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Letter to the Editor

Menopause and the Loss of Skeletal Muscle Mass in Women

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Dear Editor-in-Chief

Sarcopenia, the age-related decline in skeletal muscle mass and function, is one of the main contributors to morbidity and physical disability (1). In women, menopause may contribute to sarcopenia, which not only affects very old women but can also have impact on middle-aged adults (2). Changes in the gonadal hormones during the menopause transition appear to be a strong determinant of skeletal muscle mass in women. If the menopausal transition triggers the mechanisms underpinning sarcopenia in women, then menopause may be a critical time to introduce strategies to mitigate the changes in muscle mass and function that contribute to physical disability and frailty later in life. Thus, it is crucial to elucidate the extent to which menopausal transition augments sarcopenia, and whether this muscular deterioration is specifically associated with the loss of sex hormones. Menopause is: 1) the consequence of both gonadal and chronologic aging; and 2) the period that both estradiol and testosterone decrease. The complex hormonal changes during the menopause transition make it difficult to isolate the effects of a single cause of sarcopenia in women.

Compared to premenopausal women, cross-sectional studies (3, 4) have demonstrated that lean or muscle mass is lower in postmenopausal women. However, less is known about whether skeletal muscle mass and the prevalence of sarcopenia differ between the menopausal stages. Using a cross-sectional study (5), we recently determined that perimenopausal transition is a vulnerable period for the loss of muscle mass. One hundred forty four healthy women (aged 30-70 yr) were classified as premenopausal (n=30), early (n=31) and late perimenopausal (n=30), and early (n=26) and late postmenopausal (n=27).

Appendicular lean mass (ALM) index, calculated by ALM adjusted by the square of height, was assessed using dual-energy x-ray absorptiometry (5).

The protocol was approved by the Colorado Multiple Institutional Review Board and participants provided written informed consent.

Compared to early perimenopausal women, ALM index was 10 and 9 % lower in late peri- and post-menopausal women, respectively, with no other significant differences between groups. In line with this data, the prevalence of sarcopenia was 7, 3, 30, 27, and 32% in pre-, early and late peri-, and early and late post- menopausal women, respectively, showing a greater difference between early and late peri-menopausal women. Our findings highlighted the need to investigate the major hormonal factors and its underpinning mechanisms contributing to the menopause-mediated loss of skeletal muscle mass.

Hormone therapy (HT) studies exploring lean body and skeletal muscle mass in postmenopausal women have provided mixed results. Whereas some studies (6, 7) have demonstrated that HT preserves skeletal muscle mass in postmenopausal women, others (8) have shown no effect. However, the loss in estradiol is still believed to be the most important contributor in meno-

pause-associated loss of muscle mass. We recently found that 1-week administration of transdermal estradiol in early-postmenopausal women (≤6 yr past menopause; n=13) increased the ratio of nuclear to cytosolic estrogen receptor α protein (a surrogate marker of genomic estrogen receptor α activation) by 60% in skeletal muscle, compared to women treated with transdermal placebo (9). Using those skeletal muscle samples, our recent study (10) suggested that estradiol also reduced skeletal muscle protein breakdown markers, assessed by fork-head box O3 (FOXO3) de-phosphorylation, an activation form of FOXO3, and muscle RING-finger protein 1 (MuRF1) content in early-postmenopausal women; although there was an adverse effect of estradiol on protein breakdown in late-postmenopausal women (≥10 yr past menopause; n=14). Our data suggest that estradiol may play a role in skeletal muscle protein metabolism, and is associated with genomic estrogen receptor α activation in muscle.

Future studies should further investigate the specific mechanisms by which estradiol and estrogen receptors (ERα and β, and GPER) regulate protein metabolism, which may contribute to increased prevalence of sarcopenia in women.

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Conflict of interest

The authors declare that there is no conflict of interest.

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