Musculoskeletal Infection Society

33rd Annual Open Scientific Meeting

MUSCULOSKELETAL INFECTION SOCIETY

August 4-5, 2023

SALT LAKE CITY, UTAH

IN PERSON AND VIRTUAL MEETING

Please join us!

34TH Annual Open Scientific Meeting

of the

Musculoskeletal Infection Society

MUSCULOSKELETAL INFECTION SOCIETY

August 2-3, 2024

Visit

www.msis–na.org

for updates

Objectives

At the conclusion of this educational activity, participants will:

- Understand the open questions in the management of musculoskeletal infections, including optimal surgical approaches and systemic antibiotic therapy.

- Discuss challenging clinical cases of musculoskeletal infection, including diagnostics and management strategies.

- Evaluate the utility of various irrigation solutions and local antibiotic therapy.

Intended Audience

This course is designed for member and nonmember clinicians, including orthopaedic surgeons, infectious disease specialists, PAs, NPs, podiatrists and other health care providers who manage the care of patients with musculoskeletal infections.

Continuing Education Credit

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the American Academy of Orthopaedic Surgeons and the Musculoskeletal Infection Society. The American Academy of Orthopaedic Surgeons is accredited by the ACCME to provide continuing medical education for physicians.

The American Academy of Orthopaedic Surgeons designates the MSIS 33rd Annual Open Scientific Meeting, August 4-5, 2023, in Salt Lake City, Utah (live and virtual) for a maximum of **11.25** ***AMA PRA Category 1 Credits™***. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Alex McLaren, MD

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Special Thanks

To the Members who answered the call to serve when additional help was needed with Abstract and Presentation Reviews

Barry Brause, MD	Carlos Higuera-Rueda, MD	Mike O'Malley, MD
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MUSCULOSKELETAL INFECTION SOCIETY

33rd Annual Open Scientific Meeting
August 4-5, 2023
Salt Lake City, Utah

Agenda

Friday, August 4, 2023
Capitol Ballrooms

7:00am	Registration Opens
7:00-8:30am *Ballroom Foyer*	**Breakfast** **Visit Exhibitors and e-Posters**
7:45am	**Welcome, Disclosures** Laura Certain, MD PhD, MSIS President
Session I	**BASIC SCIENCE** **Moderators:** Alaina Ritter, MD, and Jeremy Shaw, MD
8:00am	Mapping Biofilm on Knee and Hip Explants: Evaluating the Role of Polymeric Components in Periprosthetic Joint Infection *Jack Brooks, Katarina Sikiric,* ***Douglas Chonko****, Matthew Pigott, Anne Sullivan, Paul Stoodley*
8:06am	Bacterial Survivors Become Opportunistic Pathogens Following Presurgical Skin Preparation Due to a Blind Spot in an FDA Standard ***Hannah Duffy****, Nicholas Ashton, Abbey Blair, Dustin Williams, Nathanael Hooper*
8:12am	A Novel Benzalkonium-Chloride Topical Solution Ahead of Efficacy and Safety Concerns for Current Preoperative Antiseptic Formulations *Diana Fernández-Rodríguez, Jeongeun Cho,* ***Emanuele Chisari****, Javad Parvizi*

8:18am Commonly Used Antiseptic Solutions Do Not Compromise Osseointegration in a Clinically Established Mouse Model for Cementless Knee Arthroplasty
***Mohammed Hammad**, Anastasia Oktarina, Vincentius Suhardi, Andrew Thomson, Qingdian Li, Kevin Döring, Alberto Carli, Mathias Bostrom, Xu Yang*

8:24am Discussion

8:33am Scaffold-Based Vaccination with PAMPs for Periprosthetic Joint Infection in a Murine Model
***Alexander Tatara**, Shanda Lightbown, Hamza Ijaz, Michael Super, Sandra Nelson, David Mooney*

8:39am Comparison of *In Vitro* Efficacy of Antibiotic Cement Against Common Prosthetic Joint Infection Pathogens
***Matthew Dietz**, Elizabeth Stewart, Brian McGowan, Emily Hunt, Dylan Thomas, Matthew Squire*

8:45am Testing a Rapidly Polymerizable Hydrogel Wound Dressing for Far-Forward Care of War-Time Traumatic Blast Wounds in a Murine Model of Open Fracture
*Christopher Hamad**, Zeinab Mamouei**, Adolfo Hernandez, Rene Chun, Christopher Hart, Chad Ishmael, Amaka Enueme, Elizabeth Pumford, Andrea Kasko, Nicholas Bernthal*

8:51am Vancomycin and Gentamicin Loaded Stimulan Beads are More Effective at Killing *Staphylococcus aureus* Synovial Sluid Aggregates than Intra-Articular Concentrations of Vancomycin Alone *In Vitro*
*Amelia M Staats, Phillip Laycock, Paul Stoodley**, Devin Sindeldecker***

8:57am Implant Materials Affect Biofilm Formation
*David Kerr, Jerry Chang**, Thorsten Seyler***

9:03am Discussion

SYMPOSIUM #1 **It Grew What Now? Periprosthetic Infections Caused by Unusual Pathogens**
Moderators: Irene Sigmund, MD, and Sandra Nelson, MD

9:10am ***Mycobacterium fortuitum***
Jenny Aronson, MD, Infectious Disease
Stanford University, Redwood City, CA

Mycoplasma
Laila Woc-Colburn, MD, Infectious Disease
Emory University, Atlanta, GA

Blastomyces
Laura Damioli, MD, Infectious Disease
University of Colorado, Aurora, CO

10:10am **Break**
Visit Exhibitors and e-Posters

Session II **CLINICAL STUDIES**
Moderators: Nicolas Cortes-Penfield, MD, and Brian Klatt, MD

10:35am A "Dry Tap" in PJI Workup of Total Hip Arthroplasty Is Not Reassuring For the Absence of Infection
Emily Treu, *Nathan Behrens, Brenna Blackburn, Christopher Pelt, Daniel Cushman, Michael Archibeck*

10:41am Robotics and Navigation Do Not Affect the Risk of Periprosthetic Joint Infection Following Primary Total Hip or Knee Arthroplasty
*Scott LaValva**,** Yu-Fen Chiu, Mia Fowler,* ***Alberto Carli***

10:47am Outcomes of a Collaborative Orthopaedic-Infectious Disease Clinic
Allison Lastinger*, Matthew Dietz*

10:53am Discussion

11:00am Safety Profile of Seven-Day Antibiotic Irrigation for the Treatment of Chronic Periprosthetic Joint Infection: A Prospective Randomized Phase II Comparative Study
Bryan Springer, Brian deBeaubien, ***Nicolas Piuzzi****, Hari Parvataneni, Andy Glassman, Carlos Higuera*

11:06am A Phase 1b Open-Label, Dose-Escalating Study to Evaluate the Safety and Tolerability of PLG0206, an Antimicrobial Peptide, in Patients Undergoing, Debridement, Antibiotics, and Implant Retention (DAIR) for Treatment of a Periprosthetic Joint Infection (PJI) Occurring after Total Knee Arthroplasty (TKA): Interim Analysis
David Huang*, Nicolas Piuzzi, Antonia Chen, Christopher Pelt, David Rodriguez-Quintana, Despina Dobbins, Matthew Dietz*

11:12am Extended Oral Antibiotics Increase Tetracycline Resistance in Patients Who Fail Two-Stage Exchange
***Laura Certain**, Brenna Blackburn, Jeremy Gililland, Sandra Nelson, Antonia Chen, Jessica Seidelman, Alaina Ritter, Research Consortium (AARC)*

11:18am Extended Oral Antibiotic Prophylaxis: Defining its Role in All-Comers Undergoing Primary and Aseptic Revision Total Joint Arthroplasty
***Kyle Bundschuh**, Brian Muffly, Ayomide Ayeni, Sameer Khawaja, Anthony Karzon, George Guild, Kevin Heo*

11:24am Discussion

SYMPOSIUM #2 **Infection Mimics**
Moderators: Angela Hewlett, MD, and Andy Miller, MD

11:30am **Clinical Case Presentation**
Angela Hewlett, MD
University of Nebraska, Omaha, NE

What Not to Miss: Pyoderma Gangrenosum as a Mimic of Surgical Site Infections
Lauren Madigan, MD, Dermatology
University of Utah, Salt Lake City, UT

CRMO/SAPPHO as Osteomyelitis
Polly Ferguson, MD, Pediatric Rheumatology
University of Iowa, Iowa City, IA

Crystalline-Induced Arthritis in a Prosthetic Joint
Ryan Jessee, MD, Rheumatology
Greensboro, NC

12:30pm **Lunch**
Ballroom Foyer Box Lunch
Visit Exhibitors and e-Posters

Session III **CLINICAL STUDIES**
Moderators: Poorani Sekar, MD, and Irene Sigmund, MD

1:30pm Establishment and Validation of a Synovial Fluid CRP Clinical Decision Limit for Periprosthetic Joint Infection
*Carl Deirmengian, Krista Toler, John Miamidian, **Alex McLaren***

1:36pm Association of Preoperative NarxCare Scores with the Fate of Two-Stage Reimplantation Revision Total Joint Arthroplasty
*Vivek Singh, **Jesus Villa**, Katherine Rajschmir, Tejbir Pannu, Justin Limtong, Carlos Higuera-Rueda*

1:42pm Single-Stage Exchange Arthroplasty has Comparable Results to Two-Stage Exchange Revision in Select Patients with Periprosthetic Hip and Knee Infection
***Ryan Sutton**, Juan Lizcano, Andrew Fraval, Bright Wiafe, Paul Courtney, Scot Brown*

1:48pm Discussion

1:58pm Patients with Positive *Cutibacterium* Culture Following Total Hip (THA) and Total Knee Arthroplasty (TKA) Often do not Meet MSIS Criteria for Infection
***Benjamin Levy**, Tracy Borsinger, Paul Werth, Wayne Moschetti*

2:04pm Expanded Gram-Negative Antimicrobial Prophylaxis Reduces Surgical Site Infection in Hip Fracture with Arthroplasty
*Scott Roberts, Richard Martinello, Lee Rubin, **Marjorie Golden***

2:10pm A Retrospective Cohort Study on the Impact of Suppressive Antimicrobial Therapy after DAIR for PJI in 3 Countries
***Don Bambino Geno Tai,** Paul Jutte, Aaron Tande , Benjamin Langworthy , Matthew Abdel, Elie Berbari, Gina Suh, Wierd Zijlstra, Alex Soriano, Marjan Wouthuyzen-Bakker*

2:16pm Discussion

SYMPOSIUM #3 Spine Infections: Case-Based Discussion of Open Questions in Management

2:30pm Laura Damioli, MD, Infectious Disease
University of Colorado, Aurora, CO

Brian Karamian, MD, Orthopaedics
University of Utah, Salt Lake City, UT

Brandon Lawrence, MD, Orthopaedics
University of Utah, Salt Lake City, UT

Jeremy Shaw, MD, Orthopaedics
University of Pittsburgh, Pittsburgh, PA

3:30pm	**Break** **Visit Exhibitors and e-Posters**
Session IV	**CLINCAL STUDIES** **Moderators:** Jakrapun Pupaibool, MD, and Matthew Dietz, MD
3:50pm	Accelerated Severity of Illness Score Enhances Prediction of Complicated Osteomyelitis in Children *Tahmina Jahan, **Norman Lapin**, Michael O'Connell, Chan-Hee Jo, Yuhan Ma, Naureen Tareen, Lawson Copley*
3:56pm	Effect of Preoperative Antibiotic Therapy on Operative Culture Yield for Diagnosis of Native Joint Septic Arthritis ***Ryan Khodadadi**, Pansachee Damronglerd, Jack McHugh, Said El Zein, Brian Lahr, Brandon Yuan, Omar Abu Saleh, Gina Suh, Aaron Tande*
4:02pm	Risk Factors for Repeat Irrigation & Debridement in Native Joint Septic Arthritis ***Gabriel Linden**, Sophie Lipson, Vineet Desai, Jared Alswang, Scott Ryan, Antonia Chen, Matthew Salzler*
4:08pm	Assessing the Utility of Vertebral Body / Disc Space Fluid Cell Differential in the Diagnosis of Native Vertebral Osteomyelitis ***Said El Zein**, Brian Lahr, Brett Freedman, Matthew Howard, Aaron Tande, Elie Berbari*
4:14pm	Discussion
4:22pm	Does the CDC Surgical Wound Classification Adequately Predict Post-Operative Infection in Orthopaedic Trauma? ***Elizabeth Cho**, Hanna House, Andrew Marten, Marina Feffer, Julie Agel, John Scolaro, Meir Marmor, Ashley Levack*
4:28pm	Outcomes Following Implant Retention for Fracture-Related Infections ***Hussam Tabaja**, Brandon Yuan, Nicholas Rhodes, Aaron Tande*
4:34pm	Multisite Study of the Management of Musculoskeletal Infection after Trauma: The MMUSKIT Study ***Jessica Seidelman**, Alaina Ritter, Malcolm DeBaun, Christian Pean, Laura Certain, Sandra Nelson, MMUSKIT Study Group*
4:40pm	Discussion

4:50pm **Live Survey of the MSIS**
Antonia Chen, MD

6:30pm **President's Reception and Hall of Fame Induction**
Olympus Ballroom Cocktails and Southwest Dinner Buffet
Dress: Business Casual

Saturday, August 5, 2023
Capitol Ballrooms

6:30-8:30am **Breakfast**
Ballroom Foyer **Visit Exhibitors and e-Posters**

7:00-7:45am **MSIS Business Meeting** (**MSIS Members only**)
Capitol Ballroom

7:55am **Options for Publication**
Laura Certain, MD, PhD

Session V **BASIC SCIENCE**
Moderators: Alaina Ritter, MD, and Elie Ghanem, MD

8:00am Efficacy and Tissue Toxicity of Topical Antiseptics
*David Kerr, **Jerry Chang***

8:06am Novel Activated Zinc Anti-Biofilm Irrigant Superior to Commercially-Available Irrigants
*Derek Hill, **Nash Reigle**, Brandon Nutt, Paul Attar, Korey Goldsmith, Michael Scarborough, Ahmed Siddiqi*

8:12am Operating Room Air May Harbor Pathogens: The Role of an Ultraviolet Air Filtration Unit
***Diana Fernández-Rodríguez**, Nicolina Zappley, Javad Parvizi*

8:18am Chondrocyte Invasion is a Mechanism for Persistent *Staphylococcus aureus* Infection
***Jerry Chang**, David Kerr, Thorsten Seyler*

