Veterinary Bioscience: Cardiovascular System

WEEK 2 – THE HEART AS A PUMP

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INTENDED LEARNING OUTCOMES

At the end of this lecture you should be able to:

Explain how the electrical and mechanical events of the heart are linked to achieve effective pumping. In particular you should be able to:

- 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

KEYWORDS

After load, cardiac output, diastole, systole, end diastolic volume, ejection fraction, fractional shortening, Frank Starling curve, preload, stroke volume.

LECTURE 9 – DETERMINANTS OF CARDIAC OUTPUT: THE MECHANICS OF SYSTOLE AND DIASTOLE

DETERMINANTS OF CARDIAC OUTPUT

Cardiac output is measured in mls per minute- it is the product of heart rate (beats/minute) and stroke volume (mls). Heart rate, as we have previously discussed, can be modified by activity of the sympathetic and parasympathetic nervous systems on the SA node. Stroke volume can be modified ventricular filling and by changes to contractility of cardiac myocytes. In this

lecture we will look in more detail at the function of the heart pump, and how changes in cardiac filling, and the pressure in the arteries affects output from the heart.

THE CONCEPTS OF PRELOAD AND AFTERLOAD:

Preload is the degree of tension on a muscle when it begins to contract. For cardiac contraction, preload is generally considered to be the volume of blood in the ventricle at the end of diastole, (i.e. end diastolic volume). So, filling of the heart by blood returning from the veins determines preload. Afterload is the load against which the cardiac muscle exerts its contractile force. (i.e. the pressure in the arteries)

The importance of these concepts lies in the fact that the nature of contraction of cardiac muscle depends on pre and after load, and that pre and after load can vary both in physiological and pathological states.

PRE-LOAD: LENGTH/TENSION RELATIONSHIPS

Frank-Starling Law of the Heart: the energy released during contraction depends on the initial fibre length. (or *the force of contraction is related to the degree of stretch of the heart*.) Force is required to stretch a resting muscle to different lengths. This force is called **resting tension**. When a muscle is stimulated to contract whilst length is held constant, it develops an additional component of tension called **active tension**.

TOTAL TENSION = RESTING TENSION + ACTIVE TENSION

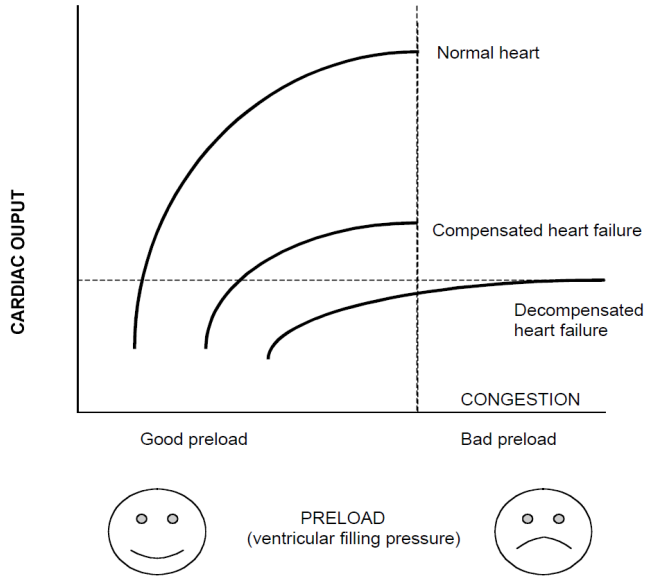
Tension developed by cardiac muscle depends very much on the muscle length at which contraction occurs. (Very short or very long muscle lengths develop little active tension.) So, contractility is defined as the change in peak isometric force (isovolumic pressure) at a given initial fibre length (end diastolic volume)

The length-tension relationship can be partly explained in terms of sliding filament hypothesis. As the muscle fibre is stretched, more cross-bridges can form and force increases. This relationship is similar to skeletal muscle, but the curve is steeper in cardiac muscle, probably because of a length dependent increase in Ca^{++} sensitivity to troponin.

SIGNIFICANCE OF FRANK-STARLING LAW

The length-tension relationship of heart muscle allows for **equalization of output** from left and right sides of the heart. For example, 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. In response to exercise, central venous pressure rises. This leads to an increase in end diastolic volume, and an increase in stroke volume from both the left and right ventricles.

The Frank-Starling Law is often expressed as a **ventricular function curve**, because end diastolic volume (mL) is related to cardiac muscle fibre length, and stroke volume is related to muscle tension. Ventricular function curves are used to compare the performance of normal and failing hearts, and also to describe the effect of physiological stimuli and drugs on cardiac performance.



