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UNDERSTANDING THE DISEASE

Understanding cardiovascular physiology of ageing

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Introduction

Ageing is not fully understood; however, a gradual deterioration of organ function will occur over the lifespan [1]. This leads to reduced reserves that might not affect older adults in daily life; however, when given intensive care (stress) old patients are more vulnerable to adverse events. Comorbid diseases are frequent, and separating effects of age from disease is difficult. This short narrative overview will describe the most important age-dependent changes in the cardiovascular system for the practising intensivist.

Changes in cardiac function

Altered cellular function, cardiac shape, plasticity and valvular stiffening all contribute to reduced cardiovascular reserve (Fig. 1).

Myocardial cellular and cardiac tissue changes

The heart undergoes age-specific changes. With normal ageing muscle mass is largely conserved, although there are structural changes. Myocardial thickness develops asymmetrically, with intraventricular thickness predominating, microscopically the result of a decrease in number but increase in the size of cardiac myocytes [2]. General fibrosis and calcification occur, with an increase in the fibrous extracellular matrix, fat deposition and tissue calcification (Fig. 1). At a cellular level, deteriorating Ca^{2+} handling is important. Reduced Ca^{2+} reuptake in the myocytes leads to a prolongation of the action potential, and several complex changes in calcium-related ion currents and other factors slow cellular reactions responsible for controlling the periodicity of heartbeats. These changes contribute to the reduction in stressed HR responses, and the increase in incidence of arrhythmias with age. Changes in the lipid content of the cell membranes and an inability to effectively clear reactive oxygen species reduce the capacity of the myocardium to react to stressors such as ischaemia.

Myocardial function changes

Systolic function is little affected by normal ageing and at rest the heart retains a normal ejection fraction (EF) of at least 50% with variability associated with gender and ethnicity [3]. During stress and exercise the reduced cardiovascular reserve becomes apparent. With age the increased stiffness of the myocardium leads to a slower filling of the ventricle and a reduced cardiac filling during the early (passive) diastolic phase, leaving the heart more dependent on the active filling phase during atrial contraction. At high heart rates or atrial fibrillation this may lead to reduced ventricular filling and that a patient with a stable heart failure decompensates. These changes partially explain a recently described geriatric syndrome "heart failure with preserved EF". This is a common form of HF in patients aged 65 years or older, and is associated with marked exercise intolerance, high readmission rates and 1-year mortality of 30% [4]. Recently, right heart catheterization [5] in healthy participants aged 20–80 years demonstrated an increased pulmonary artery pressure/capillary wedge pressure to cardiac output (CO) ratio with increasing age. The currently used threshold for excess left ventricular filling pressure (25 mmHg) was present in 30% of elderly participants (over 60 years old).

A progressive decrease in maximum oxygen consumption (VO_2 max) occurs: by the age of 80 years, a 50% reduction [6]. This must be caused either by reduced CO and/or oxygen consumption by tissue. A decreased

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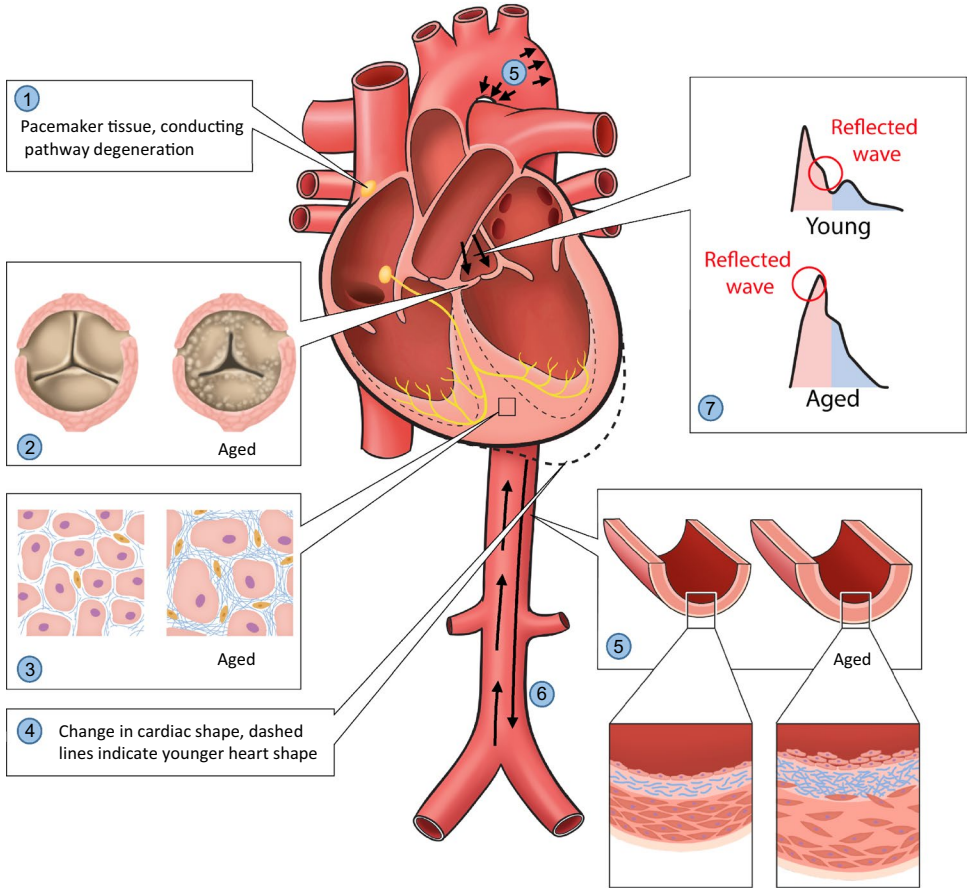

