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DEVELOPMENT OF A NOVEL METHOD TO ASSESS SKELETAL MUSCLE ATROPHY IN COLLAGEN INDUCED ARTHRITIS (CIA) MODEL

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BACKGROUND

Muscle quality in rheumatoid arthritis (RA) is a new concept that involves morphological features and function. A measurement that associates cell morphology with clinical and physical parameters has not been reported in the literature. CIA is a RA mice model characterized by loss of muscle mass similar to human RA, thereby it is a convenient model to study the disease impact in muscle physiology. Our main goal was to develop an index to measure the morphometry of muscle fibers in RA and correlate the morphological features with the muscle functional performance in CIA.

MATERIALS AND METHODS

18 DBA/1J mice were induced using complete Freund's adjuvant and a booster after 18 days induction. Along experimental phase, we evaluated muscle strength using grip strength test and clinical disease score after onset of disease. 16 healthy mice were used as control. After 25 days CIA induction, 8 CIA and 8 controls were euthanized for muscle evaluation in mild disease and, at day 50, 8 CIA and 8 control mice were euthanized for evaluation in severe disease. Tibialis anterior were collected for myofiber histological analysis. Using the Image Pro Plus software (Media Cybernetics, China), we segmented muscle fibers and assessed its area and its regularity (the last through an index named Muscle Fiber Irregularity Index, MFII). The index works as a threshold to set to screen the degree of normal, atrophic and hypertrophic based on the morphometry if muscle fibers. Values are compared to area and shape of control (healthy) fibers. Frequency analysis and Pearson Correlations were used and statistical significance was considered as $p<0.05$.

RESULTS

We found 1.5% atrophic muscle fibers in control animals. Mild CIA showed the same atrophic muscle fibers percentage compared to control. However, severe CIA showed 11.8% of atrophic muscle fibers. Decrease muscle strength in CIA over time were associated with a greater atrophic muscle fiber proportion ($r=-0.8$, $p=0.021$) and increased disease score ($r=-0.8$; $p=0.019$).

CONCLUSION

Here we developed a new, objective method applied to screen for muscle quality through the morphometry of muscle fibers. Muscular Morphometric Analysis (MusMA) has potential to be used in combination with clinical parameters in several human pathophysiological analysis. Besides that, we can

speculate that although muscle strength is associated with atrophic cell percentage, loss of strength does not only depend of atrophy, but disease activity also seems to influence muscle strength reduction.