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Characterization of muscle in OI Model mice

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Osteogenesis imperfecta (OI) is a congenital connective tissue disorder characterized by decreased bone mineral density and increased bone fragility and susceptibility to fracture. In addition to skeletal fragility, patients with OI reportedly have muscle weakness although currently no systematic evaluation of muscle function or morphology in humans or animal models of the disease has been performed. Normal type I collagen is coded for two genes located on different chromosomes: COL1A1 and COL1A2. The oim/oim mouse is homozygous for a null mutation in the COL1A2 gene and is a phenocopy of human type III OI (severe disease phenotype). Heterozygous mice (oim/+) harbor the null mutation in only one allele of the COL1A2 gene and model human patients with type I OI (mild disease phenotype). We wanted to determine whether the reported muscle weakness in OI patients is due to a muscle pathology. We analyzed the muscle mass, fiber morphology, and cross-sectional area of muscles fibers of the hind limb muscles (quadriceps, gastrocnemius, plantaris, tibialis anterior and soleus), as well as the fiber type composition of the soleus muscle of wildtype (wt), heterozygous (oim/+), and homozygous (oim/oim) mice. Our results demonstrate that the muscle mass/body mass, fiber morphology, cross-sectional area of hindlimb muscles, as well as fiber type composition of the soleus muscle of oim, oim/+ relative to wt (+/+) mouse muscles were not significantly different between the genotypes. We correlated our morphologic findings with a functional contractile assay and determined that muscle tension-force generation and nerve conduction are not impaired in oim/oim or oim/+ mice. These findings suggest that oim and oim/+ mice do not have inherent muscle pathology. This knowledge is important in our ultimate understanding of skeletal muscle in OI model mice and ultimately, humans with this disease.