Using the *Articularis Genu* to Test Peri-Articular Muscle Health During Knee Osteoarthritis

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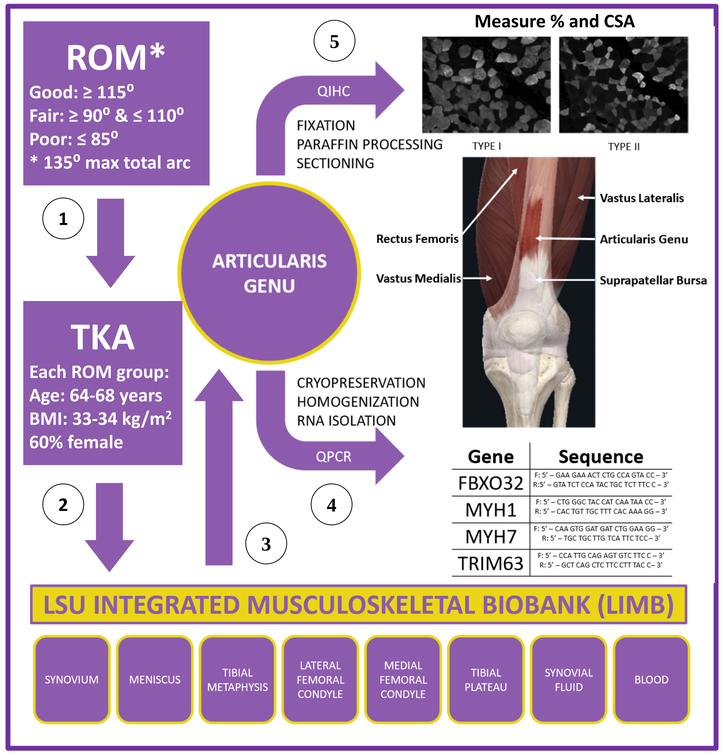
Introduction

Aging quadriceps are composed of slow-twitch, oxidative type-I myofibers, in predominance to fast-twitch, glycolytic type-II myofibers (IIa, IIx, and IIa/x subtypes).[1-3] Myofibers differentially express myosin heavy chains (MHC), such as those encoded by *MYH7* and *MYH1*, in myocytes around type-I and type-IIx fiber isoforms, respectively. Fiber distribution and quality in each of the quadriceps varies between older individuals, dependent on activity and exposure to insults such as osteoarthritis (OA).[1-3] OA-related joint disuse alters fiber distribution favoring type-II with higher occurrences of type-IIa/x hybrids.[4-6] OA quadriceps also manifest targeted atrophy of type-II fibers, specifically in the *Vastus lateralis* (VL)[4] and *Vastus medialis* (VM)[6]. Together, these changes act as hallmarks of poor peri-articular muscle quality.[4] Deep to and continuous with the *Vastus intermedius* (VI) is the *Articularis genu* (AG). The AG is the intra-articular muscle of the knee that coordinates retraction of the suprapatellar bursa during extension[7] and has a similar mechanism of action, concurrent innervation, and fiber distribution closest to the VI, with a type-I (~70%) over type-II ratio of ~2.3 in aging populations.[8] The AG is removed during total knee arthroplasty (TKA) and the only knowledge of its sensitivity to OA is ultrasound-based evidence of atrophy, leading to functional limitations as measured by isometric extension exercises.[9] Our objective is to expand this knowledge by analyzing fiber counts and size in banked OA AGs using quantitative immunohistochemistry (QIHC) coupled with QPCR of genes likely regulated in support of changes in AG structure. We predict that the sensitivity of AG fibers to OA will be similar to published data on the VM and VL during OA and that changes in fiber type distribution percentages and cross-sectional area (CSA) will associate with total range of motion (ROM). If our preliminary results support our hypothesis, we aim to refine a platform to assess OA quadriceps health using the AG as a surrogate.

Methods



Results

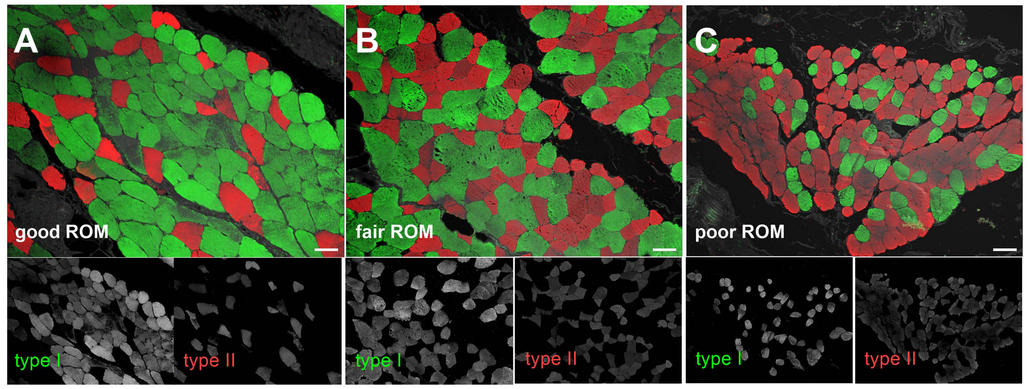


Figure 1. Co-detection of slow MHC (green; type-I) and fast MHC (red; type-II) myofibers by QIHC and confocal microscopy. Total patient sample (n=40) was grouped by (A) good (n=10), (B) fair (n=19), and (C) poor (n=11) ROM.