8:24am Polymicrobial Infection with *Candida albicans* and *Staphylococcus aureus* Increases Bacterial Biofilm Formation in a Murine Model of Periprosthetic Joint Infection
***Zeinab Mamouei**, Christopher Hamad, Rahul Sobti, Jack Pearce, Adolfo Hernandez, Rene Chun, Aaron Kavanaugh, Fabrizio Billi, Nicholas Bernthal*

8:30am Discussion

8:40am Systemic Versus Increasing Intra-Articular Doses of Vancomycin in a Prosthetic Joint Infection Rat Model: Efficacy and Impact on Mitochondria
***Nour Bouji**, Elizabeth Stewart, John Hollander, Ethan Meadows, Dylan Shaver, Matthew Dietz*

8:46am A Refillable Drug Delivery Device that Sustains Local, High Dose Antibiotic Therapy Manages Biofilm Implant-Related Infection in a Sheep Model of Long Bone Open Fracture
Dustin Williams, Robert Falconer, ***Nicholas Ashton***

8:52am Gentamicin-Loaded Bone Cement is Effective Against Representative Small Colony Variants: An *In Vitro* Study
Jeongeun Cho, ***Emanuele Chisari**, Diana Fernández-Rodríguez, Javad Parvizi*

8:58am Discussion

SYMPOSIUM #4 ***Cutibacterium acnes* and the Skin Microbiome**
Moderator: Laura Certain, MD, PhD

9:10am **Anatomy Promotes Neutral Coexistence of *C. acnes* Across Facial Skin**
Tami Lieberman, PhD, Systems Biology
Massachusetts Institute of Technology, Cambridge, MA

***C. acnes* in Shoulder PJI**
Paul Pottinger, MD, Infectious Disease
University of Washington, Seattle, WA

10:10am **Break**
Visit Exhibitors and e-Posters

SYMPOSIUM #5 **Fracture-Related Infection**
Moderators: Jessica Seidelman, MD, and Malcolm DeBaun, MD

10:30am **Preclinical Models of Infected Fracture**
Joseph Wenke, PhD, Orthopaedics
University of Texas Medical Branch, Galveston, TX

Antibiotic Management of Infected Fracture Fixation
Gina Suh, MD, Infectious Disease
Mayo Clinic, Rochester, MN

Orthopaedic Heresy: Fact and Fiction
in the Care of Chronic Osteomyelitis
David Lowenberg, MD, Orthopaedics
Stanford University, Redwood, CA

12:00pm **Introduction of Incoming President: Thorsten Seyler, MD PhD**
Laura Certain, MD, PhD
Presentation of Awards
Jon T. Mader Award; Jeanette Wilkins Award; e-Poster Award
Closing Remarks: *Laura Certain, MD, PhD*

12:15pm Adjourn

We look forward to seeing you again in August 2024!

Session I

23-APP-1193 Mapping Biofilm on Knee and Hip Explants: Evaluating the Role of Polymeric Components in Periprosthetic Joint Infection
*Jack Brooks, Katarina Sikiric, **Douglas Chonko**, Matthew Pigott, Anne Sullivan, Paul Stoodley*

23-APP-1176 Bacterial survivors become opportunistic pathogens following presurgical skin preparation due to a blind spot in an FDA standard
***Hannah R Duffy**, Nicholas Ashton, Abbey Blair, Dustin L Williams, Nathanael Hooper*

23-APP-1086 A novel benzalkonium-chloride topical solution ahead of efficacy and safety concerns for current preoperative antiseptic formulations.
***Diana Fernández-Rodríguez**, Jeongeun Cho, Emanuele Chisari, Javad Parvizi*

23-APP-1154 Commonly Used Antiseptic Solutions Do Not Compromise Osseointegration in a Clinically Established Mouse Model for Cementless Knee Arthroplasty
***Mohammed Hammad**, Anastasia Oktarina, Vincentius J Suhardi, Andrew Thomson, Qingdian Li, Kevin Döring, Alberto V Carli, Mathias Bostrom, Xu Yang*

23-APP-1162 Scaffold-based Vaccination with PAMPs for Periprosthetic Joint Infection In A Murine Model
***Alexander Tatara**, Shanda Lightbown, Hamza Ijaz, Michael Super, Sandra Nelson, David Mooney*

23-APP-1121 Comparison of In vitro Efficacy of Antibiotic Cement Against Common Prosthetic Joint Infection Pathogens
***Matthew J Dietz**, Elizabeth Stewart, Brian McGowan, Emily Hunt, Dylan Thomas, Matthew Squire*

23-APP-1212 Testing a Rapidly Polymerizable Hydrogel Wound Dressing for Far-Forward Care of War-Time Traumatic Blast Wounds in a Murine Model of Open Fracture
*Christopher Hamad, **Zeinab Mamouei**, Adolfo hernandez, Rene Chun, Christopher Hart, Chad Ishmael, Nicholas Bernthal, Amaka Enueme, Elizabeth Pumford, Andrea Kasko*

23-APP-1148 Vancomycin and gentamicin loaded Stimulan beads are more effective at killing Staphylococcus ureus synovial fluid aggregates than intra-articular concentrations of vancomycin alone in vitro
*Amelia M Staats , Phillip Laycock , **Paul Stoodley** , Devin Sindeldecker*

23-APP-1134 Implant Materials Affect Biofilm Formation
*David Kerr, **Jerry Chang**, Thorsten Seyler*

1193 Mapping Biofilm on Knee and Hip Explants: Evaluating the Role of Polymeric Components in Periprosthetic Joint Infection

Authors: Jack Brooks, Katarina Sikiric, **Douglas Chonko**, Matthew Pigott, Anne Sullivan, Paul Stoodley

Background And Rationale: Periprosthetic joint infection (PJI) is a severe complication that occurs following primary total joint arthroplasty (TJA), leading to increased patient morbidity and mortality. Bacterial biofilms often preside in these infections, with their tolerance of antibiotics and host immunity posing major treatment challenges. It is not known if some component materials are more prone to biofilm formation than others.

Study Question: This study aims to characterize specific locations on periprosthetic knee and hip explants that are more favorable to bacterial attachment and further analyze the specific material impacts of these components on biofilm formation.

Methods: Explanted components from 31 hip and knee TJA revision cases were evaluated using implant surface culture (ISC). ISC involves applying a thin agar coating over the implant surface, followed by incubation, observation, and imaging of colony outgrowth over a period of 9 days. Selected microbes were identified and subsequently compared to clinical culture and the 2013 Musculoskeletal Infection Society's PJI diagnostic criteria. A detailed statistical analysis was then completed to further assess biofilm growth by differences in material and location.

Results: ISC showed a sensitivity of 93% and a specificity of 62.5% compared to clinical culture. When compared to MSIS criteria, the sensitivity and specificity measured 100% and 91%, respectively. Biofilm was commonly found on component edges and in cavities, especially on the non-articulating surface between the tibial tray and polyethylene insert. Statistical analysis confirmed that the polyethylene insert of the knee was more conducive to biofilm growth than metallic components in ISC positive cases ($p=0.0052$). Residual PMMA on individual components was also identified as a surface with notable biofilm formation.

Discussion: ISC offers a useful technique for locating bacterial growth on explanted hardware. This method identifies polymeric materials as more conducive to biofilm growth. In addition, examples of notable growth between the tibial tray and polyethylene insert continue to suggest this area as a protected space for bacteria from the diffusion of antibiotics.

Conclusion: Biofilm was successfully mapped to specific locations and materials of explanted hardware components from knee and hip revision cases. Polymeric components displayed increased biofilm growth compared metallic hardware.

1176 Bacterial survivors become opportunistic pathogens following presurgical skin preparation due to a blind spot in an FDA standard

Authors: **Hannah R Duffy**, Nicholas Ashton, Abbey Blair, Dustin L Williams, Nathanael Hooper

Background And Rationale: Bacterial survivors of preoperative skin preparations (PSPs) pose a significant infection risk, especially when hardware is involved. PSPs are approved by the FDA using a skin sampling process known as the Cup-Scrub method. In this technique, a sterile cup is placed on the skin following PSP. Broth is pipetted into the cup and the skin is agitated with a rubber spatula to suspend bacteria. As this method does not consider deep-dwelling bacteria, we developed a model for PSP testing which uses full-thickness skin samples excised from the pig back that account for microbes in deeper skin regions. In this study, we compared our process, known as the Tissue-Blend method, with the Cup-Scrub method to estimate the number of bacterial survivors in skin following a chlorhexidine gluconate (CHG) PSP.

Study Question: To what extent do the Cup-Scrub and Tissue-Blend methods leave viable bacteria in deep skin regions following PSP?

Methods: We applied the Cup-Scrub and Tissue-Blend methods to the backs of 7 Yorkshire pigs following alternating scrubs of 4% CHG and alcohol (n=5 sites/pig) and on control skin as a relative baseline (n=5 sites/pig). With 4 treatment groups, 20 samples were taken from each animal for a total of 140 samples.

Results: The average log10 reduction for the Cup-Scrub and Tissue-Blend methods were 1.57 +/- 0.45 and 0.23 +/- 0.48 log10 CFU/cm2, respectively. Initial values using the Cup-Scrub and Tissue-Blend methods were 2.62 +/- 0.21 and 3.46 +/- 0.24 log10 CFU/cm2, respectively. The difference in bioburden between the Cup-Scrub and Tissue-Blend sampling techniques in both the control and CHG areas were statistically significant ($p<0.001$).

Discussion: Most surgical site infections (SSIs) stem from skin flora bacteria. This dangerous and costly complication is principally prevented by PSPs. The current sampling standard used for FDA approval of PSPs, or the Cup-Scrub method, underreports the bioburden present in the skin when compared to the Tissue-Blend model leading to a preventable infection risk. The high CFU/cm2 signal following PSP application with the Tissue-Blend method shows the importance of readdressing current PSP approaches to mitigate SSI.

Conclusion: A significant percentage of bacteria in the deep tissue regions survive PSP, creating a blind spot in the standard that we use to measure PSP efficacy before surgery.

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1086 A novel benzalkonium-chloride topical solution ahead of efficacy and safety concerns for current preoperative antiseptic formulations.

Authors: Diana Fernández-Rodríguez, Jeongeun Cho, **Emanuele Chisari,** Javad parvizi

Background And Rationale: Prevention of healthcare-associated infections (HAI), like surgical site infections (SSIs), has become a top priority for the medical community and object of rating and grading of healthcare institutions. Presurgical reduction of the bioburden on the skin has been suggested as a way to reduce SSI incidence. Currently available skin decolonization products are chlorhexidine gluconate (CHG) based. The rise in resistance of organisms to CHG, together with cases of CHG hypersensitivity prompted us to design a novel skin antiseptic solution.

Study Question: Can bacteria be detected on skin after the use of chlorhexidine gluconate? Does the susceptibility of common infecting microorganisms causing surgical site infections differ between chlorhexidine gluconate and benzalkonium-chloride?

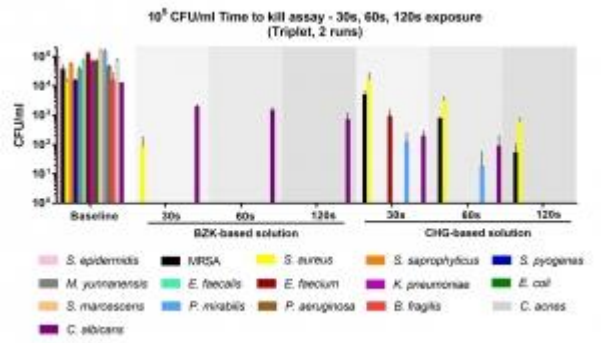
Methods: We conducted an observational clinical study using next-generation sequencing to assess the residual microbiota after the application of a preoperative antiseptic solution containing CHG at 2% as the active ingredient. Results were then replicated in in vitro testing according to the ASTM protocol E2315-16 in comparison with another common antiseptic. A formulation based on benzalkonium chloride (BZK) at 0.129% was chosen according to available evidence and regulatory restrictions.

Results: As part of an ongoing study, we noticed a high rate of bacteria retrieved after the topical CHG application on a total of 15 (42.85%) patients. S. epidermidis and C. acnes were the most frequent strains observed; however, Enterobacterales and anaerobes species were also identified. Later, our in vitro efficacy tests confirmed that the CHG-based solution had a limited activity towards Gram-positive, Gram-negative and fungi species at 30 seconds of exposure. After 120 seconds, CHG was not able to clear all the S. aureus bioburden. By contrast, after 30 seconds of exposure, all bacterial strains were killed by our in-house BZK formulation, but C. albicans was still found at 120 seconds of exposure (666.7 Â± 535.4 CFU/ml, $p<0.01$).

Discussion: We detected a limited efficacy for CHG-based formulations in in vivo and in vitro assays. Our in-house BZK-based solution was effective against all Gram-positive, Gram-negative, and anaerobic bacterial strains, after 30s of exposure.

Conclusion: The rapid action of BZK, together with its proven safety, makes it a promising product for skin decolonization in the future.

Attachments:



1154 Commonly Used Antiseptic Solutions Do Not Compromise Osseointegration in a Clinically Established Mouse Model for Cementless Knee Arthroplasty

Authors: **Mohammed Hammad**, Anastasia Oktarina, Vincentius J Suhardi, Andrew Thomson, Qingdian Li, Kevin Döring, Alberto V Carli, Mathias Bostrom, Xu Yang

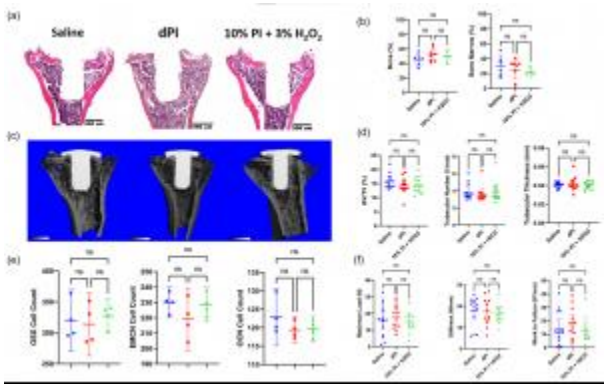
Background And Rationale: Synergistic use of povidone-iodine (PI) and hydrogen peroxide (H2O2) has shown promising results in PJI management; however, there is a prevailing concern among orthopedic surgeons regarding the utilization of higher concentration antiseptic irrigation solutions such as 10% PI mixed with 3% H2O2 even when shown better results in terms of bacterial eradication and/or clinical outcomes in PJI management. This apprehension is grounded in the potential cytotoxic effects at the peri-implant interface, which may adversely impact osseointegration leading to complications, including but not limited to aseptic loosening.

