Cardiometabolic Risk, Obesity & Inflammation: What Does it all Mean for Individuals Aging with Spinal Cord Injury?

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Cardiometabolic Risk

• The term ‘cardiometabolic risk’ has recently supplanted ‘metabolic syndrome’
• Better defines CVD and endocrine risks
• CMR represents unique combinations of risk factors that may impart a health hazard
• CMR clustering linked to CVD-related morbidity and mortality
  – Worsens non-linearly with the identification of additional risk factors
Cardiometabolic Risk

- Studies examining cardiometabolic syndrome have found that its principal clinical outcome is cardiovascular disease
- People who develop CVD do so based upon the synergies of multiple risk factors
- Many CMR factors and clustering are disturbingly prevalent in persons with SCI
- But is this commensurate with CVD?

McNeill, 2005; Fried, 1998; Smith, 2007; Bauman & Spungen, 2008; Nash, 2009)
Longitudinal Aging Evidence

• CVD is the leading cause of death in long-term SCI (30+ years)
• 35% of all deaths in those with SCI 60 and older
• After excluding deaths during the first year post-injury, CVD is the most common cause of death
• 41% of all deaths in the Boston Cohort Study

DeVivo, 1999; Whiteneck, 1992; Hartkopp, 1997; Yekutiel, 1989
Factors Contributing to Cardiometabolic Risk

- Genetics
- Age
- Overweight/Obesity

Insulin Resistance Syndrome
- Insulin Resistance
- Lipids
- BP
- Glucose

Cardiometabolic Risk

Global Diabetes/CVD Risk

Factors
- Abnormal Lipid Metabolism
  - LDL ↑
  - ApoB ↑
  - HDL ↓
  - Triglycerides ↑

- Age, Race, Gender, Family History
- Smoking, Physical Inactivity
- Hypertension
- Inflammation, Hypercoagulation
Atherogenic Lipid Profile After SCI

- Normal total cholesterol
- Normal or elevated LDL
- Normal or elevated triglycerides
- **Consistently low HDL**
- Significantly elevated TC:HDL ratio

Bauman & Spungen, 2008; Nash & Mendez, 2007
Insulin Resistance

• 1/3 – 1/2 of people with SCI live in a state of insulin resistance
  – Tetra > Para
• Physical inactivity, obesity, sympathetic dysfunction may be causes
• Often missed with routine testing

Duckworth, 1980 and 1983; Nash 2006; Nash & Gater, 2007; Bauman, 1994; Bauman, 1999; Groah & Nash, 2010
UNITED STATES OBESITY TRENDS
Obesity After SCI

• Obesity is at epidemic proportions
• Obesity is due to
  – Obligatory lean muscle loss
  – Blunted sympathetic NS
  – Positive energy balance
• Obesity is UNDERestimated by BMI in people with SCI
• Central adiposity is most strongly associated with cardiometabolic syndrome

Nash & Gater, 2007; Maruyama, 2008; Myers, 2007
Metabolic Syndrome after SCI

- Castillo, JSCM, 2007
  - N=487 veterans with SCI
  - Mean age 55.2 yrs, 48.7% tetraplegic
  - 56.5% BMI > 25 kg/m²
  - 37% dyslipidemia
  - 63.4% HDL < 40
  - 56.5% hypertension
  - 44.8% metabolic syndrome

- Defined as central obesity + any 2 of the following:
  - TG >= 150 md/dl
  - Low HDL-C
  - High BP
  - Fasting glucose >= 100 md/dl
Attack of the Fat!

• Insulin resistance
• Hypertension
• Dyslipidemia
• Thromboembolism
• Inflammation
Inflammation

• Process by which body responds to injury or infection
• Important in the pathophysiology of atherosclerosis
  – CRP, hs-CRP
• Systemic inflammatory biomarkers predict cardiovascular events
• Atherosclerosis is accelerated in various inflammatory rheumatic diseases
Inflammation and Obesity

- Individuals genetically predisposed to high BMI have elevated CRP
- Adipose releases certain cytokines (IL-6) that stimulate the release of CRP
- CRP increases blood levels of cellular adhesion molecules, endothelin-1, and decreases NO
- Hence, atherosclerosis is a chronic inflammatory vascular condition
Acute Inflammation: Outcome

**ACUTE INFLAMMATION**
- Vascular changes
- Neutrophil recruitment
- Mediators

**INJURY**
- Infarction
- Bacterial infections
- Toxins
- Trauma

**Progression**

**CHRONIC INFLAMMATION**
- Angiogenesis
- Mononuclear cell infiltrate
- Fibrosis (scar)

**RESOLUTION**
- Clearance of injurious stimuli
- Clearance of mediators and acute inflammatory cells
- Replacement of injured cells
- Normal function

**INJURY**
- Viral infections
- Chronic infections
- Persistent injury
- Autoimmune diseases

**Healing**

**FIBROSIS**
- Loss of function
  - Connective tissue replacement

**Healing**

**Pus formation (abscess)**
SCI and the Pro-Inflammatory State

- Added risk of systemic inflammation due to skin breakdown and infections
- Accelerates vascular wall stress and atherogenesis
- Recent attention on blood levels of pro-inflammatory cytokines as triggers for CVD
  - Several exceed cut-off scores for elevated CVD risk

Frost, 2005; Lee, 2006; Liang, 2008; Manns, 2005; Morse, 2008; Wang, 2007
Homocysteine and C-Reactive Protein Summary

- 44% of SCI patients studied in a large sample had a homocysteine level associated with an increased mortality ratio
- 62% of SCI patients studied had moderate to high CRP levels
KNOWLEDGE BASED ON RISK FACTORS AND NOT DISEASE STATUS
Importance of Prevention

• Obesity pandemic (SCI at greater risk)
  – Primary trigger for cardiometabolic risk clustering
• ATPIII guidelines identify obesity as the primary target for intervention in cardiometabolic syndrome
• Sensory deficits may mask acute cardiovascular symptoms and obscure disease progression
• More profound impact on the health, well-being, and function of persons with SCI than those without SCI
Questions