# The Aging Cardiovascular system

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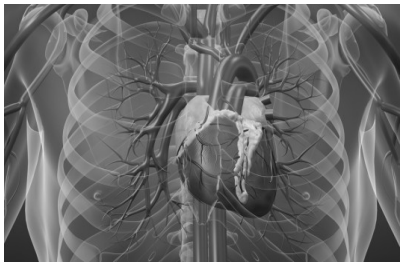
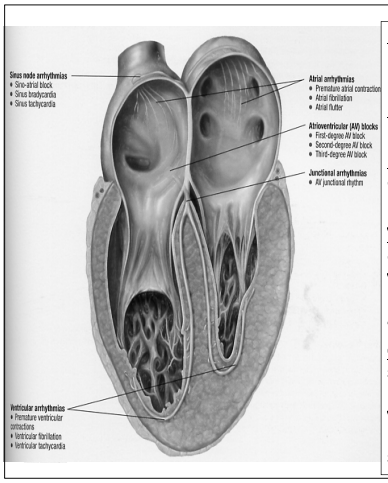
## Cardiovascular system

- Heart
- Blood vessel
- Blood






Myocardium: Cardiac muscle *syncytium* (multi-nucleated)

Endocardium: Internal layer of heart

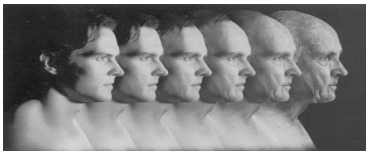
Pericardium: External connective tissue layer of heart

Valves: openings between cardiac chambers (atrial ventricular) or between heart the arteries (aorta and pulmonary)

Conduction system: sinoatrial node (SA) is the pacemaker; also atrial ventricular node (AV), Bundle of His, Purkinje system

## Aging & Cardiovascular physiology

- A continuum progressing throughout the individual's life
- A process that is genetically programmed but modified by environment
- Physiologic aging occur more rapidly or more slowly than the chronologic age



## Aging & Cardiovascular physiology

- Physical condition can radically affect cardiovascular function in the elderly
- Changes in physical activity can profoundly change cardiovascular function

**Table I.** Aging Changes in the Cardiovascular System and Their Consequences

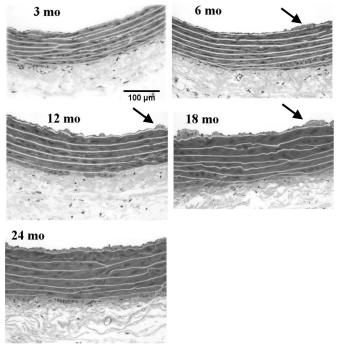
| CHANGE | CONSEQUENCE |
|---|---|
| Decreased compliance of the arterial tree | Increased afterload on left ventricle and development of LVH |
| Myocardial cell hypertrophy, increased interstitial fibrosis, dropout of cardiac myocytes, and delayed inactivation of ICa-L channels | Increased cytosolic $Ca^{++}$<br>Maintenance of contractility<br>Prolongation of action potentials<br>Delayed relaxation<br>Decreased left ventricular compliance<br>Increased contribution of atrial contraction to left ventricular end-diastolic volume |
| Apoptosis of sino-atrial pacemaker cells, fibrosis, and loss of His bundle cells | Slower intrinsic heart rate<br>Varying degrees of AV block |
| Fibrosis and calcification of the fibrous skeleton of the heart and valves | Aortic valve sclerosis and stenosis<br>AV block |
| Decreased responsiveness to β adrenergic stimulation and reactivity to baroreceptors and chemo receptors | Increased circulating catecholamines |

AV=atrioventricular; LVH=left ventricular hypertrophy; ICa-L=L-type $Ca^{++}$ current

## Changes in the cardiopulmonary anatomy & physiology

1. Decreasing elasticity of the aortic compliance
2. Dropout of myocytes; LV afterload
3. LV hypertrophy and decreased diastolic pressure
4. Apoptosis of atrial pacemaker cells
5. Fibrosis and calcification of the fibrous skeleton of the heart
6. Decreased responsiveness to β-adrenergic receptor stimulation and decreased reactivity to baroreceptors and chemoreceptors

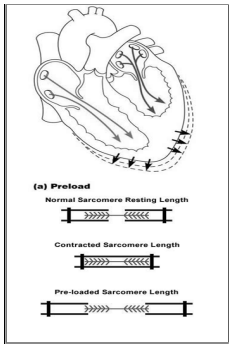
## Decreasing elasticity of the aortic compliance

