 beat/min Cardiac output almost remains <u>constant</u> 🤷‍♀️
  Why?
  Because heart rate decrease but stroke volume will increase , as we mention before they are interdependent (change together in opposite direction)

طيب ليش؟ ليش إذا صار عنا decrease in heart rate رح يصير عنا increase in stroke volume؟
Because when heart rate decrease the ventricle will have enough time for maximum filling so we will have good filing and good ejection so stroke volume will increase and cardiac output will be constant .

- **What will happen if heart rate decreases below 50 beat/min?**
  We will have increase in stroke volume but the increased can't compensate the high slow heart rate , therefore the Cardiac output is decreased.

- **If the heart rate <u>increases up to</u> 200 beat/min in this case the stroke volume is decreased, why?**
  - Because we don't have enough time for filling so;
  - ➡️ No good ejection ➡️ No good diastolic volume ➡️this will effect the cardiac output .
  - In this case cardiac output remain constant , or may be increase slightly because we have increase in heart rate➡️ from increasing in heart acceleration

- **But if we have increase in heart rate <u>more than</u> 200** ➡️diastolic period shorten too much and stroke volume is markedly <u>decrease</u> the cardiac output will also be <u>decreased</u> ➡️because the <u>decreased</u> stroke volume <u>not compensated</u> by Heart acceleration.
- **يلا على السلايد الي بعده**👏🏻🚶🏻‍♂️

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Slide 4 (Regulation of heart rate)

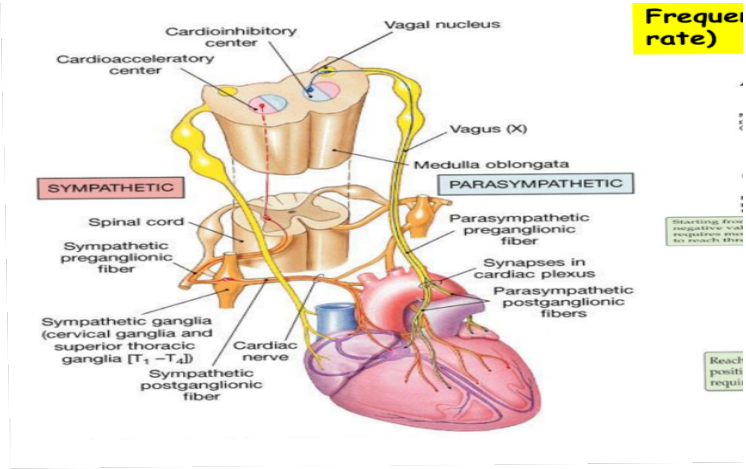
- **Mechanism that regulate the heart rate can be divided into 2 categories:**✌🏻
  - **Neural mechanism**
  - **Humoral mechanism**

- **And the <u>Neural mechanism</u> have 3 Types** 👌:
  1. **Autonomic regulation**
  2. **Reflex regulation**
  3. **Regulation by higher centers** 🔥

Slide 5 (Autonomic control)

(Autonomic means sympathetic and parasympathetic control)

متل ما بنشوف بالصورة الي تحت⬇️



Both sympathetic and parasympathetic divisions of autonomic nervous system have an effect on heart rate.

وطبعاً نحنا بنعرف انو معظم الأعضاء بالجسم في عندها dual innervation الي همه ⬇️

(Sympathetic and parasympathetic)

يعني أعضاء الجسم بتحصل innervation من التنين sympathetic and parasympathetic بس بالعادة بكون واحد اكتر من التأثي على حسب ال organ الي عنا .

So heart have dual innervation but it's normally , at rest : parasympathetic control is the dominant mechanism, therefore the parasympathetic control of SA node(responsible of heart rate)is the dominant mechanism not sympathetic therefore the basal heart rate is less than the intrinsic heart rate.

What do we mean in intrinsic heart rate?

Intrinsic heart rate is the rate of discharge of SA node when the heart is completely de-innervated.

يعني لو عملنا⬇️

release of the heart from the body we will don't have innervation and the intrinsic heart rate will be very high and higher than basal because the basal heart rate =(70-80) but the intrinsic =(100-110) and this in the de-innervation .

