
SATURDAY, SEPTEMBER 12, 2009

7:30 A.M. – 8:00 A.M.
CONTINENTAL BREAKFAST
IN EXHIBIT HALL - Cotillion Ballroom

7:00 A.M. – 8:00 A.M.
PAST PRESIDENTS'/NEW MEMBERS' BREAKFAST

7:00 A.M. – 8:00 A.M.
WOMEN SURGEONS IN VASCULAR SURGERY
BREAKFAST - Wellington Ballroom

8:00 A.M. - 9:45 A.M.
SESSION IV
PRESIDING: Jon S. Matsumura, MD
Gilbert R. Upchurch Jr., MD

19. Fiber Type-Specific Oxidative Damage in the Gastrocnemius of Patients with Peripheral Arterial Disease

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OBJECTIVE: Myopathy characterized by mitochondrial dysfunction and oxidative damage contributes to the pathophysiology of peripheral arterial disease (PAD). Quantifying oxidative damage in PAD muscle may permit disease staging aimed at prediction of ischemic complications, need for aggressive therapy, and evaluation of therapeutic intervention. In this study, we evaluated the hypothesis that increased oxidative damage in ischemic muscle of PAD patients can be quantified in needle biopsies, correlates with disease severity, and is myofiber type specific.

METHODS: Muscle biopsies were taken from the gastrocnemius of 21 PAD and 14 control patients, with a Bergstrom needle. Protein carbonyls and 4-hydroxy-2-nonenal (HNE) adducts, biomarkers of oxidative damage, were quantified in individual myofibers of slide-mounted tissue by quantitative fluorescence microscopy. Oxidative damage was determined as mean pixel intensity in gray-scale units (gsu). Adjacent sections of 5 PAD and 5 control patients were labeled with anti-myosin I and II antibodies, permitting quantification of oxidative damage in specific myofiber types. Myofiber area was measured based on sarcolemma labeling.

RESULTS: Mean carbonyl and HNE content were increased 36% (723 gsu vs. 533 gsu, $p < 0.01$) and 27% (427 gsu vs. 335 gsu, $p < 0.05$), respectively, in PAD compared to control muscle (Figure). Both carbonyl and HNE content exhibited a significant negative correlation with Ankle/Brachial Index ($r = -0.65$ and -0.43) and positive correlation with disease severity ($r = 0.67$ and 0.49). PAD muscle contained 52% type I, 31% type II, and 17% hybrid (type I/II) fibers compared to 53%, 42% and 5%, respectively, in controls. Among pooled fibers of the 5 PAD and 5 control patients, hybrid fibers exhibited significantly greater oxidative damage than both type I and II fibers. All fiber types in the PAD muscle had significantly lower myofiber area compared to control muscle (Figure).

CONCLUSION: Myofiber area of all fiber types was significantly decreased in PAD muscle consistent with myopathy. Oxidative damage was significantly increased in PAD muscle; with greater damage in hybrid fibers and a trend towards a higher proportion of hybrid fibers in PAD muscle. Oxidative damage in the gastrocnemius of PAD patients was a significant predictor of disease severity.