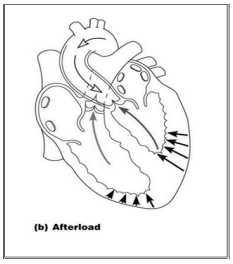



Miller S J et al. Am J Physiol Heart Circ Physiol 2007;293:H2634-H2643

- Increased resistance to ejection of blood from the left ventricle
- Velocity with which the pulse wave travels to the periphery and reflects back increases
- Increased aortic systolic pressure developed by the LV for any given stroke volume and increased ventricular afterload

## Dropout of myocytes; LV afterload

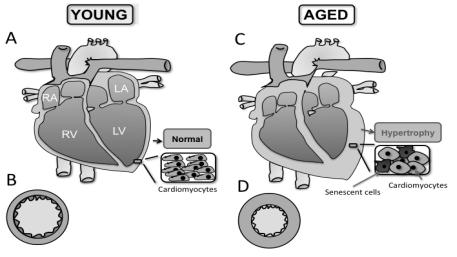



- Increased LV afterload
- Results in modest LV hypertrophy

## LV hypertrophy and decreased diastolic pressure

- There is the pressure responsible for subendocardial perfusion
- There is subendocardial ischemia and interstitial fibrosis
- There is prolongation of contraction and relaxation times



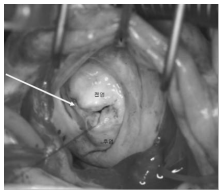

*Agricultural and Biological Science*, 2013

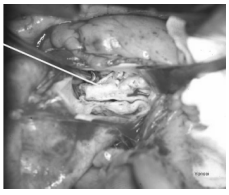
## Apoptosis of atrial pacemaker cells

- The number of atrioventricular nodal cells is preserved
- There is fibrosis and cellular loss in the His bundle

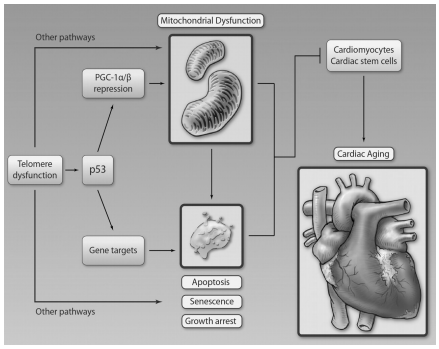
Fibrosis and calcification of the fibrous skeleton of the heart

- Composed of the annular rings and fibrous trigones
- Calcification of the baseds of the aortic cusps





Decreased responsiveness to β-adrenergic receptor and decreased reactivity to baroreceptors and chemoreceptors




Moslehi J et al. Circulation Research. 2012;110:1226-1237

What is differences at rest and during exercise responses with aging?

Cardiac changes at rest

- Minor ↓in HR
- CO output maintained by ↑SV
- ↑ejection of blood during late systole
- ↓Early diastolic filling rate
- ↓EDV not – enhanced atrial contribution to LV filling
  – beware AF, particularly if tachycardic

Cardiac changes during exercise

- ↓in maximum HR(↓response to β adrenergic stimuli)
- ↓in cardiac output – reduced by 30% between ages 20 and 80
- Maximum SV not reduced – but maintained in different manner
- Frank Starling mechanism

Cardiac output at rest and with exercise

At rest

Early studies :decrease of cardiac output with aging at rest and with exercise
Current studies :Cardiac output at rest is maintained by compensating for a slower heart rate by increasing the stroke volume
- Wall stress remains normal

Exercise
- Decrease in the maximal oxygen consumption
- Decrease in the maximum heart rate compared to younger subjects.
- Maintain stroke volume (end-diastolic volume)

## Cardiac output at rest and with exercise

- Increase in circulating norepinephrine and epinephrine
- Decreased responsiveness to adrenergic stimuli
- Delay in arterial relaxation in response to exercise increases vascular impedance with increasing age
- Increased plasma catecholamines can help compensate for the decrease of β-adrenergic responsiveness

## Frank starling mechanism

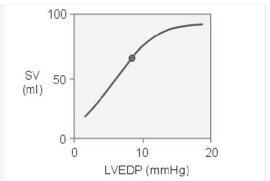



*Figure 1.* Frank-Starling mechanism. Increasing venous return to the left ventricle increases left ventricular end-diastolic pressure (LVEDP) and volume, thereby increasing ventricular preload. This results in an increase in stroke volume (SV). The "normal" operating point is at a LVEDP of ~8 mmHg and a SV of ~70 ml/beat.