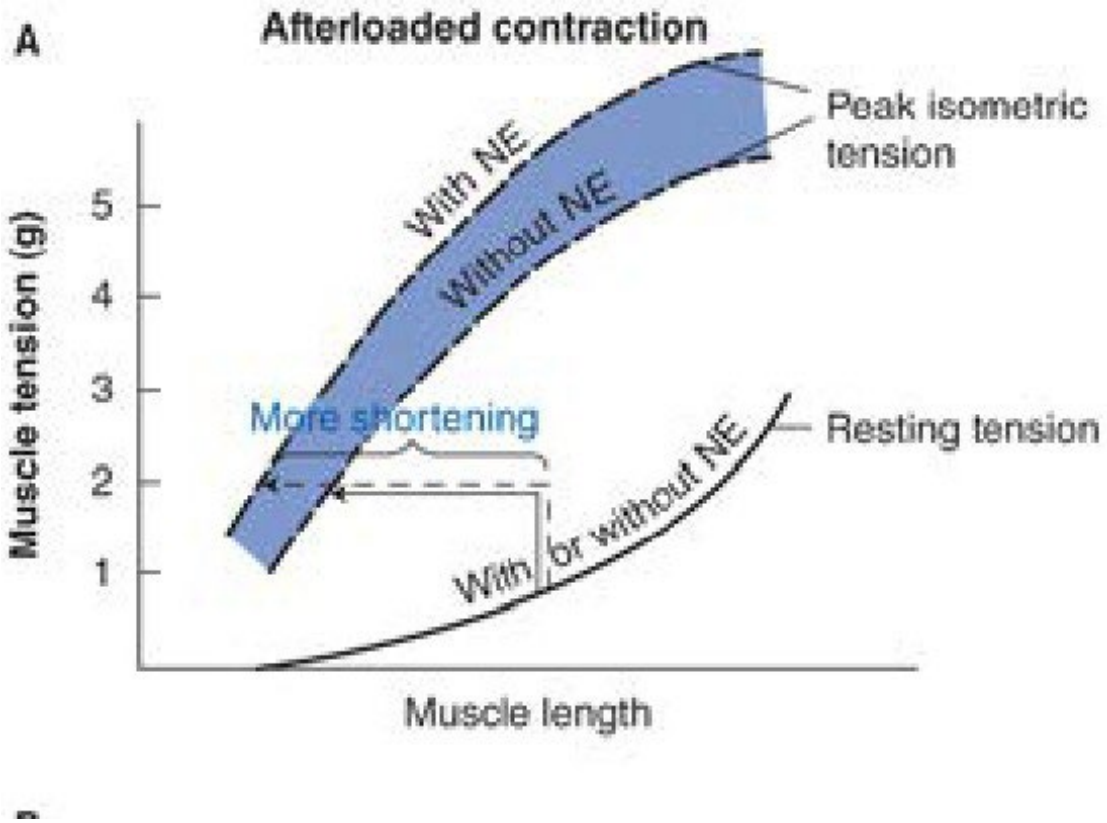
EFFECT OF AFTERLOAD

Another consequence of Starling's Law is that it allows for stroke volume to be maintained in the face of an increase in blood pressure, or afterload. Increased blood pressure leads to higher afterload, and a reduction in volume of blood ejected from the heart with each beat. The resultant increase in end systolic volume and end diastolic volume increases cardiac muscle stretch, thereby increasing force of contraction and stroke volume. (However, when either preload or afterload increase, cardiac work and cardiac oxygen consumption increase.)

MODULATORS OF CARDIAC MUSCLE CONTRACTILITY: INOTROPY

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. **Noradrenaline (NA)** released from sympathetic nerves is the most important physiological regulator of cardiac muscle contractility. NA is a positive inotrope- it increases contractile force and shifts the ventricular function curve upwards

NA binds to β- adrenoceptors on the cell membrane. This increases cAMP levels and cAMP-mediated phosphorylation of Ca channels increases Ca entry during the action potential. NA also increases the rate of relaxation by increasing the activity of Ca^{++}-ATPase pump in the sarcoplasmic reticulum



Mohrman DE & Heller LJ. Cardiovascular Physiology. 3rd Ed. 1991p 43

Drugs may also function as either positive or negative inotropes. For example, digoxin inhibits the membrane bound Na^+-K^+ exchange process, leading to an increase in intracellular calcium, and a positive inotropic effect.

An increase in **heart rate**, also increases cardiac contractility. This can be attributed to increased intracellular Na^+, due to increased frequency of AP's, and increased Ca in the sarcoplasmic reticulum, due to decreased diastolic interval over which Ca can be extruded from the cell.

LUSITROPY

Equally important to cardiac mechanics and effective pumping is the capacity of the heart to relax effectively between beats to enable cardiac filling. This characteristic of heart function is referred to as lusitropy. In certain disease states the heart becomes "stiff' so that relaxation and cardiac filling is incomplete.

MEASUREMENTS OF HEART FUNCTION

Heart function may be measured volumetrically- for example by measuring stroke volume, end diastolic volume, end systolic volume or ejection fraction, or it may be measured in terms of dimensions- for example one dimensional distances of the ventricle at different times in the cardiac cycle. Fractional shortening is the fraction of any diastolic dimension (recorded with echocardiography) that is lost in systole and is used to measure the function of the cardiac muscle. These measures will be discussed further in the seminar on cardiac imaging.

FURTHER READING

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