طيب لو كان عندي innervation لل heartشو حتكون؟🤔😏

If we have innervation of the heart it will be <u>Parasympathetic</u> and it will inhibit the intrinsic heart rate that's will be (70-80) <u>not</u> (100-110) therefore the heart rate will be less.

The parasympathetic of the heart:

Originate from ➡️nucleus tracts solitaries

Originate from ➡️dorsal motor nucleus of vagus

Originate from ➡️nucleus ambiguous

- **And the vagus nerve from these places 👆 mainly supply the atria ,(SA node) and AV node very little supply to ventricle**

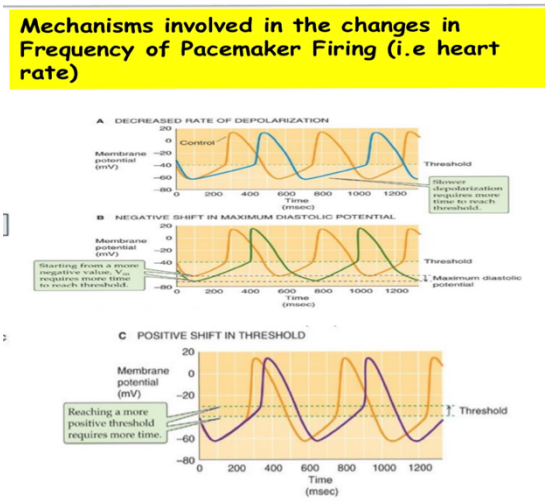
وبقدر احكي انه لا يؤثر على ال ventricle تمامًا وهاد الاشي الو أهمية(سؤال النا ,السؤال تحت أيها الشغفيون دورو على الإجابة يلا)

<u>What is the important of no parasympathetic innervation for ventricle?!!</u>🤔😀 بما أنكم فاضيين اشغال فكرو بهاد السؤال وهو الكم فقط(فلنتفكر🤦‍♂️)

- **We have two branches for vagus nerve:**
  - **Right vagus nerve**
  - **Left vagus nerve**

Right vagus nerve predominantly supplies SA node while the left vagus nerve predominantly supplies AV node

Parasympathetic vagus stimulation decreases the heart rate



بمعنى اخر أتطلع على الرسم ال curve العلوي : بنلاحظ على هاد ال curve انه ال parasympathetic vagus stimulation decreases the heart rate by decreasing the slope of the prepotential phase.

- **Pre potential phase to reach threshold needs longer time ➡️ less firing➡️less heart rate**
- **(Pre potential is the phase 4)**

So vagus stimulation effect the SA node:

- **Decreases the slope of prepotential decreases the slope of phase 4 and the rhythmicity of the pacemaker cells (SA node) is reduced resulting in the bradycardia.**

- **Parasympathetic has➡️negative cronotropic effect any agent the modulate heart rate is an agent that has either positive or negative cronotropic so in this case the parasympathetic stimulation or the vagus nerve or the acetylcholine(because the acetylcholine is the neural transmitter release from parasympathetic)so the acetyl COA or the vagus they are negative cronotropic agents because the have a negative effect on the heart rate they reduce the heart rate.**

- **As we say the stimulation of vagus nerve result in reduction in the heart rate and this happened because of longer time for the prepotential to reach the threshold and this happened result of secretion of acetylcholine from the vagul nerve endings and the acetyl COA Effect on SA node remains for a short time as acetyl CoA is rapidly destroyed by a specific enzymes known as acetylcholinesterase.**

Now lets talk about sympathetic effect 🧠🥰

- **Sympathetic effect too but in stress and exercise.**

- **Sympathetic supplies all parts of the heart (SA node , AV node , atrial regions and ventricular regions and all parts of the conduction system)**

- **Sympathetic has positive <u>cronotropic</u> effect (increase the <u>heart rate</u>)**

- **At the same time sympathetic has positive <u>ionotropic</u> effect (ionotropic have relationship with <u>contractility of the heart</u>)**

- **Sympathetic innervation increases the heart rate therefore :**

(positive cronotropic) also increases the contractility of the heart (positive ionotropic)

Why sympathetic effect the contractility?