Study Question: This study aims to compare the impact of these irrigants on osseointegration and the initial strength of the bone-implant interface. We hypothesized no impact of these antiseptic irrigation solutions on (1) trabecular bone microarchitecture and biomechanical pull-out properties; and (2) no cytotoxic effects on osteoblast differentiation in our established mouse model for tibial implantation.

Methods: A total of 40 C57BL/6 mice were randomly allocated into three groups: a dilute 0.3% PI group, a 10% PI mixed with 3% H2O2 group, and a saline group. Mice underwent bilateral tibial implantation surgery and irrigation solutions were applied intraoperatively. Assessments were performed at postoperative days 1 and 28, including plain radiographs, microCT evaluation, histological analysis, immunohistochemistry, and biomechanical pull-out testing.
Results: Biomechanical pull-out testing showed no differences in the bone-implant interface strength across groups. Histological analysis indicated no differences in bone and bone marrow percentage areas among treatment groups, both at postoperative day 1 and 28. Immunohistochemical analysis demonstrated no differences in peri-implant osteocalcin, osterix, or endomucin-positive cells among groups. MicroCT scans revealed no differences in peri-implant trabecular bone parameters including BV/TV, Tb.N., and Tb.Th.

Discussion: The use of antiseptic irrigation solutions showed no differences in osseointegration parameters when compared to the control group, demonstrating safety and absence of toxicity.

Conclusion: Dilute 0.3% povidone-iodine and a 1:1 combination of 10% povidone-iodine mixed with 3% hydrogen peroxide can be safely used during primary and revision total joint arthroplasty without compromising osseointegration.



1162 Scaffold-based Vaccination with PAMPs for Periprosthetic Joint Infection In A Murine Model

Authors: **Alexander Tatara**, Shanda Lightbown, Hamza Ijaz, Michael Super, Sandra Nelson, David Mooney

Background And Rationale: There are currently no available vaccines to prevent staphylococcal periprosthetic joint infection (PJI). We have designed an injectable biodegradable scaffold that elicits a stronger immune response than traditional vaccine technologies. We previously demonstrated that this system can be loaded with pathogen-associated molecular pattern molecules (PAMPs) from Escherichia coli to prevent sepsis. In this study, we evaluated the effects of Staphylococcus aureus PAMPs versus lysate as vaccine antigen in a murine model of PJI.

Study Question: Does a scaffold-based vaccine system loaded with PAMPs provide protection against S. aureus PJI in a murine model?

Methods: Injectable vaccines were prepared as previously described (Super and Doherty et al., Nat Biomed Eng 2022). Lysate was enriched for S. aureus Xen29 PAMPs using mannose-binding lectin-Fc as previously described. Mice received subcutaneous injections of vaccines loaded with lysate enriched for PAMPs ("PAMPs," n=8), unmodified lysate ("Lysate," n=5) on Days 0 and Day 14 for vaccination and booster or given no vaccine ("Unvaccinated," n=5). On Day 35 (Fig. 1A), a Kirschner wire was implanted into the distal femur protruding into the joint and inoculated with 1,000 CFU S. aureus Xen29, a methicillin-susceptible bioluminescent strain. Uninfected mice also underwent surgery as a control (n=5). Mice had sera drawn for antibody analysis, underwent bioluminescent imaging to track infection kinetics, and were euthanized on Day 49 for bacterial burden evaluation.

Results: The PAMPs and Lysate groups had significantly greater anti-staphylococcal IgG compared to unvaccinated mice before and after infection (Fig. 1B). The PAMPs group had a more rapid decrease in bioluminescent signal compared to Lysate and unvaccinated mice (Fig. 1C). On Day 49, the PAMPs group had significantly lower bacterial burden than the Unvaccinated group (Fig. 1D).

Discussion: This scaffold-based vaccine system resulted in a robust anti-staphylococcal humoral response. Only vaccine systems loaded with PAMPs resulted in significantly less bacteria at endpoint. In addition, 25% of mice in the PAMPs group had no culturable bacteria on their implant whereas this sterilizing effect was not seen in any other infected group.

Conclusion: S. aureus PAMPs in combination with a scaffold vaccine system reduces bacterial burden in a murine model of PJI.

Attachments:

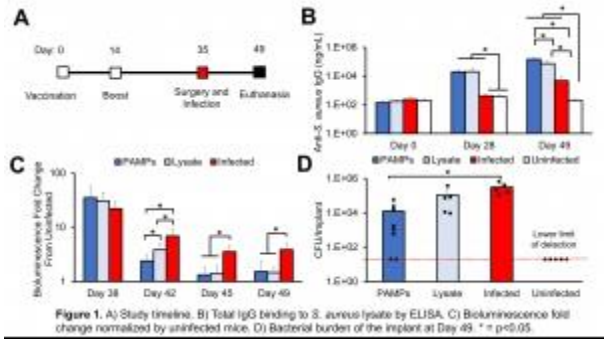


Figure 1. A) Study timeline. B) Total IgG binding to S. aureus lysate by ELISA. C) Bioluminescence fold change normalized by uninfected mice. D) Bacterial burden of the implant at Day 49. * = p<0.05.

1121 Comparison of In vitro Efficacy of Antibiotic Cement Against Common Prosthetic Joint Infection Pathogens

Authors: **Matthew J Dietz**, Elizabeth Stewart, Brian McGowan, Emily Hunt, Dylan Thomas, Matthew Squire

Background And Rationale: Antibiotic loaded bone cement (ALBC) is an important tool for the treatment of PJI. What is not known is the impact newer medium viscosity cements have on the elution of antimicrobials and how this compares to current standards.

Study Question: The purpose of this study was to compare the in vitro elution of two aminoglycosides eluted from different polymethylmethacrylate (PMMA) viscosities and two different types of cement to assess efficacy against four common PJI pathogens.

Methods: PMMA disks were created for: Palacos medium viscosity + gentamicin and Palacos R+ G, Simplex + Tobramycin, and their respective controls without antibiotics. Eluent from each of the five days was then frozen for later analysis with a Kirby-Bauer Assay. Filter paper disks loaded with the eluent were placed, in duplicate, for four samples for each of the three lots providing twenty-four samples per day for comparison. Disks along with controls were then placed onto a solid 4mm Muller Hinton Agar Plate (150mm) on which a standardized lawn of a pathogen had been created. Organisms evaluated were Staphylococcus aureus (ATCC 6538P), Methicillin-resistant S. aureus (ATCC BAA-1717), Staphylococcus epidermidis (ATCC Evans 49134), Methicillin-resistant S. epidermidis, (Evans ATCC 1191). Images were obtained at eighteen hours using and the zone of inhibition (ZOI) for each disk was calculated. Correlation of ZOI and standard curves for concentrations of antibiotic were calculated and comparisons between each cement per day of elution were calculat

Results: A maximum concentration and effectiveness were found at Day 1 for all cements against S. Epi 49134: with the greatest ZOI for Simplex with Tobramycin ($p < 0.0001$). There was a significant decrease in the ZOI for each cement and each organism per day ($p < 0.0001$). Both PMV+G and PR+G were significantly greater than Simplex with Tobramycin ($p < 0.0001$) for all organisms.

Discussion: A newly available medium viscosity cement demonstrates similar antibiotic elution characteristics to previously established standard viscosity cement. The eluted antibiotic decreases per day but is still present five days after creation providing growth inhibition of bacteria.

Conclusion: This study provides evidence that a medium viscosity ALBC can provide adequate elution and is efficacious against common PJI related pathogens.

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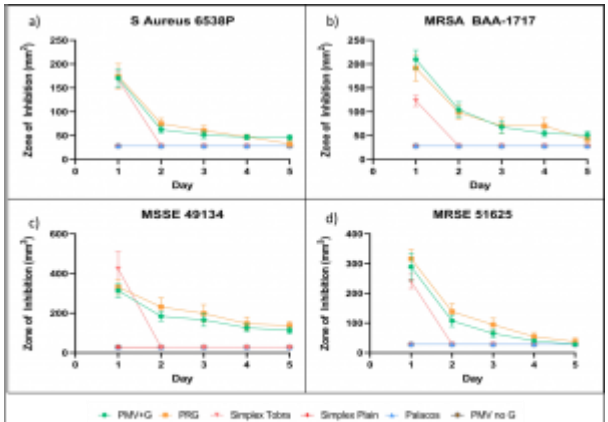


Figure 1. Zone of inhibition (ZOI) recorded from antibiotic elution from six cement types both with antibiotics (gentamycin or tobramycin) or no antibiotics against common prosthetic joint infection pathogens. Inbition demonstrated against a) MSSA b) MRSA c) MSSE, and d) MRSE.

1212 Testing a Rapidly Polymerizable Hydrogel Wound Dressing for Far-Forward Care of War-Time Traumatic Blast Wounds in a Murine Model of Open Fracture

Authors: Christopher Hamad, **Zeinab Mamouei**, Adolfo hernandez, Rene Chun, Christopher Hart, Chad Ishmael, Nicholas Bernthal, Amaka Enueme, Elizabeth Pumford, Andrea Kasko

Background And Rationale: Soldiers in far-forward environments often sustain blast wounds that cause significant soft tissue disruption and fracture. These special operation soldiers are often days away from hospital facilities and are susceptible to infection, blood loss, pain, and amputation. The goal of this project is to develop a hydrogel wound sealant that can be efficiently applied in the field to provide antibiotic, pro-coagulant, and analgesic care to soldiers. These modalities will be examined in our murine model of open fracture.

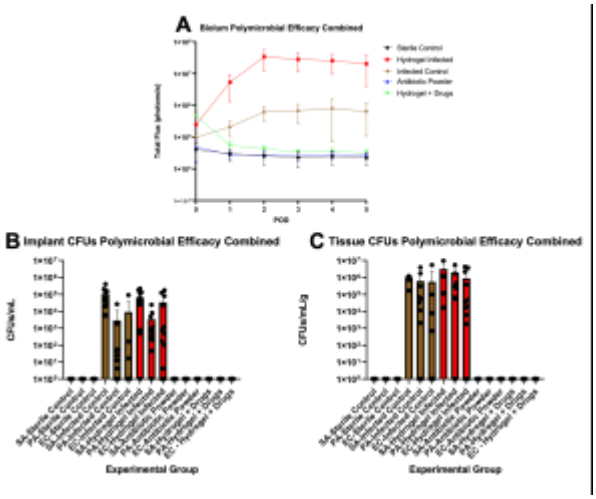
Study Question: Can a hydrogel wound dressing prevent polymicrobial infection and promote clot stability in a murine model of open fracture?

Methods: An established murine open fracture model was utilized in this study. Wound beds were inoculated with three organisms to develop a polymicrobial infection: 1E5 colony forming units (CFUs) S. aureus (Xen36), 1E2 CFUs P. aeurginosa (Xen41), and 1E3 CFUs E. coli (Xen14). Drugs utilized were vancomycin and tobramycin antibiotics, lidocaine for analgesia, and tranexamic acid (TXA) as a pro-coagulant. Experimental groups were as follows: sterile control, infected control, infected (unloaded) hydrogel, four drug hydrogel, and intrawound four drug powder. In vitro Thromboelastographic (TEG) studies were utilized to determine rates of clot lysis. Analgesic efficacy was tested utilizing a rodent gait analysis platform (DigiGait).

Results: Mice treated with drug loaded hydrogel or intrawound drug powder were able to prevent wound bed infection when challenged with polymicrobial inoculum. This was visualized on longitudinal bacterial bioluminescence and implant and tissue CFUs (Figures 1A-C). Hydrogel successfully eluted TXA and prevented clot lysis as measured via TEG analysis. This was demonstrated by maximum amplitude (MA - clot strength) and % lysis in 30 minutes (Ly30) values of >44 and

Discussion: In this murine model, our hydrogel wound dressing successfully prevented infection, stabilized clot formation, and efficiently mixed and polymerized within 2 minutes.

Conclusion: This hydrogel wound dressing successfully prevented polymicrobial infection and clot lysis. Future large animal studies will be required for testing prior to field application.



1148 Vancomycin and gentamicin loaded Stimulan beads are more effective at killing Staphylococcus ureus synovial fluid aggregates than intra-articular concentrations of vancomycin alone in vitro

Authors: Amelia M Staats , Phillip Laycock , Paul Stoodley , **Devin Sindeldecker**

Background And Rationale: The considerable antibiotic tolerance of synovial fluid-induced bacterial aggregates has been reported by multiple research groups.

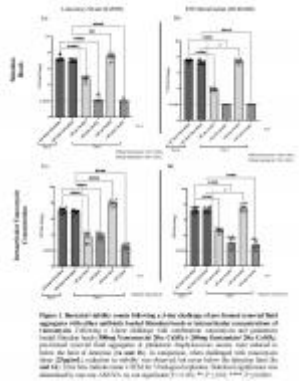
Study Question: Do vancomycin-gentamicin combination antibiotics released from high purity synthetic calcium sulphate Stimulan beads more effectively kill antibiotic-tolerant aggregates of S. aureus compared to direct addition of intra-articular vancomycin concentrations from IV administration?

Methods: Bioluminescent MRSA S. aureus, SAP231, or a PJI clinical isolate, were diluted in either Ringer's Solution (RS) or 10% bovine synovial fluid in RS to induce aggregation. The cultures were challenged with either 4 antibiotic loaded Stimulan beads or 25ï□g/mL of vancomycin for 3 days at 37ï,°C on a rocker. Four beads were used to match the approximate bead to dead space volume ratio in a knee following revision surgery. At Day 3, the aggregates were broken, and the bacteria enumerated by the plate count dilution method. The log reduction was calculated, and statistical significance determined by one-way ANOVA. Representative images of SAP231 were collected using an In vivo Imaging System (IVIS) to assess the loss in metabolic activity.

Results: In 2 of the 3 biological replicates Stimulan beads reduced bacterial viability in both the synovial fluid aggregate and planktonic samples of both strains to below the limit of detection (LOD) (>7 log reduction). These findings were corroborated by IVIS imaging which displayed a loss in bioluminescence. Vancomycin alone yielded an approximate 3 and 4 log reduction of the planktonic cells and aggregates, respectively, however, reduction to below the LOD was never achieved.

