

Investigating Age-Related Changes In Skeletal Muscle In The C57BL/10 Mouse Model To Identify Opportunities For Therapeutic Intervention

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Abstract

Background: Europe's rapidly aging population, with adults aged 65 and over now accounting for 21.6 percent, increases the urgency of understanding age-related muscle decline. Sarcopenia, the progressive loss of muscle mass and force, affects not only the limb muscles but the diaphragm as well, thereby impairing breathing and increasing complications in older adults. Given this growing demographic shift, investigating diaphragm and skeletal muscle remodeling in aged mice is essential for understanding the mechanisms of age-related sarcopenia and identifying therapeutic interventions to preserve respiratory performance later in life.

Aim: To investigate age-related remodeling in the C57BL/10 mouse by analysing muscle fibre size, central nucleation, immune infiltration, collagen deposition, and oxidative/glycolytic enzyme activity across the diaphragm, soleus, gastrocnemius, and EDL muscles.

Methods: Tissues from 6 and 24-month-old C57BL/10 mice were analysed using H&E to assess central nucleation and immune infiltration, Sirius Red to quantify collagen deposition, and laminin immunolabelling to measure fibre size. Oxidative and glycolytic enzyme activity was evaluated with SDH and GPDH staining. All images were quantified using ImageJ.

Results: Muscle fibre cross-sectional area was unaffected by age across all four muscles examined (diaphragm, soleus, gastrocnemius, and extensor digitorum longus) and was similar in 6-month and 24-month-old mice, regardless of muscle type. Collagen deposition showed an upward trend with increased age across all muscles, but this was significantly increased in the gastrocnemius ($***p < 0.001$; $p = 0.0009$) of 24-month-old mice indicating pronounced fibrosis. Succinate dehydrogenase activity showed no significant age-related changes, remaining comparable across the diaphragm, soleus and EDL but showing a trending decrease in the gastrocnemius. GPDH activity showed a downward trend in gastrocnemius and extensor digitorum longus with age but was not significant. Centrally nucleated fibres, markers of muscle regeneration, showed no significant age-related change, but did show a trending increase with age in the soleus. No significant age-related change was seen in immune infiltration. However, an upward trend in the infiltrate area was observed with age in the gastrocnemius and extensor digitorum longus.

Conclusion: Aging did not produce significant structural or metabolic changes in the skeletal muscles of C57BL/10 mice. The gastrocnemius showed the greatest vulnerability, with increased fibrosis and trends toward metabolic and inflammatory decline, whereas the diaphragm and soleus remained comparatively resilient.