Chief Resident Research Presentations

Thursday
March 10, 2016
7:00–8:30 am

LOCATION
Richard L. Menschel Education Center
Hospital for Special Surgery
2nd Floor, 535 East 70th Street

David Dare, MD
Alexia Hernandez-Soria, MD
Brian Rebolledo, MD

Morgan Swanstrom, MD
Samir Trehan, MD
Ekaterina Urch, MD
Stephen Warner, MD, PhD

Lewis Clark Wagner, MD, Award for Excellence in Clinical/Translational Orthopaedic Research
and
Russell F. Warren, MD, Award for Excellence in Basic/Translational Orthopaedic Research

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Presentation Schedule

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7:00 am  Increased Lateral Tibial Slope is a Risk Factor for Pediatric ACL Injury: An MRI-Based Case-Control Study of 152 Patients  
David Dare, MD

7:13 am  Systemically Administered Micelles Containing Simvastatin to Improve Fracture Healing in Aged Mice  
Alexia Hernandez-Soria, MD

7:26 am  Arthroscopy Skills Development with a Surgical Simulator: A Comparative Study in Orthopaedic Surgery Residents  
Brian Rebolledo, MD

7:39 am  Effect of Screw Perpendicularity on Compression in Scaphoid Waist Fractures  
Morgan Swanstrom, MD

7:52 am  Novel Serum and Synovial Fluid Biomarker of Periprosthetic Osteolysis  
Samir Trehan, MD

8:04 am  Biceps Tenodesis: A Comparison of Tendon-to-Bone and Tendon-to-Tendon Healing in a Rat Model  
Ekaterina Urch, MD

8:17 am  Superior Outcomes after Operative Fixation of Patella Fractures using a Novel Plate Construct: A Prospective Cohort Study  
Stephen Warner, MD, PhD
Increased Lateral Tibial Slope is a Risk Factor for Pediatric ACL Injury: an MRI-based Case-Control Study of 152 Patients.

David M. Dare MD; Peter D. Fabricant MD MPH; Moira M. McCarthy MD; Brian J. Rebolledo MD; Daniel W. Green MD MS, Frank A. Cordasco MD MS; Kristofer J. Jones MD

Introduction:
Increased posterior tibial slope measured on plain radiographs is associated with elevated risk of ACL rupture in adults. It is unclear, however, if tibial slope is also of significance in children and adolescents. The purpose of this case-control study was to 1) determine if alterations in posterior tibial slope are associated with ACL rupture in pediatric and adolescent athletes, and 2) to quantify changes in tibial slope by age.

Materials and Methods:
Magnetic resonance images of the knee were reviewed by three raters blinded to each other in a 1:1 sample of cases and age/gender matched controls. 76 skeletally-immature ACL-injured knees were compared to 76 knees without ACL injury. The mean age was 14.8 +/- 1.3 years old and 46% of both groups were male. The posterior slope of the articular surface of the medial and lateral plateau was measured, employing a method similar to that used in the adult literature. Our technique, however, differed in that tibial slope was measured no the cartilage surface, not the subchondral bone. Comparisons between knees were made with t-tests and spearman correlation analysis was used to assess changes in tibial slope with advancing age.

Results:
Increased slope of the lateral tibial slope (LTS) was significantly increased in the ACL-injured compared to control knees (5.7° ± 2.4° vs 3.4° ± 1.7°, P<0.001). There was no statistically significant difference in the slope of the medial tibial plateau (MTS) in the ACL-injured and control knees (5.4° ± 2.2° vs 5.1° ± 2.3°, P=0.42). There was no difference in LTS between males and females (4.46° and 4.58°, P = 0.75). Receiver operating characteristic (ROC) analysis of the LTS revealed that a cutoff of lateral posterior tibial slope >4° resulted in a sensitivity of 76% and a specificity of 75% for predicting ACL rupture in this cohort. MTS and LTS decreased, or flattened, by 0.18° (P=0.028) and 0.21° (P=0.009) per year, respectively, as adolescents age.

Conclusion:
LTS is significantly associated with an increased risk of ACL injury in pediatric and adolescent patients. MTS was not associated with risk of injury. Posterior slope was found to decrease, or flatten, with age. A cutoff of >4° for the lateral posterior slope is 76% sensitive and 75% specific for predicting ACL rupture in this cohort. LTS did not influence the incidence of ACL injury differently between genders.