Discussion: The vancomycin-gentamicin loaded Stimulan beads effectively cleared both planktonic S. aureus as well as pre-formed synovial fluid aggregates over a 3-day challenge. Compared to the addition of intra-articular joint fluid concentrations of vancomycin, the beads yielded both higher bacterial reductions and complete killing in 2 of the 3 biological replicates.

Conclusion: This study suggests that the higher concentration of antibiotics from local release together with combination antibiotics enhanced the killing of S. aureus in vitro whether present as suspended single cells or biofilm-like aggregates compared to intra-articular vancomycin from IV administration alone.
Attachments:



1134 Implant Materials Affect Biofilm Formation

Authors: David Kerr, **Jerry Chang**, Thorsten Seyler

Background And Rationale: Bacterial surgical-site infections are a significant cause of morbidity and mortality globally, and lead to additional medical and surgical treatments, increased costs, and worse outcomes for orthopaedic patients. Bacteria forming extracellular biofilms are particularly resistant to antibiotic and surgical treatments when surgical implants are present.

Study Question: We compared the ability of staphylococcus aureus to form biofilms on common surgical implant materials.

Methods: Test implants composed of hand-polished stainless steel (HPSS), titanium (Ti), titanium alloy Ti6Al4V (TiAlV), cobalt chrome alloy Co28Cr6Mo F1537 (CoCr), hydroxyapatite (HA), ultra-high molecular weight polyethylene (UHMWPE), polyether ether ketone (PEEK), and poly(methyl methacrylate) (PMMA) bone were coated with biofilms and quantified by CFU count, confocal microscopy and electron microscopy. Surface roughness and water contact angles were assessed with optical profilometer and optical zoom imaging.

Results: After 72 hours, biofilms grew more readily on non-polished 3D-printed metals and plastics, such as PMMA, TiAlV, and ultra-high molecular weight polyethylene (UHMWPE) compared to polished and machined metals, such as HPSS, Ti, CoCr (ANOVA $p<0.0001$).

Discussion: Implant materials and characteristics have a strong correlation with biofilm formation, with rougher and more hydrophobic materials predicting greater affinity for biofilm formation. In addition to being mechanically weak and a poor antibiotic release profile, PMMA is also rougher and more hydrophobic than the metal implants, and thus provides an additional surface for bacteria to readily form biofilm.

Conclusion: These results may inform implant designs and surgeons may choose materials with reduced biofilm affinity in both septic and aseptic procedures.

Session II

23-APP-1077 A "Dry Tap" in PJI Workup of Total Hip Arthroplasty Is Not Reassuring For the Absence of Infection
Emily Treu, *Nathan Behrens, Brenna Blackburn, Christopher Pelt, Daniel Cushman, Michael Archibeck*

23-APP-1182 Robotics and Navigation Do Not Affect the Risk of Periprosthetic Joint Infection Following Primary Total Hip or Knee Arthroplasty
Scott LaValva, ***Alberto Carli****, Mia Fowler, Yu-Fen Chiu*

23-APP-1146 Outcomes of a Collaborative Orthopaedic-Infectious Disease Clinic
Allison Lastinger*, Matthew Dietz*

23-APP-1109 Safety Profile of Seven-Day Antibiotic Irrigation for the Treatment of Chronic Periprosthetic Joint Infection: A Prospective Randomized Phase II comparative study.
Bryan Springer, Brian deBeaubien ***Nicolas Piuzzi****, Hari Parvataneni, Andy Glassman , Carlos Higuera*

23-APP-1071 A Phase 1b open-label, dose-escalating study to evaluate the safety and tolerability of PLG0206, an antimicrobial peptide, in patients undergoing, debridement, antibiotics, and implant retention (DAIR) for treatment of a periprosthetic joint infection (PJI) occurring after total knee arthroplasty (TKA): Interim Analysis
David B Huang*, Nicolas Piuzzi, Antonia Chen, Christopher Pelt, David Rodriguez-Quintana, Despina Dobbins, Matthew Dietz*

23-APP-1110 Extended Oral Antibiotics Increase Tetracycline Resistance in Patients who Fail Two-Stage Exchange
Laura Certain*, Brenna Blackburn, Jeremy Gililland, Sandra Nelson, Antonia Chen, Jessica Seidelman, Alaina Ritter, Research Consortium (AARC)*

23-APP-1196 Extended Oral Antibiotic Prophylaxis:Defining its Role in All-Comers Undergoing Primary and Aseptic Revision Total Joint Arthroplasty
Kyle Bundschuh*, Brian Muffly, Ayomide Ayeni, Sameer Khawaja, Anthony Karzon, George Guild, Kevin Heo*

1077 A “Dry Tap” in PJI Workup of Total Hip Arthroplasty Is Not Reassuring For the Absence of Infection

Authors: **Emily Treu**, Nathan Behrens, Brenna Blackburn, Christopher Pelt, Daniel Cushman, Michael Archibeck

Background And Rationale: Synovial fluid analysis is critical in the diagnosis of prosthetic joint infection (PJI). Attempted total hip arthroplasty (THA) aspiration results in a dry tap in up to 50% of cases. This outcome can mistakenly be interpreted as suggesting the absence of infection.

Study Question: What is the rate of culture positive PJI in patients with a previous dry tap of a total hip arthroplasty?

Methods: We reviewed all THA aspirations performed between 2014 and 2021 at a single academic institution. Aspirations were categorized as successful (â‰¥0.5 mL) or unsuccessful (

Results: 275 consecutive THA aspirations were reviewed. 100 resulted in a dry tap (36%). The dry tap cohort had significantly more fluoroscopic-guided aspirations than the successful aspiration cohort (64% vs 48.9%, p=0.0061). No difference was seen in age (p=0.9317), BMI (0.3377), needle size (p=0.4198), or indication for aspiration (p=0.247) between cohorts. Of the 100 patients with dry taps, 15 underwent repeat aspiration and 48 underwent revision surgery within 90 days of their initial dry tap. Of the 15 repeat aspirations performed, 6 (40%) were successful in obtaining fluid and 2 yielded positive culture results. Of the 48 patients who underwent revision surgery, 15 (31.3%) of these resulted in two or more positive cultures.

Discussion: This consecutive series of 275 attempted aspirations of THA resulted in a 36% dry tap rate (100/275). Of the 100 dry taps, 15 were found to have PJI based on two or more positive cultures at the time of revision surgery. An attempted repeat aspiration was successful 40% of the time, demonstrating the value of repeat attempts when clinical suspicion is high.

Conclusion: An attempted aspiration of a THA that results in a dry tap should not be considered indicative of the absence of infection given the high rate of PJI identified after the initial dry tap in our patient series.

1182 Robotics and Navigation Do Not Affect the Risk of Periprosthetic Joint Infection Following Primary Total Hip or Knee Arthroplasty

Authors: Scott LaValva, **Alberto Carli**, Mia Fowler, Yu-Fen Chiu

Background And Rationale: The use of computer-navigation (CN) or robotic-assistance (RA) during primary total hip (THA) or knee (TKA) arthroplasty has yielded many benefits due to more accurate component positioning. The utilization of these tools is generally associated with longer operative times and also necessitates additional surgical equipment and personnel in the operating room. Yet to date, the risk of developing prosthetic joint infection (PJI) associated with technology use has not been thoroughly evaluated.

Study Question: Does the use of CN or RA during TKA or THA influence of risk of PJI with 90 days of surgery?

Methods: We retrospectively reviewed 11,727 patients (13,015 knees) who underwent TKA and 12,726 patients who underwent THA at a single institution. The TKA and THA cohorts were stratified into conventional (conv), RA, and CN groups. Propensity score matching (PSM) was performed based on age, sex, BMI, Charlson Comorbidity Index (CCI) score, and smoking status. Univariate and logistic regression analyses were performed among groups to evaluate differences in surgical time and PJI rate. Separate analyses were performed for TKA and THA.

Results: After PSM, there were 10,348 patients in the conv-TKA versus CN-TKA analysis and 1,486 patients in the conv-TKA versus RA-TKA analysis. For THA, there were 4,052 patients in the THA versus CN-THA analysis and 5,356 in the THA versus RA-THA analysis. In the TKA cohorts, significantly longer operating times were noted in the RA-TKA group (14 minutes) compared to conv-TKA (p

Discussion: Despite longer operative times associated with the use of CN or RA, the use of these tools was not associated with an increased risk of PJI within 90 days of TKA or THA. These findings are reassuring given the growing adoption of intraoperative technologies in arthroplasty.

Conclusion: The risk of PJI was not influenced by the use of computer navigation or robotic assistance.

Attachments:

Table I. Results of the logistic regression analysis evaluating the impact of computer navigation and robotic assistance on the risk of prosthetic joint infection within 90 days of surgery.

Analysis	Odds Ratio for PJI	95% Confidence Interval	P-Value
Computer Navigated THA vs. Conventional THA	0.996	0.431 – 2.302	0.992
Robotic Assisted THA vs. Conventional THA	0.799	0.315 – 2.029	0.637
Computer Navigated TKA vs. Conventional TKA	0.61	0.33 – 1.15	0.13
Robotic Assisted TKA vs. Conventional TKA	0.50	0.091 – 2.73	0.42

1146 Outcomes of a Collaborative Orthopaedic-Infectious Disease Clinic

Authors: **Allison Lastinger**, Matthew Dietz

Background And Rationale: In July 2017, we implemented an Ortho ID clinic at our tertiary referral center where prosthetic joint infection (PJI) patients are seen by their orthopedic surgeon and infectious disease physician in a combination appointment. The main goals of this clinic were to improve communication between specialties and the patient, improve patient outcomes by measuring readmissions and length of hospital stay, and decrease patient travel and no-show rate.

Study Question: Did implementation of the Ortho ID clinic improve communication, improve patient outcomes, and decrease patient travel and no-show rate?

Methods: After IRB approval, a retrospective review of all two-stage revision patients cared for before and after the clinic's implementation were compared to assess readmission and length of stay. Patient travel time saved was calculated and the no-show rate for appointments was assessed. We sent a survey to the orthopedic providers including MD's, APP's and nurses to assess their perception of communication since the clinic was started. Standard descriptive statistics were used to compare and assess the outcomes.

Results: From 2011-2017, the mean number of admissions for a patient undergoing a two stage revision was 3.50 (SD 2.0) compared to 2.58 from 2018-2022 (SD 1.2) [p 0.0002]. The mean number of hospital days decreased from 30.8 (SD 27.4) prior to the clinic to 21.9 (SD 21.09) after the clinic [p 0.0114] which translates to an estimated cost avoidance of $2.9 million per year. The mean distance traveled for clinic appointments by patients throughout their PJI care was 610.8 miles which was cut in half by the combination clinic. This also led to a decrease in the no-show rate from 18.24% prior to the clinic existence down to 6.85%. The survey of orthopedic providers showed that they communicate with the ID provider often or always since the clinic started compared to rarely and sometimes prior to the start of the clinic. The survey showed improved surgeon satisfaction with caring for PJI patients.

Discussion: Caring for patients with PJI requires a multidisciplinary team. We were able to demonstrate that a combined Ortho ID clinic leads to improved patient outcomes and cost avoidance to the institution. This data should be used to support resources for similar clinics and expanding multidisciplinary care between orthopedics and infectious diseases to care for other patients with musculoskeletal infections.

Conclusion: Seeing patients in this multidisciplinary clinic improved patient outcomes and surgeon satisfaction.

1109 Safety Profile of Seven-Day Antibiotic Irrigation for the Treatment of Chronic Periprosthetic Joint Infection: A Prospective Randomized Phase II comparative study.

Authors: Bryan Springer, Brian deBeaubien , **Nicolas Piuzzi**, Hari Parvataneni, Andy Glassman , Carlos Higuera

Background And Rationale: Periprosthetic joint infection (PJI) remains a major complication following total joint arthroplasty. Systemic IV antimicrobials yield poor outcomes because bacteria routinely form biofilms, and systemic therapy is unable to obtain the minimum biofilm eradication concentration (MBEC). Therefore, this study evaluated the safety of a novel method of optimized local delivery of antibiotics when compared to a standard two-stage exchange arthroplasty.

Study Question: Is local delivery of high-dose antibiotic safe in treatment of chronic PJI compared to two-stage exchange?

Methods: This was a Phase II, multicenter, prospective randomized clinical trial of the safety of a 7-day two-stage exchange arthroplasty with local antibiotic irrigation compared to a standard two-stage exchange. The experimental group included irrigation using 80 mg tobramycin daily with a 2-hour soak followed by hourly irrigation using 125 mg of vancomycin with a 30-minute soak resulting in 21 cycles per day via a novel intramedullary irrigations device. The control group received an antibiotic loaded cement spacer with vancomycin (average 8.4 g) and tobramycin (average 7.1 g). Both groups received 12 weeks of systemic antibiotics following Stage 2 surgery. Safety measures included: Adverse events, peak vancomycin/tobramycin serum concentrations (experimental group), blood transfusion and mortality. Total operative time for both groups were recorded.

Results: Thirty-seven patients were randomized to the experimental group and 39 to control. There was no difference in baseline demographics or comorbidities. The incidence of study antibiotic- and procedure-related SAEs in the experimental group was low. There were no antibiotic medication related adverse events with 2 SAEs related to antibiotic instillation. 188 vancomycin peak measurements taken in the experimental group, 127 samples had detectable serum level concentrations (69%), with all concentrations well below the maximum acceptable trough threshold of 20 • g/mL, and an average mean highest observed concentration of 6.1 • g/mL on Day 7 (with a max of 19 ug/mL.). Of the 103 tobramycin peak measurements, there were 46 samples with detectable levels (45%), with all well below the maximum clinically acceptable peak threshold of 18-24 • g/mL, and an average mean highest observed concentration of 0.67 ug/mL on Day 5. There was no difference in the amount of blood transfused per subject (Experimental -655 ml vs Control -792 ml; p=0.4188). Two (2) deaths occurred in each group. The overall OR time was significantly less in the experimental group (198 vs 166 minutes p=0.0068).All subjects in the experimental group were successfully reimplanted between 7-10 days compared to 73% of in the control group.

