464

Loading of the medial knee ligaments and anterior cruciate ligament during clinical tests of anteromedial rotatory instability

Andrew Pechstein[1], Erin Berube[1], Mark Amirtharaj[1], Emma Reznick[1], Thomas Wickiewicz[1], Paul Christos[2] and Carl Imhauser[1]
[1]Hospital for Special Surgery and [2]Weill Cornell Medical College

OBJECTIVES/GOALS: Injury to the medial knee ligaments (sMCL, dMCL, POL) and anterior cruciate ligament (ACL) can cause anteromedial rotatory instability (AMRI). AMRI can cause knee instability and ACL graft failure, but it is unclear how the sMCL, dMCL, POL, and ACL resist AMRI. We aimed to characterize the in-situ forces of the sMCL, dMCL, POL, and ACL under loading conditions involved with AMRI. METHODS/STUDY POPULATION: We characterized the in situ forces of the sMCL, dMCL, POL, and ACL under 1) isolated external tibial rotation torque (ER), 2) isolated anterior tibial force (Ant), and 3) combined ER+Ant loading. Twenty-eight human cadaveric knees (18 male; mean age, 48±13; 21–65 years) were tested on a robotic manipulator with force sensing. Tibiofemoral kinematics were recorded under isolated ER (4Nm, 0–90°), isolated Ant (134N at 0–90°), and combined ER+Ant (4Nm +100N at 15, 30, 90°). The sMCL, dMCL, POL, and ACL were dissected in random order. The in situ force (N) in the sMCL, dMCL, POL, and ACL at the peak applied load for each loading condition was calculated using superposition and compared with Kruskal–Wallis tests with post hoc pairwise testing using a Bonferroni–Holm correction for multiple comparisons ($\alpha = 0.05$). RESULTS/ANTICIPATED RESULTS: Under isolated ER, the force in the sMCL (32–52N) from 0°-90° exceeded that of the ACL, dMCL, and POL at each flexion angle (p0.05). Force in the ACL was the second highest (26–6N from 0°-90°). Force in the dMCL and POL was low (≤12N). Under isolated Ant, the ACL carried the highest force at all flexion angles (≥113N) (p0.05), but at 90° the sMCL carried the highest force of all ligaments (p0.05). At 90°, force in the dMCL diminished (DISCUSSION/SIGNIFICANCE OF IMPACT: We show that the sMCL is the major stabilizer to external rotation torques and combined anterior and external loading conditions related to anteromedial rotatory instability across the arc of knee flexion, while the dMCL, POL, and ACL play a less prominent role, with the exception of the ACL and dMCL near full extension.

465

Genomic return of research service core with the precision health function of ICTS

Jenny McKenzie, Sarah Hartz, Chris Gurnett, Dustin Baldridge, Kevin Bowling, Jorge Luis Granadillo De, Jessica Mozersky, Laura Bierut and Patricia Dickson
Luque, Washington University in St. Louis

OBJECTIVES/GOALS: Returning genetic research results to participants can improve community engagement and enhance health equity. Providing research investigators with a convenient and cost-effective pathway for returning genetic findings, along with ensuring the necessary criteria for validity and utility, may reduce the barriers to returning results. METHODS/STUDY POPULATION: The ICTS Precision Health Genomic Return of Research Service Core (ICTS PH gROR) developed a process of returning genetic findings to participants who have indicated their preference to be notified of any findings that may impact their health. The service includes returning primary findings (actionable results discovered as part of the Investigator's approved IRB study) and/or secondary findings [clinically actionable genes by the American College of Medical Genetic and Genomics (ACMG)]. Participants with positive findings will receive a written report, generated by a board-certified clinician specializing in genetics or molecular genetic pathology. A visit with a genetic counselor provides additional resources and guidance on the identified health risks. RESULTS/ANTICIPATED RESULTS: Centralizing a service for the return of genetic results will ensure best-practices and minimize the burden. By offering results at no cost to the participant or their family, the service promotes accessibility and removes financial barriers that could otherwise prevent individuals from benefiting from genetic insights. Furthermore, by involving expert oversight committees and genetic counselors in the process, participants will receive accurate information and appropriate guidance, enhancing their understanding of the results and empowering them to address any potential health risks. Subsidizing the service with the CTSA grant keeps the costs predictable and manageable for investigators. DISCUSSION/SIGNIFICANCE OF IMPACT: This approach recognizes the importance of informed consent, ethical considerations, and the potential social implications associated with genetic findings. Through open communication, participants are actively involved in the decision-making process and have the opportunity to seek further resources and support.

466

The role of anemia and its treatment with iron in the development of oxygen-induced retinopathy

Ellen Ingolfsland, Raghavendra Rao and Kaoru Terai
University of Minnesota

OBJECTIVES/GOALS: The objective of this research is to characterize the role of anemia and its treatment with iron in the development of oxygen-induced retinopathy and to identify possible mechanisms of action for future investigation. METHODS/STUDY POPULATION: Newborn rats were exposed to cyclic hyperoxia (50%) hypoxia (10%) for 14 days to induce oxygen-induced retinopathy (OIR). Half of the pups were phlebotomized to induce anemia. Half of anemic and control pups received high-dose iron, while the other half received standard, low-dose iron. Retinas were dissected at postnatal day 20, and vascular outcomes were measured to determine phenotype. Comparisons will be made by two-way ANOVA. Additional future studies are planned: 1) electroretinogram to measure retinal function, 2) measure of retinal hypoxia and angiogenic protein levels to evaluate the effect on hypoxia-sensitive angiogenesis, 3) serum and retinal iron measures to determine iron status, 4) flow cytometry and cytokine array to evaluate immune cell response, and 5) exploratory single-cell RNA sequencing. RESULTS/ANTICIPATED RESULTS: Preliminary vascular outcomes are pending. We anticipate that retinas of anemic pups treated with low-dose (standard of care) iron will exhibit iron deficiency and hypoxia and reduced severity of OIR. Retinas of anemic and non-anemic pups treated with high-dose iron will exhibit iron excess and increased severity of OIR. However, retinal function will be reduced in anemia and rescued with treatment with high-dose iron. We further anticipate that anemia and iron-deficiency will down-regulate overall immune cell fractions, which will correlate with reduced cytokine and chemokine levels, suggesting a reduced immune response. Finally, we expect vascular endothelial cells and pericytes in anemic pup retinas to show increased angiogenic gene

https://doi.org/10.1017/cts.2024.1057 Published online by Cambridge University Press