Sex and Gender Differences in Sarcopenia

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The **SWHR ISIS Network on Musculoskeletal Health** strongly endorses the goal of the AIM Coalition to promote research on the causes of and treatments for the loss of skeletal muscle mass and function with aging, which is a condition referred to as sarcopenia.

There is an urgent need to develop effective strategies for the prevention and treatment of sarcopenia in older adults. The likelihood is high that the underlying causes of sarcopenia are different in women and men and will require the identification of sex-specific therapeutic targets.

There are biological and clinical rationales that highlight the need to expand knowledge on sex and gender differences in the etiology and consequences of sarcopenia.

- The biological rationale for such an emphasis is based, in part, on existing preclinical and clinical evidence that gonadal hormones both directly and indirectly influence skeletal muscle quantity and quality.
- The clinical rationale is that sarcopenia may be a root cause for the higher prevalence of frailty, disability, and loss of independence in elderly women than men.

<u>Examples of the need for a focus on sex differences:</u>

- Gonadal function is a direct mediator of the sex dimorphism in the hypertrophy of skeletal muscle mass during puberty. Similarly, the loss of gonadal function with aging is likely a determinant of the development of sarcopenia in older adults, but this is not well understood.

- Estrogens are not thought to have anabolic effects on skeletal muscle. However, the suppression of ovarian function in young women may trigger a decline in muscle mass and the withdrawal of estrogens in menopausal women appears to accelerate the loss of muscle mass (muscle quantity) and the decline in specific muscle force (muscle quality). The mechanisms by which estrogens regulate skeletal muscle metabolism have received little attention.

- Physical activity declines with advancing age and is thought to contribute to the development of sarcopenia. In laboratory animals, gonadectomy causes a dramatic decline in spontaneous physical activity. It is not clear whether age-related changes in gonadal function regulate physical activity in humans.

- Inflammation and oxidative stress have been implicated in the etiology of sarcopenia. Adipose tissue is a potent source of pro-inflammatory cytokines, suggesting that sex differences in total and regional adiposity could influence risk for sarcopenia.