Level of Evidence: Level III, case-control
References:

Systemically Administered Micelles Containing Simvastatin Improve Fracture Healing in Aged Mice

Hernandez-Soria, Alexia1; Chen, Yen Hsun1,2; Johnson, Adam1,2; Zhang, Yijia3; Wang, Dong3; Van Der Meulen, Marjolein1,4; Bostrom, Mathias1; Dahia, Chitra1; Purdue, Ed1; Goldring, Steven R.1; Daluiski, Aaron1

1. Hospital for Special Surgery, New York, NY, United States. 2. Weill Cornell Medical College, New York, NY, United States 3. University of Nebraska Medical Center, Omaha, NE, United States. 4. Cornell University, Ithaca, NY, United States

Introduction:

Impaired fracture healing in the elderly is a costly and significant health care problem. Previous molecular profiling of healing fracture callus tissue from young and aged mice demonstrated reduced BMP expression levels in the aged mice (1). One potential treatment strategy to enhance fracture repair in the elderly is augmentation of BMP signaling in the callus tissue. Statins induce BMP2 expression in osteoblast lineage cells and enhance fracture healing (2); however, the systemic delivery dose required for bone anabolism results in adverse non-target organ toxicity. Local application of statins with carriers such as hydrogels or other scaffolds can deliver clinically effective drug levels, but require surgical introduction of the drug or device (3,4). In a previous study our group prepared a micelle-forming macromolecular pro-drug of simvastatin (SIM-PEG) and demonstrated the ability of the systemically administered pro-drug to preferentially localize at fracture sites and to enhance fracture repair (5). In this study we sought to demonstrate that SIM-PEG micelles could induce BMP2 expression in MC3T3 cells, a murine pre-osteoblast cell line. We hypothesized that the systemically administered micelles containing simvastatin (SIM-PEG) could improve fracture healing in aged mice.

Materials and Methods:

SIM-PEG micelles were synthesized (5). MC3T3 cells were treated with SIM-PEG, and expression of BMP2 and the BMP2 target gene DKK1 was evaluated by quantitative PCR. Open, stabilized right femur fractures were created in 52 7-wk female C57Bl/6 mice and 102 8-9 month retired breeder female (aged) C57Bl/6 mice. The 8-9 month old mice received a retro-orbital injection of SIM-PEG (n=51) or saline (n=52) on post-op day (POD) 1 and POD 7. The young mice received a retro-orbital injection of saline on POD 1 and POD 7. Mice were euthanized on POD 14, 21 and 28 and fracture repair was assessed by micro-computed tomography (MicroCT, μCT 35, Scanco Medical, Brüttisellen, Switzerland) for evaluation of tissue mineral density and bone volume fraction. Fracture repair at POD 21 and 28 was also assessed biomechanically by torsion testing (MTS 858 Bionix, Eden Prairie, MN). Two-tailed T-tests were used to compare different groups over time for the qPCR, μCT and torsion testing; p-value below 0.05 was considered statistically significant.

Results:

SIM-PEG induced BMP2 expression in MC3T3 cells within 48 hours of treatment. MicroCT analysis showed a statistically significant increase in bone volume fraction (BV/TV) of the fracture callus in young control mice compared to old control mice at POD 14 (n= 9-12; p<0.05), indicating delayed healing in the old animals. Additionally, BV/TV was significantly improved in the old SIM-PEG treated mice compared to the old control mice at POD 14 (p<0.005), indicating faster mineralization and improved speed of fracture healing in older SIM-PEG treated animals, although not equivalent to healing rates in the young animals. No significant differences were seen radiographically, by μCT evaluation, or biomechanically in the later healing stages.
Conclusions:

Similar to free simvastatin, the engineered micelle form of simvastatin, SIM-PEG, is pharmacologically active and induces BMP2 expression in a murine pre-osteoblast cell line. The increase in fracture callus BV/TV at POD 14 in the SIM-PEG-treated aged mice provides evidence that the pro-drug is biologically active and is able to partially restore the delayed fracture healing in aged mice. We speculate that this effect may be attributable to statin-induced up-regulation of BMP2 expression in callus tissue. The lack of differences seen at later healing time points suggests a temporal relationship of the BMP-2 pathway and its influence in fracture repair. SIM-PEG shows promise as a single-dose therapy for enhancing fracture healing in the aged population.