Discussion: Local antibiotic delivery method is safe with minimal systemic antibiotic exposure. There was no difference in the rates or severity of the SAEs between groups. Further research is being conducted to examine the efficacy of PJI eradication using local antibiotic irrigation

Conclusion: Local antibiotic delivery method is safe with minimal systemic antibiotic exposure. There was no difference in the rates or severity of the SAEs between groups. Further research is being conducted to examine the efficacy of PJI eradication using local antibiotic irrigation

1071 A Phase 1b open-label, dose-escalating study to evaluate the safety and tolerability of PLG0206, an antimicrobial peptide, in patients undergoing, debridement, antibiotics, and implant retention (DAIR) for treatment of a periprosthetic joint infection (PJI) occurring after total knee arthroplasty (TKA): Interim Analysis

Authors: **David B Huang**, Nicolas Piuzzi, Antonia Chen, Christopher Pelt, David Rodriguez-Quintana, Despina Dobbins, Matthew Dietz

Background And Rationale: Periprosthetic joint infection (PJI) is one of the most severe complications associated with total joint arthroplasty. New treatments are needed. PLG0206 is an investigational, rationally designed cationic antimicrobial peptide that is broad-spectrum, rapidly acting, and active against antibiotic-tolerant biofilm producing bacteria that cause PJI.

Study Question: The primary objective of this study was to prospectively assess the safety and tolerability of PLG0206 administered via an irrigation solution for the treatment of PJI after TKA during DAIR when used as an adjunct standard-of-care antibiotic therapy. A secondary objective of this study was to assess the efficacy of PLG0206 on clinical outcomes at Days 21, 42, 90 post-DAIR procedure.

Methods: PLG0206 was evaluated for safety, tolerability, and efficacy when administered as a single dose irrigation for a 15-minute exposure in the wound cavity of patients undergoing DAIR for treatment of PJI after TKA (clinicaltrials.gov identifier NCT05137314). Two cohorts of patients received a single irrigation with a solution of PLG0206 at 3 mg/mL (n=7) or 10 mg/mL (n=7). This study was IRB (Institutional Review Board) approved and conducted at twelve sites in the United States from March 3, 2022, to present, and will continue assessing safety, tolerability, and efficacy of PLG0206 for the currently enrolled patients at Days 180, 270 and 365 post-DAIR procedure. This study was not powered for efficacy and no formal statistical hypothesis testing was planned. All statistical summaries were descriptive in nature.

Results: The Table shows the patient demographic characteristics, microbiological cultures, and clinical outcomes by dose cohort and last study visit.

Discussion: Following a single 15-minute irrigation of PLG0206 to the knee wound cavity of patients undergoing a DAIR procedure for treatment of PJI occurring after TKA, PLG0206 appears safe and well tolerated. Longer term follow-up of the clinical outcomes for these patients are ongoing.

Conclusion: To date, these findings support the ongoing development of PLG0206 as an irrigation when used as an adjunct standard-of-care antibiotic therapy.

Attachments:

Patient	Culture	Dose Cohort (mg/mL)	Last Study Visit (Day)	Recurrence	Adverse Events	Adverse Event Related
1) 79 yo M right knee	[illegible]	3	180	No	None	None
2) 72 yo M left knee	Negative	3	90	No	1. Atrial fibrillation (SAE) 2. COVID-19	1. Unrelated 2. Unrelated
3) 68 yo M left knee	Negative	3	90	No	None	None
4) 62 yo M left knee	[illegible]	3	90	No	None	None
5) 55 yo M left knee	Negative	3	42	No	None	None
6) 78 yo F right knee	Negative	3	90	No	1. Pruritis, 2. skin lacerations, 3. Intraoperative hypertension 4. Acute bronchitis (SAE)	1. Unrelated 2. Unrelated 3. Unrelated 4. Unrelated
7) 77 yo M left knee	[illegible]	3	90	No	1. Headache	1. Unrelated
8) 73 yo F right knee	Negative	10	42	No	None	None
9) 64 yo F right knee	S. aureus	10	42	No	None	None
10) 68 yo M right knee	Negative	10	42	No	1. Paroxysmal atrioventricular block (SAE); 2. COVID-19; 3. Gluteal abscess s/p I&D 4. Hypotension w/ evidence of end organ damage 5. Failure to thrive	1. Unrelated 2. Unrelated 3. Unrelated 4. Unrelated 5. Unrelated
11) 64 yo F left knee	[illegible]	10	21	No	None	None
12) 68 yo M right knee	Negative	10	21	No	None	None
13) 68 yo M right knee	S. aureus	10	21	No	None	None
14) 78 yo M right knee	Negative	10	7	No	None	None

1110 Extended Oral Antibiotics Increase Tetracycline Resistance in Patients who Fail Two-Stage Exchange

Authors: **Laura Certain**, Brenna Blackburn, Jeremy Gililland, Sandra Nelson, Antonia Chen, Jessica Seidelman, Alaina Ritter, Research Consortium (AARC)

Background And Rationale: Although recent studies have demonstrated a reduction in the rate of recurrent periprosthetic joint infection (PJI) with administration of prolonged oral antibiotics at time of stage-two reimplantation, the potential for increasing bacterial resistance remains a concern.

Study Question: Does giving patients extended oral antibiotics after stage-two revision increase their risk of subsequent infection with antibiotic-resistant organisms?

Methods: We retrospectively reviewed patients from four academic medical centers who underwent two-stage exchange for PJI from 2014 to 2020. Patients were stratified based on those who had received at least two weeks of oral antibiotics at the time of stage-two reimplantation compared to those who did not receive extended antibiotics. The primary outcomes were the rates of antibiotic resistance to four classes of antibiotics in any subsequent PJI (oral beta-lactams, antifolates, tetracyclines, clindamycin). The secondary outcome was the overall rate of recurrent PJI in the two groups.

Results: Of the 421 patients who underwent two-stage exchange for PJI, 227 patients received prolonged oral antibiotics at the time of stage two reimplantation. Baseline characteristics were similar between patients who received prolonged antibiotics compared to those who did not. Fifty-five patients had a recurrent PJI (13%). The prevalence of tetracycline resistance among the recurrent infections was 62% in the group that had received extended oral antibiotics compared to 27.6% in the group that did not ($p=0.04$). The prevalence of resistance to other classes of antibiotics was not significantly different between the two groups. Recurrent PJI was diagnosed in 28 out of 227 (12%) patients who received prolonged oral antibiotics compared to 27 out of 194 (14%) patients who did not ($p = 0.63$).

Discussion: Prolonged oral antibiotics following two-stage exchange increases drug resistance in subsequent PJI, specifically to tetracyclines. In contrast to other studies, we did not find a reduced incidence of recurrent PJI in the group who received prolonged oral antibiotics.

Conclusion: Prolonged oral antibiotics after stage-two revision increases tetracycline resistance in subsequent PJI. We recommend further research in the area to refine antimicrobial protocols while considering the risks and benefits of prolonged antibiotic treatment.

1196 Extended Oral Antibiotic Prophylaxis:Defining its Role in All-Comers Undergoing Primary and Aseptic Revision Total Joint Arthroplasty

Authors: **Kyle Bundschuh**, Brian Muffly, Ayomide Ayeni, Sameer Khawaja, Anthony Karzon, George Guild, Kevin Heo

Background And Rationale: Periprosthetic joint infection (PJI) following total joint arthroplasty (TJA) can be devastating for patients both physically and psychosocially, with large economic implications for the healthcare system. Prior studies have demonstrated a reduction in PJI rate with a period of extended oral antibiotics (EOA) for high-risk patients undergoing primary TJA.

Study Question: The purpose of this study was to compare the 90-day PJI rate in all-comers, including primary and revision TJA, between patients who received EOA prophylaxis and those who did not.

Methods: 2,893 consecutive primary and aseptic revision TJAs performed by a single, fellowship-trained arthroplasty surgeon from April 2016 to December 2022 were retrospectively reviewed. Beginning January 2020, all patients received seven days of 300mg oral cefdinir twice daily (EOA protocol) immediately postoperatively. No other changes were made to pre-existing institutional infection reduction protocols. 90-day PJI rates were compared between patients who did and did not receive EOA.

Results: In all-comers undergoing primary (n=2,603) and aseptic revision (n=290) TJA, 90-day PJI rates were significantly lower between patients who received EOA prophylaxis compared to those who did not (0.42% vs. 1.16%, respectively; p=0.03). Following multiple logistic regression, subanalysis of all-comers undergoing primary TJA demonstrated lower PJI rates when EOA prophylaxis was utilized (0.24% vs. 0.75%, p=0.04; OR 3.75). When examining cases of aseptic revision TJA alone, PJI rates trended toward a significant decrease with the EOA protocol compared to without (2.01% vs. 4.97%, respectively; p=0.18; OR 2.62).

Discussion: Regardless of preoperative risk stratification, patients who underwent primary or aseptic revision TJA and received EOA prophylaxis postoperatively were 3.75 and 2.62 times less likely, respectively, to develop PJI at 90-days compared to those without EOA.

Conclusion: Future studies are needed to both determine if these results are maintained at postoperative time periods beyond 90-days following primary TJA, as well as to achieve appropriate power in the aseptic revision cohort to assess the role of EOA in this population. This prophylactic measure of additional oral antibiotics could positively impact patient outcomes, while decreasing both the financial and resource burden of septic revision procedures on the healthcare system.

Session III

23-APP-1173 Establishment and Validation of a Synovial Fluid CRP Clinical Decision Limit for Periprosthetic Joint Infection
Carl Deirmengian , Krista Toler, John Miamidian, ***Alex McLaren***

23-APP-1075 Association of Preoperative NarxCare Scores with the Fate of Two-Stage Reimplantation Revision Total Joint Arthroplasty
Vivek Singh, ***Jesus Villa****, Katherine Rajschmir, Tejbir Pannu, Justin Limtong, Carlos Higuera-Rueda*

23-APP-1070 Single-stage exchange arthroplasty has comparable results to two-stage exchange revision in select patients with periprosthetic hip and knee infection
Ryan M Sutton*, Juan D Lizcano, Andrew Fraval, Bright Wiafe, Paul Courtney, Scot Brown*

23-APP-1108 Patients with Positive Cutibacterium Culture Following Total Hip (THA) and Total Knee Arthroplasty (TKA) Often do not Meet MSIS Criteria for Infection
Benjamin Levy*, Tracy Borsinger, Paul Werth, Wayne Moschetti*

23-APP-1186 Expanded gram-negative antimicrobial prophylaxis reduces surgical site infection in hip fracture with arthroplasty
Scott Roberts, Richard Martinello, Lee Rubin, ***Marjorie Golden***

23-APP-1198 A retrospective cohort study on the impact of suppressive antimicrobial therapy after DAIR for PJI in 3 countries
Don Bambino Geno Tai *, Paul Jutte , Aaron Tande , Benjamin Langworthy , Matthew Abdel, Elie Berbari, Gina Suh, Wierd Zijlstra, Alex Soriano, Marjan Wouthuyzen-Bakker*

1173 Establishment and Validation of a Synovial Fluid CRP Clinical Decision Limit for Periprosthetic Joint Infection

Authors: **Carl Deirmengian** , Krista Toler, John Miamidian, Alex McLaren

Background And Rationale: C-reactive protein (CRP) has long served as a prototypical biomarker for periprosthetic joint infection (PJI). Recently, synovial fluid CRP (SF-CRP) has garnered interest as a diagnostic tool. Although previous studies have identified diagnostic cutoffs for SF-CRP, they have been limited in scope and employed various CRP assays without formal validation for PJI diagnosis.

Study Question: This study aimed to conduct a formal single clinical laboratory validation to determine the optimal cutoff of SF-CRP for the diagnosis of PJI.

Methods: A retrospective analysis of prospectively collected data was performed using Receiver Operating Characteristic (ROC) and Area Under the Curve (AUC) analyses. Over 2,600 institutions submitted hip and knee synovial fluid samples to a single clinical laboratory for diagnostic testing between 2017 and 2022. Samples meeting specimen integrity requirements and possessing a full biomarker dataset were included. 108,948 samples were classified as Infected, Not Infected, or Inconclusive according to the 2018 ICM criteria. Data were divided into training (n=67,242) and validation (n=28,819) sets, which only included samples classified as Infected or Not Infected. The Youden Index was employed to optimize the decision threshold.

Results: The SF-CRP clinical decision limit for PJI diagnosis was established at 4.45 mg/L, with a sensitivity of 86.3% (95% CI: 85.6%-87.0%) and specificity of 87.2% (95% CI: 87.0%-87.4%). Applying this cutoff to the validation dataset yielded a sensitivity of 86.1% (95% CI: 85.0%-87.1%) and specificity of 87.1% (95% CI: 86.7%-87.5%). No statistically significant deviation in diagnostic performance was observed between the validation and training sets.

Discussion: This study represents the largest single clinical laboratory evaluation of a SF-CRP assay for PJI diagnosis. The optimal CRP cutoff (4.45 mg/L) is 36% lower than the generally recommended value (6.9 mg/L), underscoring the importance of validating individual SF-CRP assays for PJI diagnosis.

Conclusion: A single SF- CRP assay, validated at one clinical laboratory, demonstrated an optimal diagnostic cutoff of 4.45 mg/L for PJI. This cutoff yielded a sensitivity of 86.3% and a specificity of 87.2%.

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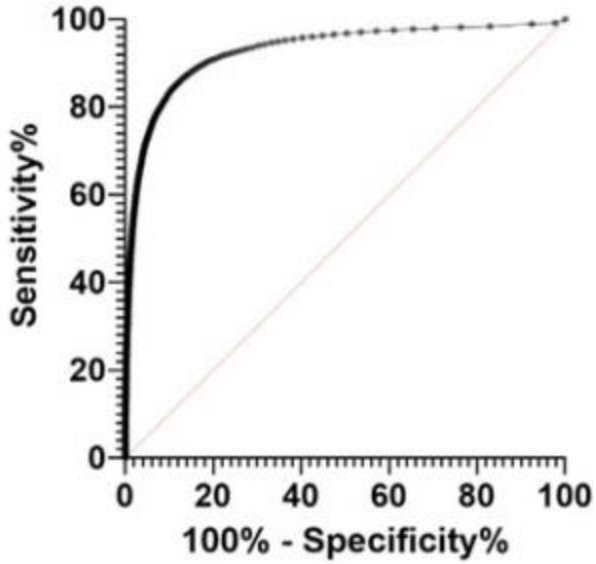

1075 Association of Preoperative NarxCare Scores with the Fate of Two-Stage Reimplantation Revision Total Joint Arthroplasty

Authors: Vivek Singh, **Jesus Villa**, Katherine Rajschmir, Tejbir Pannu, Justin Limtong, Carlos Higuera-Rueda

Background And Rationale: The association between preoperative prescription narcotic drug use and postoperative outcomes in patients who undergo revision total joint arthroplasty (rTJA) for periprosthetic joint infection (PJI) remains unexplored. The NarxCare platform utilizes the Prescription Drug Monitoring Program records to assign numerical scores that approximate a patient's overall opioid usage.

