

Possible Links of Age Related Hypertension and Evolution Imposed Features of Heart and Aorta

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Abstract: The left ventricle thickness is a limiting factor of optimal heart size and strength. Due to disappearance of all the features compromising left ventricular compliance, mammalian heart has decreased vascular density and coronary vessel diameter and it requires sufficient diastolic aortic pressure for the left ventricle perfusion. Atrial muscle and the right ventricle are perfused during the entire heart cycle. The systolic pressure in the left ventricle forces blood vessels in the muscle wall to collapse, particularly in the subendocardial muscle layer. This makes the most active part of the heart prone to hypoxia.

Optimal perfusion of the left ventricle wall requires sufficient aortic pressure during diastole, making individuals with higher diastolic pressures advantageous, in situations requiring combination of increased heart rate and output. Described mechanisms might have contributed to the hereditary quality of age-related hypertension in humans.

INTRODUCTION

Although pathophysiology of cellular mechanisms of ageing are becoming better understood, other, more diverse mechanisms limit life duration of our patients. One of the most prevalent causes of premature deaths in human medicine is atherosclerosis, often accelerated by arterial hypertension that gradually increases with age.

Despite the controversy regarding the origin of essential hypertension and accompanying vascular changes, it is generally assumed that the main cause is arteriolar constriction [1-3], although effects of large arterial vessels on high blood pressure and vice versa are getting more attention [4, 5]. For instance, among 272 tested individuals, a significant age-related increase in large and small vessels vascular resistance was reported in all hypertensive subjects and in normotensive women [6]. The increase in vascular resistance in 23 previously untreated hypertensive patients is primarily due to the changes in the large and small arterial vessels, with no evidence of generally increased arteriolar constriction [7]. It has been described that in isolated systolic hypertension, the decreased buffering function of the aorta and large arteries is partly compensated by an increase in small artery compliance [8]. It was also reported that in older adult humans with essential hypertension, lowering of arterial blood pressure following regular aerobic exercise is associated with an increase in the peak limb vascular conductance [9].

In normal adults, the mean arterial pressure (MAP) is near 90 mmHg in the aorta and large arteries. It drops almost by 60 mmHg in small arteries and resistant arterioles [1]. The remaining hydrostatic pressure is near 32 mmHg, when the blood enters in peripheral capillaries. This huge pressure gradient along arteries and arterioles shows that the high circulatory pressures are mainly limited to the prearteriolar part of the circulation.

An important question is which survival advantage forced diastolic pressure to be so high and to show tendencies to increase with age. The conventional interpretation is that in young individuals, arterial elasticity and normal responsiveness to shear stress, allow optimal blood flow under normal arterial pressure, while rigid atherosclerotic arteries in older individuals limit the blood flow, leaving increased arterial pressure, the only remaining solution to achieve near normal perfusion. Hypertension induced vessel stress accelerates atherosclerosis, resulting in a vicious circle that leads to age related hypertension and premature death due to vascular pathology.

Hicks, JW in a review of reptile circulation [10] pointed out that in some reptiles up to twofold higher pressure in systemic than in pulmonary circulations, reflects their more terrestrial way of living. It is possible that the four-chamber heart with high pressure in peripheral arteries is a prerequisite of locomotion modes that require high regional perfusion rates, which can be found in birds and mammals. This is in compliance with arterial pressure data of 24 species of mammals, weighing 0.025-4.000 kg, and of 12 bird species, weighing 0.014-110 kg, collected by Seymour, RS & Blaylock, AJ [11]. They have found that birds have higher arterial blood pressures and larger hearts than mammals, possibly reflecting their more active mode of locomotion.

LEFT VENTRICLE AS A CRITICAL COMPONENT OF THE CIRCULATORY SYSTEM DESIGN

Skeletal muscles during heavy exercise need their basal blood flow up to 32 times [1]. They are optimized for producing intermittent strong linear force and their architecture is adapted for this function (Table 1) [12]. Connective tissue between muscle fibers defines muscle architecture, limits sliding between fibers, and directs linear force of contraction. Each muscle fiber controls its internal pool of calcium ions, allowing rapid and strong contractions [1]. Muscle generated force is a sum of activities of individual fibers, regardless of fiber individual strength, velocity or endurance. Muscle diameter and vasculature can easily increase in skeletal muscles due to their privileged anatomical position on the

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Table1. Comparison of Features of Skeletal and Heart Muscles (Based on 1, 12)

Features	Skeletal Muscle	Heart Muscle
Constraints	performance depends on the summation of individual fibers of variable strength producing a linear force, while compliance during rest is not critical.	requires similar strength and velocity of muscle fibers with force acting in all direction within the muscle plane, and maintained diastolic compliance
	intracellular calcium depots secure rapid and strong contractions	intracellular depots of calcium ions are not developed
Restricted	muscle fibers are organized in linear contractile units well defined by connective tissue	fusion of cells in long and thick fibers is not allowed
	uncontrolled sliding among fibers is prevented by connective tissue	connective tissue between fibers is scarce and angiogenesis seems limited (both for new and for larger vessels)
Allowed	extracellular calcium is less important during contraction	muscle cells use extracellular calcium for contraction
	long and thick fibers with many nuclei and other organelles differ in cross section and strength	muscle fibers are of average strength due to similar cross section as tendonless chains of individual cells
	muscle develops force in a well defined direction with minimal sliding between muscle fibers	mesh of branched fibers slide in layers during contraction

body periphery, so any demand for stronger muscles can be met by local growth of muscle and vascular cells.

