Autonomic and Vascular Dysfunction in the Elderly

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- Aging:
  - Epidemiology:
    - In 2006, individuals >65 years old made up 12% of the population, but account for about one third of all surgeries performed in the US\(^1,2\)
    - The fastest growing segment of the US population consists of individuals over the age of 65; their numbers are expected to increase 53.2% by 2020\(^3\)
    - By 2050, seniors will make up 21% of the domestic population
    - The prevalence of cardiovascular disease (CVD) in American males and females aged 65-74 are 68.5% and 75%, respectively. For those aged 75+, prevalence is 77.8% and 86.4%, respectively
  - Chronological age vs. biological age
    - Chronological: unavoidable structural changes in heart & vasculature
      - Rate of chronological aging varies from individual to individual, system to system
    - Biological: net effects of changes due to chronological aging + disease states (HTN, CAT, etc.)
      - Biological age important in risk stratification for anesthesia and postop complications
        - Pre-operative “medical fitness” (a synonym for “successful aging”), rather than chronological age, is a primary determinant of post-operative outcome in the elderly surgical patient\(^4\)
- Vascular Changes
  - Arterial:
    - Structural changes that result in impairment of distensibility:
      - Extracellular matrix composition changes with aging:
        - Decreased production/quality of elastin results in an increased collagen-to-elastin ratio\(^13\)
        - Free radical attack/glycosylation of connective tissue resulting in cleavage, crosslinking, fragmentation of collagen\(^13\) – this results in the formation of advanced glycation end products [AGE]
        - Infiltration of inflammatory/atherosclerotic processes (adhesion molecules, AGE, matrix metalloproteinases, TGF-beta & other pro-inflammatory cytokines)\(^16\)
      - Nitric oxide pathway deteriorates with age
        - Loss of NO-mediated suppression of:
          - vascular smooth muscle proliferation/migration
          - leukocyte adhesion to endothelium
- flux of lipoproteins into vessel walls

- Functional changes as a result of stiffening:
  - Stiffened vessels have increased pulse-wave velocity, widened pulse-pressure, and produce cardiac strain leading to LV hypertrophy and diastolic dysfunction\(^{13}\)
  - Reduced nitric oxide-dependent vasodilation response to acetylcholine\(^{16}\)
  - Decrease in responsiveness to \(\beta\)-receptor stimulation\(^{13}\)
    - In addition to direct effects of \(\beta_1\)-receptor dysfunction on cardiac chronotropy and inotropy, decreases in \(\beta_2\)-mediated vasodilation may also impact the ability of the heart to increase ejection fraction

- Venous
  - Venous system contains \~75\% of the body’s blood volume, provides a buffer to maintain central blood volume\(^{13}\)
    - This buffer is impaired in aged veins due to decreased compliance/smooth muscle contractility\(^{15}\)
    - Elderly hearts with diastolic dysfunction are dependent on venous return to provide adequate atrial pressure to fill the ventricles\(^{13}\)
    - Elderly patients are less able to maintain their systolic blood pressure in the setting of hypovolemia (tilt table test example\(^{14}\))

- Autonomic Changes
  - Impaired baroreflex control of heart rate
    - Increased sympathetic activity
      - Basal levels of catecholamines increase with age (plasma norepinephrine increases 10-15\% per decade)\(^{13}\)
      - Age-dependent reduction in reuptake of norepinephrine by cardiac neurons – higher concentrations of norepinephrine at cardiac \(\beta_1\)-receptor\(^{14}\)
    - Decreased \(\beta\)-receptor responsiveness
      - Impaired 2\textsuperscript{nd} messenger system of the \(\beta\)-receptor (decreased Gs protein/adenyl cyclase coupling with the adrenoceptor moiety) more likely the culprit than changes in \(\beta\)-receptor density.\(^{16}\) This results in:
        - Reduced vascular dilation in response to isoproterenol/epinephrine.
          - Decreased cAMP-mediated vasorelaxation
        - Reduced inotropic response to exercise/catecholamines\(^{15}\)
          - Questionable reduction in chronotropy\(^{15}\)
          - Greater dependency on Frank-Starling mechanics to increase CO during exercise
  - Slightly diminished \(\alpha\)-receptor function
• Number of $\alpha_1$-receptors well preserved, however there is decreased vasoconstriction at same dose of $\alpha$-agonist compared with younger subjects$^{14,15}$
• $\alpha_2$-receptors show age-related loss, may have implications for intolerance of orthostatic changes
• Decreased $\alpha$-receptor function compensatory for increased sympathetic outflow?
  - Diminished parasympathetic activity$^{13}$
    • Reduced vagal tone
      - Diminished heart rate increase to large dose atropine$^{14}$
    • Reduced response to muscarinic receptor activation
      - Reduction in carbachol-induced inhibition of forskolin-activated adenyl cyclase in muscarinic receptors of aged myocardium$^{15}$
      - Autoantibodies to M2-muscarinic receptors (positively associated with idiopathic dilated cardiomyopathy) are significantly increased in the elderly$^{16}$ (significance undetermined)
  - Decreased reflex responsiveness
    • Less tolerant to orthostatic stress/blood loss
    • May in fact be helpful?
      - Hypovolemia not masked by compensatory reflexes (identify earlier)

References