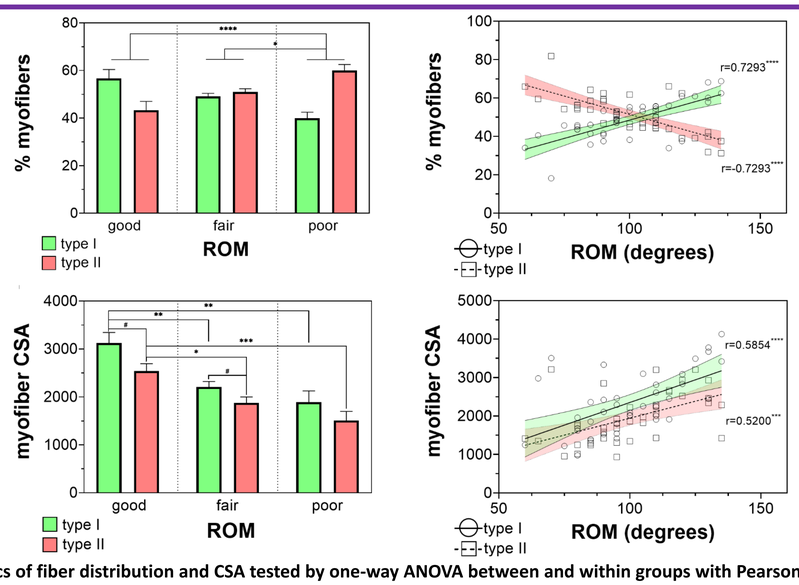


Figure 2. Metrics of fiber distribution and CSA tested by one-way ANOVA between and within groups with Pearson's correlation analyses (r) against ROM. *p<0.05 between groups and #p<0.05 within groups; **p<0.01; ***p<0.001; and ****p<0.0001.

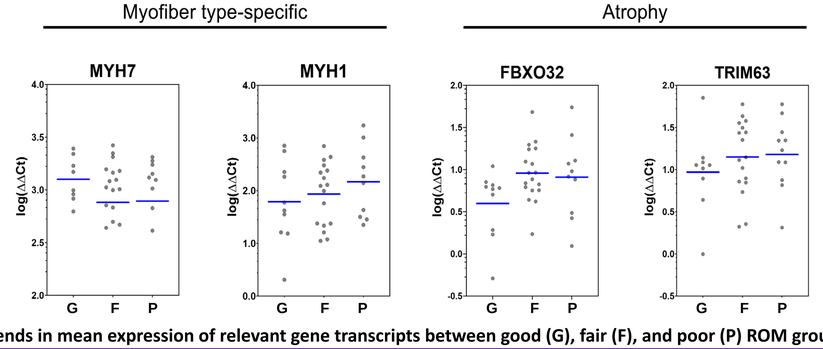


Figure 3. Trends in mean expression of relevant gene transcripts between good (G), fair (F), and poor (P) ROM groups.

Conclusions

- The AG is sensitive to OA-related deficits in ROM.
- The AG undergoes changes in fiber distribution and atrophy as a response to OA, consistent with similar studies of the VL[4] and VM[6, 10] of knee OA patients. Subtyping of increasing atrophied type-II fibers in the AG relative to poor ROM is critical, to test the prediction that type-IIa/x hybrids are elevated in wasting AGs.
- OA-related limitations in knee motility may act in synergism with aging-related muscle wasting to more severely alter the AG, with progressively severe atrophy and aberrant re-distribution of myofibers as ROM worsens.
- The AG has the potential to act as a surrogate the quadriceps in a diagnostic testing platform of peri-articular muscle status.
- More refined and in-depth analyses of banked AGs will provide insight on the global health of peri-articular muscles in patients afflicted with knee OA to potentially guide peri-operative pain management (e.g. neuromuscular electrical stimulation) and individualized strength rehabilitation strategies post-TKA.

Limitations

- Needs more power to confirm any significant differences in expression of relevant gene transcripts between ROM groups, since only trends can currently be reported.
- Lacks baseline and in-house comparative analyses of healthy AGs and age-matched muscles of the OA quadriceps, respectively.
- Minor contamination of cryopreserved AGs with synovium and fat at collection.

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