لانو بأثر على ال⬅️myocardium — الي معظمها موجود بجدران ال ventricle لذلك ال parasympathetic لا يؤثر على ال ventricles وبالتالي لا يؤثر على الmyocardial parts وبالتالي لا يؤثر على ال contractility أما ال sympathetic بأثر عليهم لهيك عنده positive ionotropic وبالنسبة لل parasympathetic فهوه كمان يؤثر على ال contractility in atrial regions ولكن انقباض ال atria not essential for filling

The sympathetic innervation to the heart is plentiful happened result from releasing of norepinephrine and sometimes result of releasing of epinephrine from adrenal medulla and both are effect beta 1 adrenergic receptors on the heart therefore we

will have increasing in calcium and sodium permeability inside the cardiac cells that will lead to increasing in the heart rate and contractility.

لو بدي أتطلع على الرسمات الموجودة فوق👆 بنلاحظ ان هي الرسمات ال٣ هيه عبارة عن ال mechanisms التي تؤدي إلى زيادة ال heart rate نتيجة ال autonomic innervation

Figure A ➡️ it's mechanism of (decreased rate of depolarization)
متل ما حكينا قبل انو ال⬇️

parasympathetic make increase in slope of prepotential so➡️ it take longer time for this phase to reach the threshold (الخط المتقطع)

Blue line represent parasympathetic effect 💙

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ال mechanism الأخرى التي من خلالها تعمل هذه ال autonomic divisions على زيادة أو نقصان ال heart rate هي عبارة عن ما يسمى بال negative shift in maximum diastolic potential
It's (Figure B)

بنلاحظ انه ال parasympathetic بيعمل على ما يسمى ال hyper-polarization يعني ال
Phase 4 start from more negative value then we will have hyperpolarization⬇️
يعني بصير عنا ⬅️negative shift

Green line represent parasympathetic effect 💚

بنلاحظ بالرسمه انه بدأ من(70-)بدلاً من (50-) مثلاً
Which means longer time is needed for diastolic potential to reach threshold ➡️andFiring the action potential 🔥therefore by this mechanism the parasympathetic innervation decrease the heart rate (والعكس بالنسبة لل sympathetic)

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3rd mechanism➡️ (positive shift in threshold)
يعني ال threshold بدل ما كانت عبارة عن 45- مثلاً رح تصير 30-وهذا معناه:
- less negative and more positive and this mechanism use by parasympathetic to decrease the heart rate (وبالتالي بعمل ➡️positive shift in threshold therefore Longer time is needed to reach threshold to fire an action potential .
(العكس تمامًا بال sympathetic)

(Figure C)

Purple line represent parasympathetic effect 💜

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Slide 6 (Reflex control)

- **The Reflex control include:**

- **Baroreceptor reflex**
- **Chemoreceptor reflex**
- **Bainbridge Reflex**
- **Cushing's Reflex**

يلا نبدأ فيهم وحده وحده🧐 :

I. Baroreceptor reflex:
what's the component of Reflex ?

- **Receptors**
- **Afferent neuron**
- **integrating Center**
- **Efferent neuron**
- **Target tissue**

In the Baroreceptor we have a <u>mechanical</u> receptors

- **called <u>Baroreceptors</u>**
- **Located in the <u>carotid sinus</u> and <u>aortic arch</u>**
  and these receptors are stimulation by high blood pressure, once they are stimulation they become active after activation they stimulate send impulses through afferent neurons to nucleus tracts solitaries .and this impulses that are generated in these baroreceptors after their stimulation by high blood pressure are transmitted to the nucleus tracts solitaries by afferent neurons
  - **Afferent neurons➡️(مكانها بال ninth and tenth cranial nerve)**
  - **Nucleus tracts solitaries ➡️(مكانها بال medulla oblongata)**

When nucleus tracts solitaries stimulate these area send inhibitory impulses to vasomotor center (VMC) ➡️ Inhibition for VMC ➡️ reduction in sympathetic activity ➡️increasing in parasympathetic activity ➡️bradycardia ➡️heart rate reduction

Heart Rate increases occur in condition in which Baroreceptor are less stimulated such as hypotension.