Study Question: The purpose of this study was twofold: (1) identify a preoperative NarxCare Score (NCS) threshold for adverse events (failed reimplantation based on the MSIS criteria) (2) identify outcome differences between patients with lower vs higher preoperative NCS.

Methods: We retrospectively reviewed patients who underwent two-stage rTJA for PJI and were re-implanted between 2014-2020. NCS prior to two-stage rTJA, patient characteristics, operative time, discharge disposition, 90-day adverse events (emergency department visit [ED], reoperation, and readmission), and whether the reimplantation failed based on the MSIS definition (Tier 3 and Tier 4) was collected. A ROC analysis was utilized to determine a preoperative NCS threshold associated with higher odds of failure. Using the established NCS threshold, we divided the study population into two cohorts for comparison: Low vs High preoperative NCS. All aforementioned outcomes were compared using multilinear/logistic regressions.

Results: A total of 68 patients were included (24 hips and 44 knees). ROC analysis yielded a preoperative NCS above 265 as predictive of reimplantation failure (AUC:0.7,p=0.005) with a sensitivity of 71.5% and specificity of 65%. Two cohorts were established based on this NCS cutoff (N=34 each) and did not statistically differ in baseline characteristics. Mean NCS for patients with a preoperative NCS <0.003).

Discussion: Preoperative NCS above 265 is associated with higher subsequent failure of two-stage reimplantation for PJI. This may aid surgeons counsel patients underoing rTJA for PJI based on their preoperative narcotic use as well as help determine the prospect of achieving a successful two-stage reimplantation.

Conclusion: Preoperative NCS above 265 is associated with higher subsequent failure of two-stage reimplantation for PJI.

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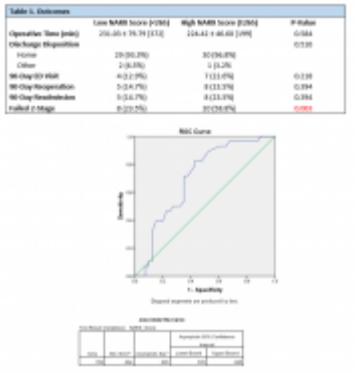

1070 Single-stage exchange arthroplasty has comparable results to two-stage exchange revision in select patients with periprosthetic hip and knee infection

Authors: **Ryan M Sutton**, Juan D Lizcano, Andrew Fraval, Bright Wiafe, Paul M Courtney, Scot Brown

Background And Rationale: Although two-stage exchange has been the standard of care for periprosthetic joint infection (PJI) in the United States, single-stage exchange is emerging as an option in select patients. The purpose of this study was to compare outcomes of patients undergoing single-stage versus conventional two-stage exchange using strict surgical indications.

Study Question: Using the same surgical indications, how do surgical outcomes compare between patients undergoing single and two-stage exchange.

Methods: We reviewed a consecutive series of 196 patients with diagnosed PJI undergoing revision total knee (TKA) and total hip arthroplasty (THA) from 2017 to 2021. Patients were excluded if they had a history of PJI, plastic surgery coverage, or extensive bone loss requiring endoprosthesis. We compared the number of patients PJI-free at one year follow-up based upon MSIS criteria and patients requiring re-revision surgery between the two-stage and single-stage groups.

Results: A total of 126 patients met the inclusion criteria (64.3%), comprised of 60 single-stage (47.6%) and 66 two-stage patients (52.4%). There were no differences in patient demographics, comorbidities or follow-up between the two cohorts. At a mean follow-up of 1.75Â±1.02 months, we found that more patients had surgical success based on MSIS PJI-free criteria in the single-stage group (90% versus 74.2%; p=0.022), and more patients required re-revision in the two-stage group due to PJI (16.7% versus 3.3%; p=0.006), however there were no significant differences in PJI-free success when comparing knee and hip revisions separately. There were no differences in microorganism profile or complications between the two cohorts, but more single-stage patients received long-term antibiotic suppression (83.3% versus 60.6%; p=0.009).

Discussion: Using our specific surgical indications, less single-stage exchange patients required re-revision and more single-stage patients met MSIS PJI-free criteria compared to two-stage patients. Single-stage patients did have a higher portion of patients on chronic antibiotic suppression, which may confound results.

Conclusion: In patients with PJI with no prior history of infection and no bone or soft tissue compromise, single-stage arthroplasty is a viable alternative to conventional two-stage exchange. Further studies with longer-term follow-up are needed to evaluate its efficacy.

Attachments:

Table 1. Clinical Outcomes

	All patients (N=126)	Single stage (N= 60)	Two stages (n=66)	p-value
Mean follow up	1.75 ± 1.02	1.71 ± 1.02	1.79 ± 1.03	*0.621*
Failure (Re-Revision)				***0.006***
PJI	13 (10.3)	2 (3.3)	11 (16.7)	
Extensor mechanism disruption	1 (0.8)	0 (0)	1 (1.5)	
Loosening	2 (1.6)	0 (0)	2 (3)	
Periprosthetic fracture	1 (0.8)	0 (0)	1 (1.5)	
Traumatic dislocation	1 (0.8)	1 (1.7)	0 (0)	
Salvage procedures	3 (2.4)	0 (0)	3 (4.5)	*0.095*
Deceased				*0.073*
No	120 (95.2)	55 (91.7)	65 (98.4)	
Yes	6 (4.8)	5 (8.3)	1 (1.5)	
1-year PJI free				***0.037***
No	14 (11.1)	3 (5)	11 (16.6)	
Yes	112 (88.8)	57 (95)	55 (83.3)	

1108 Patients with Positive Cutibacterium Culture Following Total Hip (THA) and Total Knee Arthroplasty (TKA) Often do not Meet MSIS Criteria for Infection

Authors: **Benjamin Levy**, Tracy Borsinger, Paul Werth, Wayne Moschetti

Background And Rationale: Cutibacterium, as a ubiquitous, commensal gram-positive organism, represents a diagnostic challenge for arthroplasty surgeons. The characteristics of Cutibacterium culture positivity in THA and TKA are not well understood.

Study Question: 1. How many patients with positive Cutibacterium prosthetic joint cultures meet MSIS prosthetic joint infection criteria? 2. What are the inflammatory marker levels and synovial fluid characteristics in Cutibacterium-positive THAs and TKAs? 3. What are the clinical outcomes of Cutibacterium infections in TKA and THA?

Methods: 1: Retrospective chart review of patients with Cutibacterium culture following THA or TKA. 2: Patient baseline characteristics and lab results were analyzed using T-test and chi-squared analysis. 3: Those who underwent subsequent surgery were evaluated at one year using MSIS ORT.

Results: Of those with Cutibacterium-positive cultures, 10 of 21 THAs (47.6%) preoperatively met MSIS infection criteria, while 7 of 8 TKAs preoperatively met MSIS criteria (87.5%) (p= 0.13). Mean ESR was 36.4 mm/h for THA and 51.5 mm/h for TKA (p = 0.21), with mean CRP of 35.2 mg/dL for THA and 36.8 mg/dL for TKA (p = 0.95). Mean cell count and percent polymorphonuclear (PMNs) leukocytes from intra-articular aspiration was 27,055 with 68% PMNs for THA and 22,194 with 73.9% PMNs for TKA (p = 0.72 and p = 0.70, respectively). Mean cell count and percent PMNs was 24,143 (range of 95 to 128,205) with 58.9% PMNs for monomicrobial infections and 25,903 with 78.8% PMNs for polymicrobial infections. Of patients who underwent surgical intervention following positive periprosthetic Cutibacterium culture and had one-year follow-up (n =22), 16 (72%) had successful outcomes at one year. Only ASA was significantly different between the success and failure groups.

Discussion: Cutibacterium PJI could lead to more subtle clinical and laboratory changes compared to other microbial species.

Conclusion: 1) Patients with Cutibacterium-positive cultures following TKA or THA may not meet MSIS infection criteria. 2) Inflammatory markers and fluid characteristics of Cutibacterium-positive THAs and TKAs were elevated but had more subtle changes compared to accepted values for more virulent microbial species. 3) Patients who undergo surgical intervention following a positive periprosthetic Cutibacterium culture often have successful outcomes at one year.

Attachments:

Table 3: Laboratory data with comparison between THA and TKA.

Laboratory Data	THA	TKA	p-value
Polymicrobial (%)	10 (47.6)	5 (62.5)	0.68
Time to culture positivity (mean (SD))	6.75 (2.5)	7.39 (2.6)	0.57
Number of positive cultures (mean (SD))	2.05 (1.6)	1.75 (1.5)	0.66
WBC count (mean (SD))	27,055 (3,9922)	22,195 (2,9172)	0.77
PMN % (mean (SD))	67.92 (36.5)	73.88 (29.3)	0.70
Sonicated tissues positive for *Cutibacterium* (%)			0.24
No	16 (76.2)	7 (87.5)	
Yes	5 (23.8)	1 (12.5)	
Alpha Defensin (%)			0.41
Unknown	17 (81.0)	8 (100.0)	
Negative	2 (9.5)	0 (0.0)	
Positive	2 (9.5)	0 (0.0)	
ESR mm/h (mean (SD))	36.38 (27.3)	51.50 (31.1)	0.21
CRP (mean (SD))	35.23 (63.0)	36.80 (38.0)	0.95

WBC = white blood cells; PMN = polymorphonuclear cells; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein

1186 Expanded gram-negative antimicrobial prophylaxis reduces surgical site infection in hip fracture with arthroplasty

Authors: Scott Roberts , Richard Martinello, Lee Rubin, **Marjorie Golden**

Background And Rationale: Prior reports have shown benefit to the use of expanded gram-negative antimicrobial prophylaxis (EGNAP) when there is a high incidence of surgical site infection (SSI) due to these organisms. The utility of EGNAP on SSI in the hip fracture with arthroplasty population is unknown.

Study Question: Is the use of extended gram negative antimicrobial prophylaxis EGNAP associated with a reduction in the SSI rate of patients with hip fracture following arthroplasty

Methods: A retrospective cohort study of patients admitted to Yale New Haven Hospital from January 2019 to July 2021 who sustained hip fracture and underwent arthroplasty was performed. Patients received the standard of care surgical antimicrobial prophylaxis (usually cefazolin) were compared against patients who received the standard of care in addition to EGNAP with gentamicin dosed within 60 minutes of the initial incision. Only clean wounds were included. Surgical site infection incidence was adjusted for ASA score.

Results: A total of 899 patients sustained hip fractures and received arthroplasties, 622 (n = 69.2%) who received appropriate EGNAP and 277 (30.8%) who did not. There were 4 SSIs (0.6%) in those who received EGNAP compared to 8 SSIs (2.9%) who did not receive appropriate EGNAP ($p = 0.007$). There was no difference in acute kidney injury (0.6% vs 1.4%, $p = 0.238$), hemodialysis requirement (0.2% vs 1.1%, $p = 0.055$), or post-operative C. difficile infection (0.6% vs 1.8%, $p = 0.106$) in those who received EGNAP compared to those who did not. Of the 12 SSIs, 4 (33.3%) were culture positive and 8 (66.7%) were culture negative. Three of the culture positive patients did not receive EGNAP and had an organism cultured that was susceptible to gentamicin.

Discussion: EGNAP use was associated with a reduction in the SSI rate of patients with hip fracture who underwent arthroplasty and was not associated with adverse events

Conclusion: Use of EGNAP may be a potential adjunctive strategy in reducing SSI in the hip fracture patient population.

1198 A retrospective cohort study on the impact of suppressive antimicrobial therapy after DAIR for PJI in 3 countries

Authors: **Don Bambino Geno Tai** , Paul Jutte , Aaron Tande , Benjamin Langworthy , Matthew Abdel, Elie Berbari, Gina Suh, Wierd Zijlstra, Alex Soriano, Marjan Wouthuyzen-Bakker

Background And Rationale: The landmark DATIPO trial concluded that six weeks is not non-inferior to 12-week antibiotic therapy for periprosthetic joint infections managed with DAIR. However, it is unknown if suppressive antibiotic treatment (SAT) would improve outcomes for patients with acute PJI. Therefore, our study aims to evaluate the utility of SAT after 12 weeks of therapy.

Study Question: What is the utility of SAT after 12 weeks of antibiotic therapy?

Methods: We performed a retrospective study of patients with acute hip or knee PJIs managed with DAIR at five institutions in the US, Netherlands, and Spain from 2005-2020. We analyzed the effect of SAT using a Cox model among patients after 12 weeks. The primary covariate of interest was whether the patient was on antibiotics after week 12, which was coded as a time-varying covariate. We controlled for age, sex, type of infection, modular exchange, joint, and presence of bacteremia and Staphylococcus aureus. We excluded patients whose follow-up was less than 12 weeks. We defined treatment failure as infection recurrence (same or different organism), unexpected reoperation, or death due to infection.

Results: There were 504 patients, including; U.S. (n=184), the Netherlands (n=231), and Spain (n=89). The majority were female (58%, n=292), with a mean age of 70 years ago (SD 11). Hips and knees were equally proportioned. Primary arthroplasties represented 69% of the total cohort (n=349). Sixty treatment failures occurred during the mean follow-up of 1,258, 941, and 1,594 days, respectively. We did not find a statistically significant association between SAT after 12 weeks and treatment failure (HR 1.25, p=0.45, 95% CI 0.70-2.24). This finding was consistent across different subgroups, including hip or knee joints, early or late acute infections, cohort, and a subgroup of knee joints after 180 days (Table 1).

Discussion: Different studies have conflicting results on the benefit of SAT in DAIR. While we found that the SAT did not significantly lower the risk of failure for the entire cohort, there are subgroups in whom SAT was trending towards benefit. Future research must focus on predicting patients who would benefit the most from SAT. Our study was limited by a small number of events and unmeasured confounders.

Conclusion: SAT after 12 weeks is not associated with the overall treatment success of DAIR for acute PJI.

Attachments:

Table 1: Adjusted Hazard Ratios of Suppressive Antibiotic Therapy by Subgroups

Group	Hazard ratio	p-value	95% Confidence interval
All cases	1.25	0.45	0.70-2.24
Knee joints	1.35	0.38	0.69-2.64
Hip joints	0.73	0.66	0.18-2.95
Early acute	1.61	0.24	0.73-3.53
Late acute	1.08	0.86	0.22-2.57
Knee joints after 180 days	0.97	0.93	0.46-2.03
USA Cohort	0.37	0.09	0.12-1.18
Spain Cohort	0.41	0.42	0.05-3.55

Note: Adjusted for age, sex, type of infection, modular exchange, joint, and presence of bacteremia and *Staphylococcus aureus*.

