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Expanding on Characterization of the "Forgotten Muscle" during Knee Osteoarthritis

Abstract

The infrapatellar articularis genu (AG) is linked to the quadriceps femoris (QF) muscles and can be easily sampled during total knee arthroplasty (TKA). The AG is composed of type (T)1 slow oxidative and T2 fast (mostly) glycolytic myofibers in a similar 1:1 ratio as in the QF complex. In a similar fashion as the QF, the AG can be analyzed for changes in myofiber type content, atrophy, and fibrosis of the endomysium due to joint disuse in patients afflicted with end-stage knee osteoarthritis. T2 fibers are further subtyped into 2A, 2X, and 2A/X hybrids. The latter subtype has been strongly associated with disuse in studies on the vastus lateralis during OA. Further, myofiber type switching favoring T1 normally occurs in association with aging. We have previously analyzed myofiber switching in the AG of OA patients relative to active range of motion (ROM) with progressive myofiber switching to T2 fibers relative to increasing deficits in ROM. Here, we expand on this study by testing the hypothesis that T2A/X hybrids are the predominant phenotype in the expanding numbers of T2 myofibers in severely disused OA knees. Concurrent with a prevalence of T2A/X hybrids, we anticipate measuring higher fibrosis of the AG endomysium in patients with poor ROM that associates with high collagen deposition in the neighboring synovium.

OA patient AGs (n=33) collected during TKA were processed and embedded for paraffin sectioning. AGs were grouped by poor (≤85º; n=11), fair (90º to 115º; n=11), and good ROM (≥115º; n=11). To evaluate and measure muscle fiber type content, we co-detect myosin heavy chains (MHC) specifically expressed by the different myofiber subtypes using indirect immunofluorescence. Briefly, we co-detect T1, T2A, and T2X myofibers using primary antibodies raised and carried in different species and Ig isotypes against MHC7 (mouse IgG1), MHC2 (rabbit IgG), and MHC1 (mouse IgM), respectively. These are then labeled using secondary antibodies against the corresponding source species and isotype conjugated to spectrally separate Alexa fluorophores (AF): anti-mouse IgG1 AF488, anti-rabbit IgG AF647, and anti-mouse IgM AF594. The picrosirius technique was used to stain, capture, and measure fibrosis by confocal microscopy and software assisted thresholding of stained collagen fibrils.

While studies in our lab suggest that AG disuse is associated with an increasing ratio of T2 over T1 myofibers, we expect to find that the majority of those T2 myofibers will co-express MHC1 and MHC2, effectively classifying them as T2A/X. Furthermore, we anticipate an association of fibrosis severity between the OA AG and synovium, with the highest values measured in patients with highest ROM deficits. Using the AG as a tool for assessing the extent of muscle wasting at the time of TKA will allow for discovery of correlations between biomarkers in periarticular muscle, synovial fluid, and serum. Our overarching goal is to potentially determine and evaluate a biomarker panel of muscle health in fluids derived from arthrocentesis or a simple blood draw to help guide individualized muscle rehabilitation therapies post-TKA.