II. Chemoreceptor reflex :-

- **In chemoreceptor we have <u>chemical</u> receptors in the carotid sinus called carotid bodies.**
- **Chemoreceptor stimulated by change in chemical composition of the blood as occurs in hypoxia , hypercapnia , and acidosis.**

- **Activation of chemoreceptor primarily produces Bradycardia , but heart rate may unchanged or even slightly increased by secondary effect.**

- **Mild hypoxia causes tachycardia, but moderate to severe hypoxia decreases the cardiac output by suppressing myocardial contractility by stimulation of chemoreceptors ➡️ so reduction in cardiac output and suppression for myocardial activity.**

- **Carbon dioxide changes :-**

it's effect may be direct or indirect in the myocardium

  - **The direct effect for carbon dioxide leads to depression in myocardium if I have hypercapnia**
  -
  - **The indirect effect leads to stimulation for peripheral chemoreceptor and this will effect the heart rate.**

- **Acidosis make depresses in myocardium (less contraction) why?🤔🤓**
  Because if I have reduction for intercellular ph will leads to decrease the endoplasmic reticulum calcium leads to decrease the contractility and reduction in intracellular ph lead to decrease sensitivity of mayofilament to calcium
  (Troponin sensitivity to calcium becomes less
  ➡️ So less sliding ➡️ less contraction

III. Bainbridge reflex :-

- **It's cardioaccelators reflex**
- **Leads to increase the heart rate**
- **Increase in heart rate when venous return increase**

Right atrial ⬅️Bainbridge reflex لهيك ممكن نسميه بدل right atrium يحدث بال reflex هذا ال reflex

IV. Cushing's Reflex :-

- **This reflex become active when hypotension occur that decrease blood flow to the VMC so➡️direct stimulation of VMC➡️activation of sympathetic, which cause tachycardia and vasoconstriction .**
- **But the consequent increase in pressure due to Cushing reflex stimulates the baroreceptors that finally result in bradycardia.**

Slide 7 (control by higher centers)

بعض ال⬇️
(emotional states like stress and anxiety)
بتعمل⬇️
(stimulation for higher center in the brain cortex)
والتي بدورها تؤثر على ال⬇️
(cardiovascular center)
الموجود بال⬇️
(Medulla)
وبالتالي رح يصير عندي⬇️
(firing for more sympathetic or parasympathetic)
الي بالنهاية سوف يؤدي الى⬇️
(Change in Heart rate)

وبس كدااا يلا السلاايد الي بعدو🤓🏃

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Slide 8 (Humoral control mechanism)

We have many hormones that effect the heart rate like:thyroxine, catecholamines these hormones increase heart rate.

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Slide9 (physiological variation)

We have many physiological variation that effect the heart rate.

(هالمعلومه للمعرفه ومو مطالبين فيها😄 مبدأ زيادة الخير خيرين)

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Slide 10 (Factors effecting stroke volume)

1. **Cardiac pumping power:** this is effected by the cardiac inotropic state
   - **Factors that effect cardiac pumping power**
     - Preload
     - After load
     - Contractility

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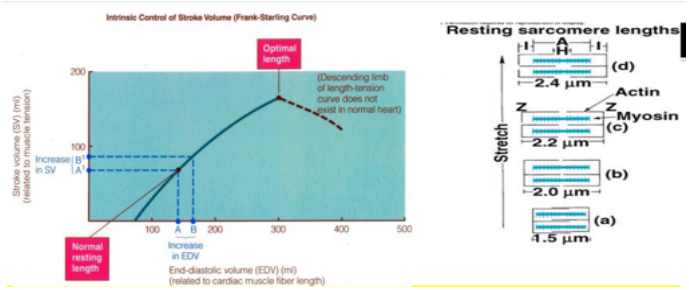
Slide 11 (cardiac preload)

نبدأ بالعوامل الان:

Preload: is the end diastolic volume.