References:


Funding Acknowledgement, if applicable:

This work has been supported by The OREF Resident Training Grant with funding provided by the Dr. Dane and Mrs. Mary Louise Miller Endowment Fund, the Rudin Foundation Grant, NIH/NCATS TL1TR000459 of the CTSC at Weill Cornell Medical College, and by NIH grant RO1 AR053325

IRB/IACUC Approval Number 03-13-09M and Approval Period 7/29/13 to 7/2/14
**Introduction**: Surgical simulation has become increasingly relevant to orthopaedic surgery education and may translate to improved operating room proficiency in orthopaedic surgery trainees. The purpose of this study is to compare the arthroscopic performance of junior orthopaedic surgery residents who receive training with a knee and shoulder arthroscopy surgical simulator to those who receive traditional didactic training.

**Materials and Methods**: Fourteen junior orthopaedic surgery residents at a single institution were randomized to receive knee and shoulder arthroscopy training with a surgical simulator (n = 8) or didactic lectures with arthroscopy models (n=6). After their respective training, performance in diagnostic knee and shoulder arthroscopy was assessed using a cadaver model. Time to completion and assessment of arthroscopic handling using a subjective injury grading index (scale: 0-10) was then used to evaluate performance in final cadaver testing.

**Results**: Orthopaedic surgery residents who trained with a surgical simulator outperformed the didactic-trained residents in shoulder arthroscopy by time to completion (-35%; P=0.02) and injury grading index (-35%; P=0.01) (Fig.1). In
addition, a trend towards improved performance of knee arthroscopy by the simulator-trained group was found by time to completion (-36%; P=0.09) and injury grading index (P=0.08) (Table 1).

**Conclusion:** In this study, junior orthopaedic surgery residents who trained with a surgical simulator demonstrated improved arthroscopic performance in both knee and shoulder arthroscopy. Still, future validation of surgical simulator training for orthopaedic surgery residents remains warranted.

**Selected References:**


**Level of Evidence:** Level II

**IRB Approval Number:** 12044

**IRB Approval Period:** 5/1/14 - 2/26/15
Table 1 – Injury Grading Index$^a$

<table>
<thead>
<tr>
<th>Arthroscopy Model</th>
<th>Simulator-trained Group (n=8)</th>
<th>Didactic-trained Group (n=6)</th>
<th>$P^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee</td>
<td>4.0 ± 1.0</td>
<td>5.3 ± 1.5</td>
<td>0.08</td>
</tr>
<tr>
<td>Shoulder</td>
<td>3.6 ± 0.9</td>
<td>5.5 ± 1.5</td>
<td>0.01</td>
</tr>
</tbody>
</table>

$^a$Values are expressed as mean standard deviation.

$^b$P values <0.05 were considered to indicate statistical significance.
Effect of Screw Perpendicularity on Compression in Scaphoid Waist Fractures

Swanstrom MM, Morse KW, Lipman J, Hearns K, Carlson MG

Introduction:

Central and perpendicular screw orientation have each been described for scaphoid fracture fixation. It is unclear, however, which orientation produces greater compression even though compression is a well-appreciated necessity in scaphoid fracture fixation. We hypothesize that perpendicular screw orientation in scaphoid waist fractures produces greater compression than pole-to-pole orientation.

Methods:

Ten preoperative CT scans of scaphoid waist fractures were classified by fracture type and orientation in both the coronal and sagittal planes. 3-dimensional models of each scaphoid and fracture plane were created. Simulated Acurtrak 2 (Acumed) screws were placed into the models in both perpendicular (PERP) and pole-to-pole (PTP) orientations. Engagement length and screw angle relative to the fracture were then measured. Compression strength was calculated mathematically from the shear area (engagement length and screw diameter), average density and acuity of angle (radians). Wilcoxon signed-rank tests and a Pearson correlation were used to compare compressive forces.

Results:

The angle between screw and fracture in the PTP group ranged from 36-84°. By definition, the PERP screw angle was 90°. Fracture orientation included five transverse, two horizontal oblique, two coronal, and one vertical oblique fracture.

There was a significant positive correlation between perpendicularity of the PTP screw to the fracture and its compression strength (r=0.69, n=10, p<0.05) (Figure 1). PERP screws had significantly more compression than PTP screws when the PTP screw to fracture angle was <80° (470N vs 353N, p<0.05). When the PTP screw to fracture angle was >80°, the PTP screw approximated the PERP screw, and there was no difference in compression between PTP (747N) and PERP (752N) screw placement (p>0.05).