- ↑EDV, dut to :
- Longer diastolic interval(↓HR)
- ↓EF – ↑amount of blood in LV at start of diastole

## Response to upright exercise

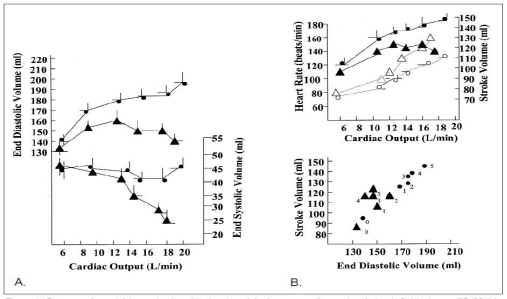



*Figure 3. Response to upright exercise in subjects where latent coronary disease is ruled out. Subjects age 65–80 (circles); age 25–44 (triangles). Panel A: In the elderly patients the end-diastolic volume increases with exercise and there is little change in the end-systolic volume. In the younger subjects, the end-diastolic volume changes little and the end-systolic volume falls. Panel B: Heart rate (dotted lines) and stroke volume (solid lines) response to exercise. In the elderly subjects the heart rate increases less than in the younger subjects and the stroke volume increases more. The greater stroke volume in the elderly results from the increased end-diastolic volume (Panel A).*
*Adapted with permission from Geokas MC, Lakatta EG, Makinodan T, et al. The aging process.* Ann Intern Med. *1990;113:455–466.*

## Changing Myocardial Function & Structure

1. Myocardial contractility
2. Preload
3. Afterload

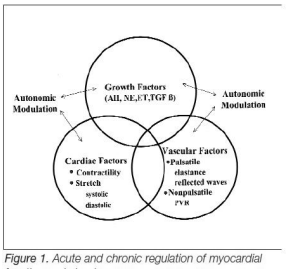
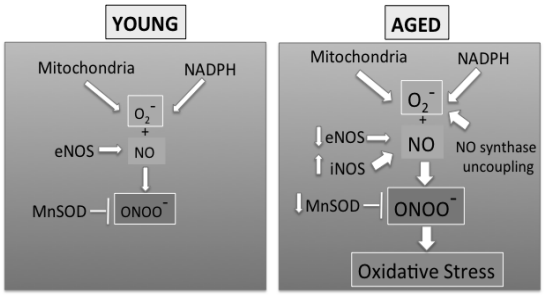



*Figure 1. Acute and chronic regulation of myocardial function and structure*
*AII=angiotensin II; NE=norepinephrine; ET=endothelin; TGF β=transforming growth factor β; PVR=peripheral vascular resistance*
*Adapted with permission from Lakatta EG, et al. The aging heart. In: Eugene Braunwald, ed.* Heart Disease. *5th ed. Philadelphia, PA: WB Saunders; 1997:1691.*

## Aging & Oxidative Stress




## Maximal Oxygen Consumption

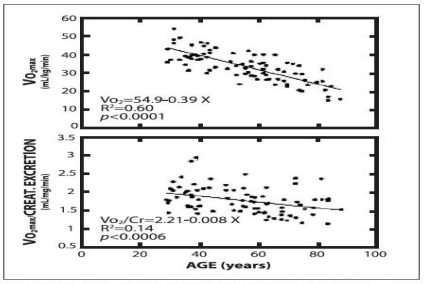



*Figure 2. Top: Maximal oxygen consumption ($VO_{2max}$) as a function of age*
*Bottom: $VO_{2max}$ normalized for creatinine (Cr) excretion (as a measure of muscle mass) as a function of age. When the decreased muscle mass is taken into account, the age-associated decrease in $VO_{2max}$ rate is markedly attenuated.*
*Reprinted with permission from* J Appl Physiol. *1988;65:1147–1151.*[16]

## Aging and B-Blockade

**Table II.** Similarities Between Aging and β Blockade During Aerobic Exercise

| | Aging | | β Blockade | |
|---|---|---|---|---|
| Maximal aerobic capacity | ↓ | | ↓ | |
| Maximal heart rate | ↓ | | ↓ | |
| Maximal end-diastolic volume | ↑ | | ↑ | |
| Maximal ejection fraction | ↓ | | ↓ | |
| Maximal cardiac output | ↓ | ↔ | ↓ | ↔ |
| Maximal plasma catecholamines | ↑ | | ↑ | |

↓=decrease; ↑=increase; ↔=no change
Reproduced with permission from Fleg JL, Gerstenblith G, Lakatta EG. Pathophysiology of the heart and circulation. In: Messerli FH, ed. *Cardiovascular Disease in the Elderly*. 3rd ed. New York, NY: Kluwer Academic Publishers; 1993:53.

## Conclusion

The major effects of aging on the cardiovascular system

- decreased compliance of the arterial system, a dropout of myocytes and atrial pacemaker cells
- increasing fibrosis of the cardiac fibrous skeleton
- decreased responsiveness to β-adrenergic stimuli

(which is in part compensated by an increase to be little decrease in myocardial contractility, but there is slowing of ventricular relaxation, an increase in the contribution of atrial contraction to end-diastolic volume, and maintenance of the cardiac output during exercise mainly through the Frank-Starling mechanism)