We have relationship between the preload and force of tension

متل ما بنشوف بالصورة الي تحت👇



- **X-axis represent preload or EDV**
- **Y-axis represent force of tension developed within muscle fibers**

- **Increase in EDV ➡️ increase in force of contraction ➡️ increase in stroke volume**

لما صار في عنا زيادة بال EDVمن ال A لل Bعلى ال x-axisتؤدي الى زيادة ال stroke Volume من A1الى B1على y-axisهذا هو عبارة عن (Frank-starling curve)

Frank-Starling low: within limits the force of cardiac pumping power contractility is directly proportional to the initial length (preload or EDV) of the cardiac muscle fibers.

EDV = preload =length of muscle fibers of the heart ⬅️يعني هدول كلهم بدلو على نفس الاشي

(هذه الصوره عبارة عن علاقة ما بين ال initial length (EDV وال tension اذاً هو length-tensio curve) وهو Frank-starling loop

هلا بالتعريف الي فوق بحكيلك انو within limits لهيك بدكم تعرفون انو في عنا limit. يحدد عن طريق ال length لل cardiac muscle

So we have optimum length that has the highest contraction of the muscle

لهيك بنلاحظ عند طول ال 2.2لل muscle fiber في عندي ال Maximum contraction في عندي maximum force tension

After this peaks length ➡️ we reach limit ➡️ after this limit ➡️ ventricular contraction decrease at either shorter or longer muscle fiber length

2,2 is the optimum sarcomere length that have the peak (limit) the maximum force of contraction and maximum tension that has the maximum stroke volume

بالرسمة الي فووق 😳👆

At 2.2 we have optimum length and optimum overlapping between actin and myosin so we will have:

- **More shortening ➡️ more velocity of shortening ➡️ more tension ➡️ more stroke volume**

- **The importance of this mechanism is that it helps the heart to eject whatever volume of blood it receives within limit.**

لهيك القلب إذا وصله دم زياده عن الطبيعي بيقدر يتعامل مع الوضع وبقدر يضخ الدم بدون أي محفز خارجي لانو بصير عنده more stretching بال ventricle يعني more length يعني more overlapping بين ال actin وال myosinوبالتالي more contraction و more stroke volume.
وهذا يجعل القلب قادر على التخلص من(🩸 extra volume of blood)

غير هي الطريقة لسا كمان عنا طريقتان😀👇 :

The 2nd mechanism is :
The Increase in stretching lead to make the troponin more sensitive for calcium so➡️ more sliding➡️ more shortening

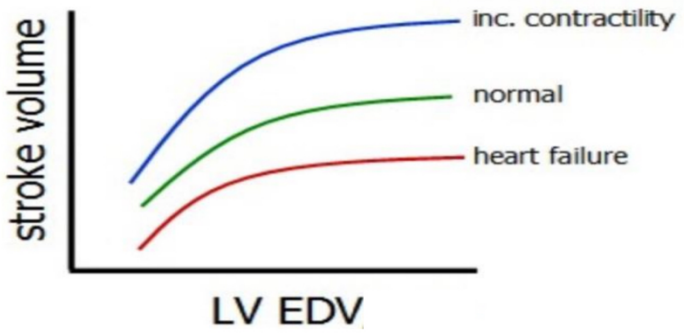
The 3rd mechanism is :
Every increase in myocyte (sarcomere) lead to decreases the muscle fiber diameter which would bring actin and myocin molecule closer to each other ➡️ which facilitate there interaction to each other ➡️ more sliding ➡️ more contraction ➡️ more stroke volume.

وهيييك بنكون خلصنا الريكورد الأول لهي المحاضرة👏🏻👏🏻 خدلك بريك وكملل🤓💪🏻

لعند الدقيقة 9:31شرح مُعاد وهو ب slide 11 لهيك حكمل من 😊 slide 12

Slide 12 (The Frank -starling curves)

Significance of Starling law



This curve in the picture is:
Length – tension curve OR Frank – starling curves
X-axis represent EDV
Y-axis represent stroke volume
and we have 3 curves:

- **Normal heart ➡️ green in color 💚**
- **Curve that represent the Frank-starling curve for heart failure ➡️ red color❤️**
- **Normal heart which is stimulated from outside (increase contractility) ➡️ blue color 💙**