Heart muscle fibers are smaller than skeletal muscle fibers by one-third and consist of anatomically joined distinct quadrangular cells, forming a syncytium with scarce connective tissue between the fiber bundles [12] (Table 1). Heart contraction is done through sliding between muscle fibers, producing a two dimensional reduction of the heart chamber surface. Modular construction of joined small cells of similar cross sections allows smooth sliding of muscle layers. Beside that, heart muscle cells share the same extracellular calcium pool for contraction [1], allowing their excitability, contractility strength, and speed to be as uniform as possible.

It needs to be noted that any passive tissue (connective tissue, vasculature etc.) stacked between the layers of muscle fiber mesh might compromise both contractility and diastolic compliance (increased rigidity through limited sliding of mesh layers). This is a possible explanation of limited redundancy of coronary circulation that takes blood from the aortic root, a point of the highest systolic and diastolic pressures and returns it to the right atrium, at the point of the lowest circulatory pressure. Human heart, as the only continuously working muscle in the body, is among the organs with the highest oxygen consumption per tissue volume (9.7 ml/100g/min) and largest arteriovenous difference in oxygen contents (114 ml/l) [1]. Even at rest, it extracts 50-60% of the blood oxygen. While atrial muscle and the right ventricle are perfused during the almost entire heart cycle, subendocardial blood vessels collapse under the systolic pressure in the left ventricle [1], making the most active part of the heart prone to hypoxia.

Described data suggest that special anatomical and functional features of the heart muscle and limited coronary circulation reflect requirements imposed by the left ventricle compliance (Table 2). Even small changes can compromise

the left ventricle coronary blood flow, its systolic or diastolic function.

Diastolic dysfunctions in hypertrophic and ischemic heart diseases are linked to increased left ventricular chamber stiffness and impaired myocardial relaxation, leading to increased left ventricular diastolic pressure and impaired filling [13, 14]. In early stages, an abnormality in relaxation phase is presented by decreased early diastolic filling and increased volume of atrial contraction. It is known that heart failure in excessive growth hormone exposure can be caused by diastolic dysfunction due to ventricular hypertrophy (increased left ventricular chamber size, or wall thickness) [15].

A possible conclusion is that during survival selection, the left heart wall thickness became the limiting factor in the heart of optimal size and strength. If the wall is too thick or contains too many blood vessels, the left ventricle becomes less compliant, leading to the diastolic dysfunction with poor diastolic filling and limited stroke volume, despite the increased heart muscle strength and muscle oxygen consumption. Selection forces have eventually resulted in a compromise between diastolic filling and systolic ejection. Optimal left ventricle function depends on aortic elasticity and the sustained left ventricle wall compliance due to scarce vasculature and fibrous tissue. In this setting, diastolic perfusion of coronary arteries is forced by the elastic recoil of aorta and large arteries that acts as a diastolic pump, using energy accumulated in elastic walls during previous heart strokes.

POSSIBLE CONSEQUENCES ON AGEING

Few consequences related to ageing seem probable. In case of limited redundancy of coronary circulation, stronger hearts required higher diastolic pressure in the aorta. Otherwise, the trade-off between increased muscle strength against reduced compliance due to additional vasculature would be unavoidable.

Table 2. Proposed Anatomical and Functional Constraints of the Heart Muscle Features Due to Optimization of the Left Ventricle Function and Coronary Perfusion

Anatomical and Functional Heart Parameters (optimal adult value (1))		Left Ventricle During Heavy Physical Exercise			Risk of Heart Wall Ischemia
		Systolic function (contraction force)	Diastolic function (end diastolic volume)	Coronary perfusion flow	
Wall thickness (8 to 12 mm)	<8 mm	reduced force	increased	improved	reduced
	>12 mm	increased force	reduced	compromised	increased
Diastolic duration (0.4 to 0.6 s)	<0.4 s	unaltered	reduced	compromised	increased
	>0.6 s		increased	improved	reduced
Systolic duration (0.2 to 0.3 s)	<0.2 s	reduced stroke volume	unaltered	improved	reduced
	>0.3 s	increased stroke volume		compromised	increased
Systolic pressure (120 mmHg)	low	reduced afterload	unaltered	unaltered	reduced O ₂ consumption
	increased	increased afterload			increased O ₂ consumption
Diastolic pressure (80 mmHg)	low	reduced afterload	unaltered	compromised	increased
	increased	increased afterload		improved	reduced

Low aortic diastolic pressure would increase chances of coronary problems during the periods of tachycardia and increased heart output. That would make individuals with higher diastolic pressures advantageous in situations requiring increased heart output and increased heart frequency. This process lasted for many generations and the rest of the body slowly adapted to new levels of arterial pressure through a complex network of resistant arterioles and regulatory mechanisms, allowing stable perfusion of brain, kidneys and other visceral organs, despite abrupt changes in cardiac output. An additional feature of increased arterial pressures is that it allowed higher flow rates in exercising skeletal muscles, thus further increasing survival chances.

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