Fig. 1 Cardiovascular changes with ageing consequent on a complex process of senescence, apoptosis and autophagy linked to decreases in sirtuins (SIRT 1), cell cycle regulators, mitochondrial dysfunction, activation of inflammatory genes, alterations in nitric oxide production and other factors [2, 8]. (1) Pacemaker and conducting pathways degenerate, slowing heart rate response to stress and increasing the risk of arrhythmias. (2) Valve stiffening and calcification, increasing afterload, turbulence and risk of valvular incompetence; murmurs are common. (3) Myocyte hypertrophy and increase in fibrinous matrix reduce plasticity and ability to respond to stress. (4) Altered cardiac shape e.g. septal hypertrophy is common reducing efficiency. (5) Vascular changes affect the intima and media leading to increasing thickness, fibrosis and loss of elasticity, resulting in a stiffer vascular system. Endothelial inflammatory tendency and changes in endothelial signaling e.g. altered nitric oxide-mediated responses contribute to dysfunction. (6 and 7) Increased pulse wave velocity results in reflected waves arriving in the central arteries during systole rather than diastole, increasing systolic pressure and increasing afterload, while resulting in the loss of augmented diastolic filling. Permission granted to use the figure from the BASIC website of the ICU, PWH, Medical Faculty, Chinese University of Hong Kong

heart rate rise in response to stress or exercise is a substantial contributor to the limited CO response. Maximum HR is reduced from around 200/min at age 20 to 140/min at age 80 as result of a depressed excitability of individual sino-atrial node myocytes [7]. The modulation of the cardiovascular system in response to exercise and stress through adrenergic stimuli also changes with age. A reduced β-adrenergic response is the consequence of reduced β-adrenergic receptor density, as well as a decline in the functional response. Observed circulating catecholamine concentrations are often increased, but are not functionally fully compensatory. These changes further contribute to an observed blunted cardio-acceleratory and CO response to stress seen in the elderly [8].

Cardiac rhythm abnormalities

The resting heart rate is not considered to be affected by age [9]. However, the general increase in fibrous content and calcification process in cardiac tissue may lead to dysfunction in the atrioventricular (AV) node with an increase in the risk of AV block. Changes in the conducting bundle branches also occur. ECG changes like increased QRS voltage, prolongation of QT interval and abnormalities in the ST wave may be markers for the future development of cardiovascular disease in

otherwise healthy individuals. The presence of bundle branch block (BBB) and atrial fibrillation (AF) are associated with underlying abnormalities in the heart like hypertrophy or atrial enlargement and are risk factors for mortality [10].

Changes in vascular function

Arteries

Several age-related changes occur in the arterial system through mechanisms such as altered signaling processes, abnormal modulation of senescence and apoptosis, and vascular inflammation [11]. There is a dilatation of large arteries and thickening of the intimal-medial layer where hypertrophy, calcium deposits and extracellular matrix changes (collagen cross-linking, and fraying of elastin fibrils) all increase vascular stiffness (Fig. 1). The resulting reduced arterial wall compliance, and hence a more rapid propagation of the stroke volume, increased pulse wave velocity (PWV) [12].

Arteries are dynamic structures and the endothelium and its glycocalyx function responsively to regulate arterial tone through the synthesis and release of vasoactive substances, among these are nitric oxide (NO) and endothelin. Ageing affects these processes, generally contributing to reduced vascular compliance, but also reducing the elderly patient's ability to respond appropriately to acute changes in blood pressure, CO and fluid status [13].

Arterial blood pressure

The systolic blood pressure (SBP) is determined by the stroke volume, arterial compliance and systemic vascular resistance (SVR), and increases with age. However, the diastolic blood pressure (DBP), reduced by the progressively increasing vascular stiffness, declines after the age of 60. The result is an increase in pulse pressure (SBP-DBP), which may be a useful indicator of arterial stiffness and prognosis in the elderly population [12]. The heart and peripheral vasculature form a single dynamic unit, and the combined effect of structural and functional changes in the myocardium and peripheral vasculature makes attempts to achieve stable blood pressure control in elderly patients in ICU substantially more difficult.

Normal ageing causes a progressive increase in the late systolic pressure peak [14]. Augmentation is the boost to late systolic pressure after the initial systolic shoulder and is normally caused by pressure wave reflection from the periphery when conduit arteries interface with high resistance arterioles [15]. Ageing-related increases in pulse and systolic pressure are thus observed. Additionally, in the young, reflected waves reach the aortic root in diastole and augment coronary artery filling, but with increasing PWV reflected waves augment pressure in late systole, potentially increasing LV afterload and reducing coronary blood flow.

Conclusion

The heart and vessels undergo major changes with advancing age, even without superimposed diseases. However, during stress compensatory responses are substantially reduced, and the appropriate management of critical illness in the elderly requires an understanding of the mechanisms of this phenomenon.

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Compliance with ethical standards

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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