لهيك بنلاحظ انو at a given end diastolic volume يعني خد أي volume من محور xواطلع لفوق

- **At a given end diastolic volume in the heart failure the normal (EDV- stroke volume curve) shifted downward and to the left and this is due to reduction in pumping power of the heart.**

- **But if we stimulate the normal heart by external mechanism such as (norepinephrine stimulation, sympathetic stimulation)frank – starling curve shifted upward and to the left.**

In this case we have increased in stroke volume, why?
Because we have two factors or two mechanism that effect the contractility of normal heart:

1) **Frank – starling mechanism:-**
   انو في امتلاء وبالتالي في length معين وبالتالي في contraction نتيجة هاد الامتلاء
2) **External stimulation by some factors called positive inotropic that's lead to increase the contractility . E.g:(epinephrine)**

What is the significance of frank-starling mechanism?
This mechanism helps the heart to pump whatever volume of blood it receives, but within limit (up to a certain limit)
So any volume of blood reach the ventricle controlled by frank mechanism
Once the heart receive more blood the ventricle stretch more and the force of contraction is increased which insure ejection of this extra-volume of blood .

- **What is the importance of frank starling mechanism in the filling heart ?**

- **Before we answer the question let's talk about normal heart**
- **Frank starling mechanism in the normal heart allows changes in the right ventricular output to match changes in the systemic venous return, how?**
- **If the systemic venous return increase the right ventricular end diastolic volume and output also increase.**

  Increase venous return ➡️increase EDV➡️increase stretching ➡️move toward optimal length ➡️increase tension➡️increase stroke volume ➡️increase cardiac output

- **Increasing in the venous return causes an increasing in right ventricular output ➡️increasing in the pulmonary venous return ➡️increasing in the left ventricular EDV and output which balances the right ventricular output**

- **Frank starling mechanism maintains equal outputs from both ventricles**

- **The important of frank starling mechanism in the heart failure:**
  In heart failure ventricular pumping power decreases so auto regulation of myocardial contractility through frank starling mechanism.

- **Reduction in pumping power leads to increase the remaining blood volume in the ventricle(this volume we called it END systolic volume)**

- **Contractility weakness ➡️pumping weakness ➡️more blood stay in the heart**

عندما يعود الدم من ال peripheral ويعود الى ال atria وبعدين يصير عندي filling هاد الاشي بدل انو صار عندي ESV كبير بالأصل وبعدين اجا دم زيادة من ال atria اثناء ال diastolic لهيك النتيجة حتكون انو حيكون عندي EDV اكتر ...لا تتسائل كتير هلأ بحكيلك ليش😁👇
(ال ESVالمتبقية اصلاً كبيره وهاد كلو بسبب انو في عنا ضعف بال contraction وفي عندي filing اثناء ال diastolicمعناها المحصلة رح تكون EDVعالي🤷‍♀️)

- **This lead to a powerful ventricular contraction according to frank-starling mechanism therefore accumulated blood in the ventricle will be pumped inspite the heart failure .**

لهيك من الممكن يصير فيه shift بال curveالي 👆upward(باتجاه ال normal)
يعني لو واحد عنده hypertension بالبدايه رح يكون عنده resistant لل pumping بالتالي بالبداية ما رح يقدر يعمل pumpingلكمية ال blood المعتادة ولكن هذا يترتب عليه انه ال ESVازدادت وبسبب الزيادة ال ESVرح يؤدي الى زيادة ال EDVلأنه اثناء عملية الامتلاء رح تُضاف ال ESVلل volume الجديد اللي جاي من ال atria اثناء ال diastolic

Increase of EDV➡️increase in force of contraction ➡️the heart pumped the usual amount of blood ➡️shif toward the normal curve

لكن هاد الاشي إذا استمر رح يصير عندي weaknessبال contractility إذا صار عندي امتلاء اكتر لانه هاد الاشي ممكن ينتج عنه hypertrophy فيؤثر بشكل عكسي على ال contractility of myocardium cells وبالتالي heart failure لهيييك بكون لازم Treatment.🤓