Session IV

23-APP-1101 Accelerated Severity of Illness Score Enhances Prediction of Complicated Osteomyelitis in Children
*Tahmina Jahan, **Norman Lapin**, Michael O'Connell, Chan-Hee Jo, Yuhan Ma, Naureen Tareen, Lawson Copley*

23-APP-1106 Effect of Preoperative Antibiotic Therapy on Operative Culture Yield for Diagnosis of Native Joint Septic Arthritis
***Ryan Khodadadi**, Pansachee Damronglerd, Jack McHugh, Said El Zein, Brian Lahr, Brandon Yuan, Omar Abu Saleh, Gina Suh, Aaron Tande*

23-APP-1129 Risk Factors for Repeat Irrigation & Debridement in Native Joint Septic Arthritis
***Gabriel Linden**, Sophie Lipson, Vineet Desai, Jared Alswang, Scott Ryan, Antonia Chen, Matthew Salzler*

23-APP-1118 Assessing the Utility of Vertebral Body / Disc Space Fluid Cell Differential in the Diagnosis of Native Vertebral Osteomyelitis
***Said El Zein**, Brian Lahr, Brett Freedman, Matthew Howard, Aaron Tande, Elie Berbari*

23-APP-1084 Does the CDC Surgical Wound Classification Adequately Predict Post-Operative Infection in Orthopaedic Trauma?
***Elizabeth Cho**, Hanna House, Andrew Marten, Marina Feffer, Julie Agel, John Scolaro, Meir Marmor, Ashley Levack*

23-APP-1115 Outcomes Following Implant Retention for Fracture-Related Infections
***Hussam Tabaja**, Brandon Yuan, Nicholas Rhodes, Aaron Tande*

23-APP-1088 Multisite Study of the Management of Musculoskeletal Infection after Trauma -The MMUSKIT Study
***Jessica Seidelman**, Alaina Ritter, Maolcom Debaun, Christian Pean, Laura Certain, Sandra Nelson, MMUSKIT Study Group*

1101 Accelerated Severity of Illness Score Enhances Prediction of Complicated Osteomyelitis in Children

Authors: Tahmina Jahan, **Norman Lapin**, Michael O'Connell, Chan-Hee Jo, Yuhan Ma, Naureen Tareen, Lawson Copley

Background And Rationale: Severity of illness (SIS) determination for children with osteomyelitis presents a formidable challenge. Existing predictive models lack consensus on outcome definition, have prolonged scoring duration, and include judgment-based parameters. This study improves on previous models.

Study Question: Can a systematic and quantitative-based definition of the outcome of complicated osteomyelitis be identified? Can a SIS be free of judgement-based predictors and available within a fraction of the time of existing models?

Methods: Children with culture-positive Staphylococcus aureus osteomyelitis were retrospectively studied to exhaustively identify adverse events (AEs). Complicated osteomyelitis outcome was systematically determined with an AE-weighted index (AEI) to establish a cutoff AEI>2 to qualify as complicated. Fifty-four parameters were analyzed through univariate analysis to identify potential predictors of complicated osteomyelitis. Successive multivariable regressions were conducted, screening chronologically distinct variables separately to minimize cross-influence. A combined regression selected final parameters for an accelerated severity of illness score (Accel-SIS).

Results: Model parameters included male sex (OR 4.1[95% CI 1.3-15]), tachypnea (7.3[2.4-23]), systolic hypotension (7.9[2.0-34]), CRP_initial>17.2 mg/dl (1.1[1.0-1.2]), Bands_initial>3.8% (1.1[1.0-1.1]), septic arthritis (3.4[1.2-9.9]), MRSA (3.7[1.1-15]), and platelet nadir (4.1[1.4-12]) for maximum score=32.7. ROC analysis found Accel-SIS AUC=0.939[0.908-0.971], superior to Mod-SIS=0.913[0.875-0.951], A-SCORE=0.865[0.812-0.918] and C-SCORE=0.853[0.806-0.900]. Accel-SIS had the lowest ceiling effect (0.5%) with a dynamic range 20 times that of other models. Using ROC cutoffs for illness severity, a hyper-severe category had significantly increased risk of complicated osteomyelitis (34/48 (70.8%) p<0.0001).

Discussion: Using ROC cutoff optimization, we introduce a hierarchical stratification of mild, moderate, severe, and hyper-severe groups with finer levels of distinction than previously possible. Separation of children based on this variable risk of complicated osteomyelitis will guide evaluation, treatment, surgical decision-making, and follow-up.

Conclusion: This study improves upon previous models by systematically defining the outcome variable and rigorously developing a score employing non-judgment-based predictors available within 48 hours.

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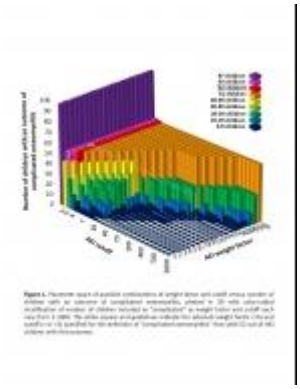

1106 Effect of Preoperative Antibiotic Therapy on Operative Culture Yield for Diagnosis of Native Joint Septic Arthritis

Authors: **Ryan Khodadadi**, Pansachee Damronglerd, Jack McHugh, Said El Zein, Brian Lahr, Brandon Yuan, Omar Abu Saleh, Gina Suh, Aaron Tande

Background And Rationale: Native joint septic arthritis (NJSA) is diagnosed by synovial fluid analysis to evaluate for evidence of infection but may be definitively established by a positive gram stain or culture. Antibiotics given prior to synovial fluid sampling have been described to alter cell count, gram stain, and culture results and are conventionally deferred until after arthrocentesis to optimize diagnostic yield. However, there is limited data on the impact of preoperative antibiotic therapy on operative culture yield in the diagnosis of NJSA.

Study Question: What is the effect of preoperative antibiotic therapy on operative culture yield for the diagnosis of NJSA?

Methods: Following IRB approval, we reviewed medical records of adults diagnosed with NJSA who underwent surgical intervention at Mayo Clinic facilities from January 2012 to December 2021. The effect of preoperative antibiotic therapy on operative culture yield was evaluated through a paired analysis of preoperative and operative cultures results utilizing logistic regression along with generalized estimating equations (GEE) to account for correlations of multiple measurements on the same subject.

Results: Results are displayed in Composite Image 1. A total of 299 patients with NJSA of 321 joints with the accompanying characteristics met study criteria (Table 1). Joint distribution, microbiology, and antibiotic administration are outlined in Table 2

Discussion: Among those treated with preoperative antibiotics, there was a significant decrease in yield between preoperative and operative cultures (68.0% to 57.1%, $p < .0001$), whereas in patients without preoperative antibiotic exposure, there was an increase in yield (60.9% to 67.4%, $p = 0.244$; Figure 1). Logistic regression analysis revealed that preoperative antibiotic exposure was more likely to decrease operative culture yield as compared to non-exposure (change, -10.9% vs. +6.5%; $p = .006$). Secondary analyses restricted to individuals who received preoperative antibiotics revealed that an increasing number of doses and earlier administration of initial antibiotic therapy were associated with lower rates of operative culture yield (Figure 2).

Conclusion: In patients with NJSA, preoperative antibiotic exposure resulted in a significant decrease in microbiologic yield of operative cultures as compared to patients in which antibiotic therapy was held prior to obtaining operative cultures.

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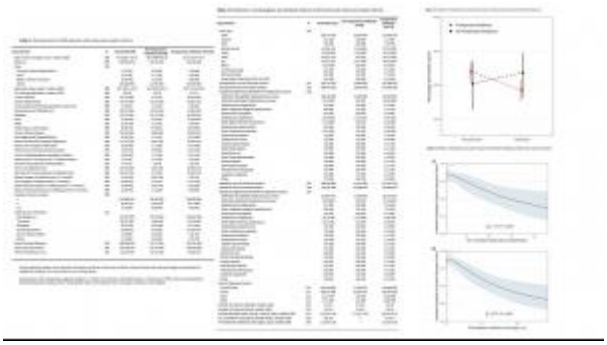

1129 Risk Factors for Repeat Irrigation & Debridement in Native Joint Septic Arthritis

Authors: **Gabriel Linden**, Sophie Lipson, Vineet Desai, Jared Alswang, Scott Ryan, Antonia Chen, Matthew Salzler

Background And Rationale: Septic arthritis is considered an orthopedic emergency which often requires prompt irrigation and debridement (I&D). Some septic arthritis cases require a repeat I&D to fully eradicate the infection, which poses further burden on the patient and provider. The purpose of this study was to identify potential risk factors that may be associated with repeat I&D after initial treatment for native septic arthritis.

Study Question: What patient factors are associated with increased incidence of repeat I&D in native septic arthritis?

Methods: Consecutive adult patients with native septic arthritis from 2015-2019 at two level one trauma centers were retrospectively identified via ICD-9 and ICD-10 codes. Patients were included if they had a clinical presentation consistent with septic arthritis, with isolation of a pathogen in synovial fluid or another source, or turbid synovial fluid without crystals. Independent-sample T-tests, Fisher's Exact Tests, and multivariate analysis were performed to determine risk factors for repeat I&D.

Results: 192 patients diagnosed with septic arthritis were included in the final analysis (36% female, 64% male). 231 joints were included in the analysis (knee, n=115; hip, n=53; shoulder, n=37; elbow, n=7; wrist, n=7; other, n=12). 67 (29%) native septic arthritis patients were IVDU and 42% of IVDU cases were associated with repeat I&D (p=0.03). This association remained significant when controlling for smoking history, diabetes, HIV status, immunocompromised status, and steroid use. Time from aspiration to first I&D, synovial white blood cells (WBC), C-reactive protein level, and erythrocyte sedimentation rate at both the initial encounter and after the first I&D were not associated with repeat I&D. Smoking, HIV status, steroid use, immunocompromised status, diabetes, and previous surgery were not associated with repeat I&D (Table 1).

Discussion: IVDU was associated with a higher incidence of repeat I&D. This study did not find associations between synovial WBC count or immunosuppressed status for repeat I&D, as previously documented in literature. Physicians treating IVDU patients with septic arthritis may wish to adjust expectations when discussing treatment outcomes, while also working to enhance the initial washout to mitigate the need for repeat I&D.

Conclusion: IVDU patients were associated with higher incidence of repeat I&D in native septic arthritis.

Attachments:

Table 1. Potential predictors of repeat irrigation & debridement (I&D) in native septic arthritis

	No Repeat I&D N=183		Repeat I&D N=48		
	n	(%)	n	(%)	p-value
Pre-aspiration antibiotics (n=226)	105	(58%)	22	(49%)	0.32
Arthroscopic I&D (n=208)	85	(53%)	26	(54%)	1.00
Arthrotomy I&D (n=208)	75	(47%)	22	(46%)	1.00
Previous surgery (n=229)	28	(15%)	9	(19%)	0.51
Intravenous drug use history (n=231)	47	(26%)	20	(42%)	**0.03***
Smoking history (n=94)	26	(38%)	13	(50%)	0.35
HIV positive (n=84)	15	(18%)	3	(10%)	0.39
Steroid use (n=95)	1	(1.4%)	1	(3.8%)	0.48
Diabetic (n=228)	36	(20%)	11	(23%)	0.69
Immunocompromised status (n=231)	84	(46%)	26	(54%)	0.35

HIV = human immunodeficiency virus
* statistically significant

1118 Assessing the Utility of Vertebral Body / Disc Space Fluid Cell Differential in the Diagnosis of Native Vertebral Osteomyelitis

Authors: **Said El Zein**, Brian Lahr, Brett Freedman, Matthew Howard, Aaron Tande, Elie Berbari

Background And Rationale: Current approaches to diagnosing suspected native vertebral osteomyelitis (NVO) rely on imaging and microbiological workup, including blood and CT-guided biopsy cultures. These existing diagnostic methods often result in ambiguity, necessitating additional tests to distinguish NVO from its mimics. Our study aims to validate pilot findings demonstrating that an elevated neutrophil differential (PMN) in vertebral bone biopsy(VB)/ disc space fluid aspirate is associated with NVO. This may allow stratification of patients with suspected NVO into those who can be monitored closely versus those who may benefit from further invasive testing or empiric antibiotic therapy

Study Question: Can a vertebral body/disc space fluid cell differential differentiate between native vertebral osteomyelitis (NVO) and NVO mimics?

Methods: This analysis examines a subset of patients from a prospective cohort study, enrolling adults referred to Mayo Clinic's neuroradiology department for spine biopsy. After collecting routine clinical specimens, the needle is rinsed with 4cc of saline into an EDTA tube for automated cell count and differential analysis. To evaluate the predictive capacity of neutrophil (PMN) differential for NVO, logistic regression models were employed, and receiver operating characteristic (ROC) curve analyses were conducted for various PMN percentage cutoff points.

Results: In this preliminary analysis, 39 patients were included, comprising 7 patients with NVO and 32 patients with alternative diagnoses. All NVO patients received antibiotics within two weeks of the spine biopsy. The median biopsy sample PMN percentage for NVO patients was 83.0 (77.5-88.0), compared to 65.0 (56.5-69.5) for those without NVO (p=0.005) (Fig 1A). The estimated relationship between the probability of NVO and each measure across the full range of percentages is illustrated in Fig 1B. The optimal ROC curve point corresponds to a PMN differential of 72.5% (sensitivity=0.86, specificity=0.81) (Fig 1C)

Discussion: These results suggest that measuring the PMN percentage in biopsy samples might be a valuable tool to differentiate between NVO and its mimics.

Conclusion: The PMN differential cutoff of 72.5% exhibited notable sensitivity and specificity for the diagnosis of NVO. Investigations are ongoing to further validate these findings

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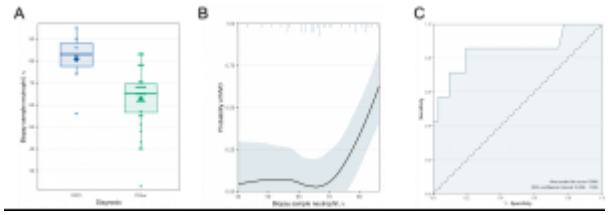

1084 Does the CDC Surgical Wound Classification Adequately Predict Post-Operative Infection in Orthopaedic Trauma?

Authors: **Elizabeth Cho**, Hanna House, Andrew Marten, Marina Feffer, Julie Agel, John Scolaro, Meir Marmor, Ashley Levack

Background And Rationale: The Centers for Disease Control (CDC) Surgical Wound Classification (SWC) is used in hospitals nationwide as part of a risk stratification model for surgical site infection (SSI). However, its utility with orthopaedic procedures remains unknown.