Discussion/Conclusions:

Increasing screw perpendicularity results in higher compressive forces. When the angle of the pole-to-pole screw to the fracture is <80°, a perpendicular screw provides superior compression than pole-to-pole. When the angle of the pole-to-pole screw to the fracture is >80°, there is no difference in compression compared to a perpendicular screw. In scaphoid waist fractures, maximum fracture compression is obtained with a screw perpendicular to the fracture, not pole-to-pole. The increased compression gained from perpendicular screw placement offsets the decreased engagement length.
Level of Evidence: Level 3

Funding Acknowledgement, if applicable: n/a

IRB/IACUC Approval Number: 2014-048
Compression strength at differing screw angles in scaphoid waist fractures.  
• indicates pole-to-pole screw; × indicates perpendicular screw
Figure 2: Simulated P2P and PERP screws in modeled scaphoid
Novel Serum and Synovial Fluid Biomarker of Periprosthetic Osteolysis

Trehan, Samir K; Jo, Jonathan; Zambrana, Lester; Purdue, Edward; Lane, Joseph M

Introduction:
Periprosthetic osteolysis (PPO) is the most frequent indication for total hip replacement (THR) failure. Currently, PPO diagnosis occurs in advanced stages that often necessitate complex revisions due to bone loss. PPO biomarkers could facilitate earlier diagnosis. Alternative macrophage activation pathway regulators, CHIT1 and CCL18, have increased periprosthetic expression in patients undergoing revision THR for osteolysis. We hypothesized that synovial fluid and serum levels of CHIT1 and CCL18 would be increased in patients undergoing revision THR for PPO versus controls without osteolysis.

Materials and Methods:
All revision metal-on-polyethylene THR patients were screened pre-operatively. Patients with active/prior infection, previous revision(s), metabolic/rheumatologic conditions and/or medications affecting bone metabolism, were excluded. According to IRB protocol and a priori power analysis, 30 patients were enrolled. Twenty “osteolysis” patients underwent revision for PPO (based on imaging and operative reports). Ten “controls” had stable implants and revision for instability (9) or mechanical symptoms (1). Pre-operative serum and intra-operative synovial fluid samples were collected. CHIT1 and CCL18 were quantified via commercially available ELISAs (Circulex and R&D Systems, respectively). Significance was assessed via two-tailed Fisher’s Exact test.

Results:
Among “osteolysis” and “control” patients, 11/20 and 4/10 were male, average age was 68 and 63 years, 9/20 and 3/10 had cemented femoral components, and average implant longevity was 15 and 5 years, respectively. CHIT1 was significantly increased in “osteolysis” versus “control” patients’ synovial fluid (3,727 versus 731 nM) and serum (98 versus 39 nM). CCL18 levels were significantly increased in “osteolysis” versus “control” patients’ synovial fluid (425 versus 180 nM), but not serum.

Conclusions:
In this prospective case-control study, CHIT1 was identified as a novel synovial fluid and serum biomarker of PPO. CHIT1 expression is induced during macrophage activation in response to wear debris. CHIT1 monitoring may facilitate early diagnosis of THR PPO and consequent avoidance of complex revisions due to implant loosening and/or bone loss. Furthermore, CHIT1 may represent a novel therapeutic target for PPO.

References:

Level of Evidence: III

Funding Acknowledgement: Louis and Rachel Rudin Foundation

IRB/IACUC Approval Number 2015-159 and Approval Period 9/24/15-7/8/16
(Above IRB information represents currently active renewal. Previous IRB #12118.)
Biceps Tenodesis: A Comparison of Tendon-to-Bone and Tendon-to-Tendon Healing in a Rat Model

Ekaterina Urch MD, Samuel A Taylor MD, Prem N Ramkumar BA, Stephen B Doty PhD, Alex E White BA, Demetris Delos MD, Mary E Shorey BA, Stephen J O’Brien MD MBA
Hospital for Special Surgery, New York, New York

Introduction: The long head of the biceps tendon (LHBT) is a well-established pain generator in the anterior shoulder. Tenodesis of the LHBT is an increasingly popular intervention for refractory biceps tendinitis. Addressing bicipital tunnel in its entirety, including both intra- and extraarticular portions, is crucial for optimized clinical outcomes. Despite extensive research on the subject, however, the optimal tenodesis location and technique remain controversial. The purpose of this was to determine the impact of tenodesis location on healing and inflammation in a rat model.

Methods and Materials: LHBT tenodesis was performed in 36 Sprague-Dawley rats to three different locations. Metaphyseal (MT) and diaphyseal (DT) tenodeses were performed by passing the LHB through a transosseous drill hole. Tendon-to-tendon tenodeses (TT) were performed by securing the LHBT to the conjoint tendon. Following surgery, four animals from each group were sacrificed at 6, 12, and 24 weeks for histological analysis. Specimens were processed with hemotoxylin and eosin (H&E), CD68 antibody (macrophage marker), and tenomodulin (Tnmd) antibody (tenocyte marker). Cellularity at the tenodesis interface was evaluated by averaging the nuclei count within 3 separate high power fields (HPF) at the tenodesis interface (tendon-to-bone or tendon-to-tendon). Inflammatory response was similarly measured by averaging the number of CD68-positive cells per HPF. The presence of tenocytes at the tenodesis interface was evaluated based on the presence or absence of a positive Tnmd reaction.

Results: Cellularity was significantly greater in the MT and DT groups at 6 and 12 weeks when compared to the TT group. No difference in cellularity was seen between the MT and DT groups at any time point. Macrophage response was significantly greater in the MT and DT groups than the TT group at both 6 and 12 weeks. (Figure 1A) No difference in CD68 reaction was seen between the groups at 24 weeks. The TT group had a strongly-positive Tnmd reaction at both 6 and 12 weeks. (Figure 1B) Tnmd reaction was absent in both bony tenodesis groups at all time points. In all cases of tendon-to-bone tenodesis, no recognizable formed tendon was seen within the bone tunnel. Rather, all specimens were characterized by dense connective tissue at the bone surface, surrounded by a large accumulation of macrophages.

Conclusions: Bony tenodesis produces a significantly greater inflammatory response at the tenodesis interface than does tendon-to-tendon fixation. Macrophage proliferation within the bone tunnel in the setting of absent formed tendon suggests tendon degeneration and calls into question the rationale behind tunnel fixation. The presence of a robust Tnmd reaction in the early healing stages in the tendon-to-tendon group suggests a regenerative healing process. Biceps tenodesis using a tendon-to-tendon transfer method optimizes healing and minimizes the inflammatory response when compared with bone tunnel tenodesis techniques in a rat model.
References:


Level of Evidence: NA

Funding: HSS Institute for Sports Medicine Research

IACUC Approval Number [08-14-03R] and Approval Period [8.21.14 – 8.20.15]
Superior Outcomes after Operative Fixation of Patella Fractures using a Novel Plate Construct: a Prospective Cohort Study


Introduction: Displaced patella fractures traditionally have been treated with anterior tension band constructs and are associated with unsatisfactory patient-reported and functional outcomes. To address these inferior outcomes, we have developed a novel fixation construct that provides multiplanar fixation through a low-profile mesh plate with minimal iatrogenic disruption to patellar vascularity. The purpose of this prospective cohort study was to determine if the new fixation construct resulted in improved outcomes compared to traditional tension band techniques.

Materials and Methods: A comparative cohort study was designed, and patients with isolated, unilateral patellar fractures were enrolled prospectively. During the study period from 2012-2014, a novel plate construct was used that spans half of the patella circumference laterally and provides multiplanar fixation through a low profile plate with additional suture fixation of the patellar tendon through the plate to address inferior pole comminution when present (Figure). A comparison cohort was drawn from patients treated from 2008-2012, where treatment consisted of traditional tension band fixation techniques. Thirty-three patients treated with a tension band and twenty-five patients treated with the novel plate construct were included in the final analyses. Subjective postoperative clinical outcomes and objective functional and strength measurements were subsequently collected in both groups. Mixed-model repeated measures analyses were used to determine between-subject and within-subject effects over the study period.

Results: The two cohorts had similar baseline characteristics. Patients with the plate construct had clinically and statistically significantly superior Knee Outcome Survey Activities of Daily Living Scale (KOS-ALDS) scores throughout the study period (p<0.001). Functional testing demonstrated modest improvements in patients with plate constructs compared to tension band constructs at twelve months. Patients in the plate cohort had significantly increased thigh circumferences (p=0.003) and decreased anterior knee pain (p<0.0001) compared to the tension band cohort.

Conclusions: Operative treatment of patella fractures using tension band constructs have resulted in impaired functional outcomes overall. In this prospective cohort study, the use of a novel fixation construct with multiplanar and interfragmentary fixation and minimal disruption of patellar vascularity enables improved clinical outcomes and functional performance.

Figure: Anteroposterior (a) and lateral (b) injury knee radiographs of a patella fracture in a 50 year old woman. 3D CT reconstructions (c) reveal an AO/OTA 34-C3 patella fracture. Anteroposterior (d) and lateral (e) knee radiographs 12 months postoperatively.
Level of Evidence: Level II, Prospective Cohort Study

Funding Acknowledgement, if applicable: N/A