Study Question: The purpose of this investigation is to evaluate the utility of the CDC SWC in predicting SSI.

Methods: Adult patients with fractures of the leg, ankle, and hindfoot treated operatively at our level I academic trauma center between 2007 and 2022 were identified. 2,792 definitive surgical encounters were included. Chart review for presence of 90-day SSI was performed among patients having repeated procedures, open fracture, abscess or wound debridement, intra-operative cultures, or infectious disease consultation (n=551).

Results: In this cohort, the overall infection rate was 2.26% (n=63). Higher SWC was significantly associated with increased infection rate (I/Clean: 0.94%, II/Clean Contaminated: 3.85%, III/Contaminated: 6.45%, IV/Dirty: 9.87%, p

Discussion: The CDC SWC has limitations for orthopaedic trauma patients, with ambiguity of classification assignment and decreased discriminatory ability within the central categories. While overall SWC correlates with infection, the relationship appears to be confounded by effect of open versus closed fractures. Other factors such as inter-observer reliability, spectrum of soft tissue injuries, and staged fixation remain challenging to classify with the descriptors available.

Conclusion: The CDC Surgical Wound Classification (SWC) has notable limitations in predicting surgical site infection amongst orthopaedic trauma patients. Alternative classification systems may have improved utility within orthopaedic trauma and warrant further investigation.

1115 Outcomes Following Implant Retention for Fracture-Related Infections

Authors: **Hussam Tabaja**, Brandon Yuan, Nicholas Rhodes, Aaron Tande

Background And Rationale: To describe outcomes following implant retention for fracture-related infection (FRI).

Study Question: What factors are associated with treatment failure following implant retention for FRI?

Methods: Retrospective study of adults (â‰¥18 years) managed for FRI at Mayo Clinic, Rochester between 2000-2021. Patients were treated with debridement, antibiotics, and implant retention (DAIR) or one-stage replacement, and antimicrobials for at least 6 weeks from presentation. Antimicrobials after 6 weeks constituted chronic suppression. Patients were passively followed from surgical debridement until last medical visit and were screened for treatment failure, defined as persistence or recurrence of infectious symptoms requiring repeat surgery after treatment. Definite radiographic bone healing was determined by a fellowship-trained musculoskeletal radiologist.

Results: A total of 101 patients presented with FRI after a median of 1.2 (interquartile range (IQR) 0.5, 2.8) months from fixation; 98 had DAIR and 3 had one-stage replacement. Chronic suppression was prescribed in 94 patients. The median follow-up from surgical debridement was 8.0 (IQR 3.8, 13.4) years. Radiographic bone healing was ultimately confirmed in 69 patients. The cumulative rate of radiographic bone healing was only estimated in patients with yearly X-rays or computed tomography (CT) scans following fixation (Figure 1). Treatment failure occurred in 26 patients, 10 of whom had recurrence after radiographic healing. The 1-year cumulative rate of treatment failure was 19.9% (95% confidence interval (CI) 13.3%-29.8%) (Figure 2). The 1-year recurrence rate after healing was 10.3% (95% CI 5.1%-20.9%). At the time of failure, 25 (96.2%) patients still had their index-infected implant and 14 (53.8%) were still on chronic suppression. Furthermore, 9 of 10 patients with recurrence after radiographic healing still had their index implant (Figure 3). A univariate Cox regression model showed that compartment syndrome, polymicrobial infection, and infections due to Enterobacter species were associated with an increased risk of failure (Table 1).

Discussion: We described rates of radiographic healing, and treatment failure specifically following implant retention for FRI.

Conclusion: Managing FRI with implant retention remains challenging with impaired bone healing and elevated failure rates. Chronic suppression until bone healing followed by implant removal may provide the best outcome.

Attachments:

1088 Multisite Study of the Management of Musculoskeletal Infection after Trauma -The MMUSKIT Study

Authors: **Jessica Seidelman**, Alaina Ritter, Maolcom Debaun, Christian Pean, Laura Certain, Sandra Nelson, MMUSKIT Study Group

Background And Rationale: Infection after fracture fixation (IAFF) is a challenging complication. The optimal treatment of these patients is unknown. Specifically, there is very little data to guide antibiotic therapy duration. The purpose of this study is to pool observational data from multiple academic medical centers to determine whether antibiotic treatment duration is associated with improved outcomes.

Study Question: The primary aim of this study was to determine if antibiotic therapy >6 weeks after surgical debridement of IAFF is associated with greater surgery-free survival.

Methods: This is a retrospective cohort study of 4 academic medical centers. We included adult patients â‰¥18 years old who underwent open reduction and internal fixation (ORIF) for long-bone trauma, subsequently had debridement surgery for infection between 14 days and 6 months after ORIF, and completed a defined course of least 2 weeks of antibiotics following debridement surgery. We excluded patients who returned to the OR prior to completion of antibiotic therapy. We defined the primary outcome as surgery-free survival after completing antibiotics. Cox Proportional Hazards models were fit with the antibiotic duration as the primary predictor. The models were adjusted for ASA score, immunosuppression, and hardware removal.

Results: 115 patients were included in the analysis. We found no statistically significant difference in surgery-free survival between patients who received >6 weeks antibiotics vs. â‰¤6 weeks [HR 1.24 (0.93-1.66); P=0.14]. Additionally, we did not find a significant association with staphylococcal vs. non-staphylococcal infections [HR 0.79 (0.34-1.86); P =0.60]. Among 53 patients who returned to the OR, the proportion of patients with a recurrent infection with the same organism or a new pathogen was similar between the >6-week and â‰¤6-week groups.

Discussion: There was no evidence in our study of improved surgery-free survival associated with >6 weeks of antibiotics following debridement surgery. Also, patients who failed therapy had a similar proportion of recurrent positive operative cultures with the same organism regardless of antibiotic duration. Our findings suggest that longer antibiotic courses may not be more curative than short antibiotic courses. Larger prospective studies are needed.

Conclusion: Longer antibiotic courses (>6 weeks vs â‰¤6 weeks) were not significantly associated with surgery-free survival among patients with IAFF.

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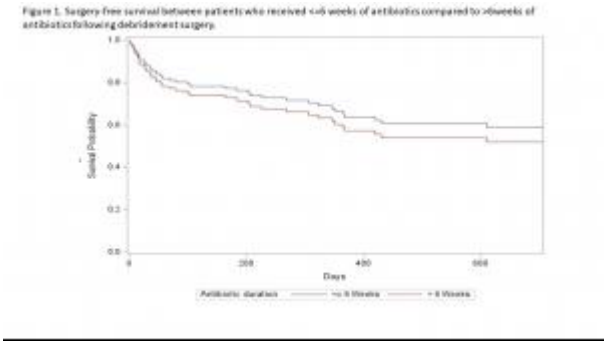

Session V

23-APP-1133 Efficacy and Tissue Toxicity of Topical Antiseptics
*David Kerr, **Jerry Chang***

23-APP-1072 Novel Activated Zinc Anti-Biofilm Irrigant Superior to Commercially-available Irrigants
*Derek Hill, **Nash Reigle,** Brandon Nutt, Paul Attar, Korey Goldsmith, Michael Scarborough, Ahmed Siddiqi*

23-APP-1085 Operating Room Air May Harbor Pathogens: The Role of An Ultraviolet Air Filtration Unit
***Diana Fernández-Rodríguez**, Nicolina Zappley, Javad Parvizi*

23-APP-1131 Chondrocyte Invasion is a Mechanism for Persistent Staphylococcus Aureus Infection
***Jerry Chang**, David Kerr, Thorsten Seyler*

23-APP-1199 Polymicrobial infection with Candida albicans and Staphylococcus aureus increases bacterial biofilm formation in a murine model of periprosthetic joint infection
***Zeinab Mamouei**, Aaron Kavanaugh, Christopher Hamad, Rahul Sobti, Jack Pearce, Adolfo Hernandez, Rene Chun, Fabrizio Billi, Nicholas Bernthal*

23-APP-1113 Systemic versus increasing intra-articular doses of vancomycin in a prosthetic joint infection rat model: Efficacy and Impact on Mitochondria
***Nour Bouji**, Elizabeth Stewart, John Hollander, Ethan Meadows, Dylan Shaver, Matthew Dietz*

23-APP-1191 A refillable drug delivery device that sustains local, high dose antibiotic therapy manages biofilm implant-related infection in a sheep model of long bone open fracture.
***Dustin Williams**, Robert Falconer, Nicholas Ashton*

23-APP-1104 Gentamicin-loaded bone cement is effective against representative small colony variants: an in vitro study
***Jeongeun Cho**, Emanuele Chisari, Diana Fernández-Rodríguez, Javad Parvizi*

1133 Efficacy and Tissue Toxicity of Topical Antiseptics

Authors: David Kerr, **Jerry Chang**

Background And Rationale: Topical antiseptics are used before and during surgery to prevent bacterial infections and may also be useful for treating bacterial infections with established glycocalyx biofilms. However, a key concern regarding the use of antiseptics is whether they adversely affect local host tissues in addition to any present bacteria, as host tissue cytotoxicity could contribute to delayed wound healing.

Study Question: The purpose of this study was to analyze the effects of clinically used antiseptics at various concentrations on biofilm formation, cell viability, and wound healing.

Methods: Fibroblasts (NIH-3T3), osteoblasts (MG63), and chondrocytes (C20A4) were cultured and used to perform scratch wound and cell viability (CCK-8) assays after exposure to various antiseptic concentrations, including acetic acid (AA), hydrogen peroxide (H2O2), chlorhexidine gluconate (CHX), and povidone iodine (PI). The efficacy of these antiseptic solutions against staphylococcus aureus biofilm formation was assessed through CFU counts and confocal microscopy.

Results: S. aureus biofilms were disrupted by all antiseptics (CFU log-reduction at 15 min. of 0.24 for 3% AA, 2.53 for 3% H2O2, 1.51 for 0.25% CHX, 2.22 for 0.13% PI, 0.18 for Saline). The anti-biofilm effect was seen on confocal microscopy with average % bacterial death at 15 min. of 46% for 3% AA, 62% for 3% H2O2, 97% for 0.25%, 67% for 0.13% PI, and 4% for saline. Assays were repeated with reduced antiseptic concentrations. Biofilm-effective antiseptic concentrations significantly decreased cell viability and mobility in CCK8 and scratch-wound assays, except for 0.13% PI. Lowest concentrations of all antiseptics and 0.13% PI were associated with closure at 24 hours, whereas the mid-range and higher concentrations of all antiseptics hindered wound closure.

Discussion: While antiseptics may be efficacious in treating S. aureus biofilms, the concentrations of antiseptics needed to achieve significant reduction in CFUs also led to decreased cell viability and mobility for fibroblasts, osteoblasts and chondrocytes. PI 0.13% was the only topical antiseptic that demonstrated anti-biofilm activity without complete inhibition of scratch wound healing for all cell lines.

Conclusion: Surgeons may wish to consider patient comorbidities and additional risk factors for delayed healing when using topical antiseptics in either aseptic or infection-related procedures.

1072 Novel Activated Zinc Anti-Biofilm Irrigant Superior to Commercially-available Irrigants

Authors: Derek Hill, **Nash Reigle**, Brandon Nutt, Paul Attar, Korey Goldsmith, Michael Scarborough, Ahmed Siddiqi

Background And Rationale: Zinc salts combined with oxidizing agents elucidate high [Zn2+], which have profound antimicrobial effects. The oxidizing agent sodium chlorite (NaClO2) has its own significant antimicrobial activity. We combined dilute zinc chloride (ZnCl2) with dilute NaClO2 to create a potent, synergistic, nontoxic antimicrobial solution (AZ100).

Study Question: We evaluated biofilm eradication of AZ100 vs multiple organisms compared to leading surgical wound irrigants. No study has compared antimicrobial irrigants this extensively against a broad array of pathogenic bacterial biofilms.

Methods: Mature biofilms of E faecium, S aureus, K pneumoniae, A baumannii, P aeruginosa, and E coli were grown in a CDC Biofilm Reactor. We exposed each to 7 irrigants for 5 minutes (in triplicate) to determine eradication of these biofilms: 0.9% normal saline solution (NSS), AZ100, hand-mixed 0.35% povidone-iodine (0.35% PI, pos control), sterile 0.5% PI, chlorhexidine gluconate (0.05% CHG), polyhexamethylene biguanide/betaine (0.1% PHMB/B), and sodium lauryl sulfate/citric acid/sodium citrate (SLS/CA/SC). Colony forming units (CFUs) were counted and reported as log recoverable CFUs (RCFU). RCFUs of each were compared to AZ100 and to 0.35% PI using Student's t-test.

Results: 126 assays were run. AZ100 demonstrated complete eradication (>4-log reduction) of 5-of-6 pathogens (3.2-log vs E coli). CHG demonstrated <2-log reduction of 5-of-6 organisms (2.5-log reduction of A baumannii). Sterile PI demonstrated 2- to 3-log reduction of all organisms. PHMB/B demonstrated <2-log reduction of 4/6 organisms, and ~3-log reduction of A baumannii and P aeruginosa. SLS/CA/SC demonstrated <2-log reduction of 3/6 organisms.

Discussion:AZ100 was the only irrigant to demonstrate >4-log eradication of a diverse array (5-of-6 organisms) of gram + and - biofilms with 5-minute exposure in vitro. AZ100 RCFU reduction was better than 0.35% PI against 4-of-6 organisms/assays ($p<0.05$). Conversely, commercially-available irrigants 0.05% CHG, sterile 0.5% PI, and 0.1% PHMB/B achieved less than 3-log eradication against 5-of-6 organisms. These commercially-available formulations were less effective than AZ100 ($p<0.05$) in 23-of-24 assays, and in 20-of-24 compared to hand-mixed 0.35% PI ($p<0.05$).

Conclusion: A novel activated-zinc solution offers a potentially superior alternative to commercially available irrigants and hand-mixed povidone-iodine against common nosocomial biofilms.

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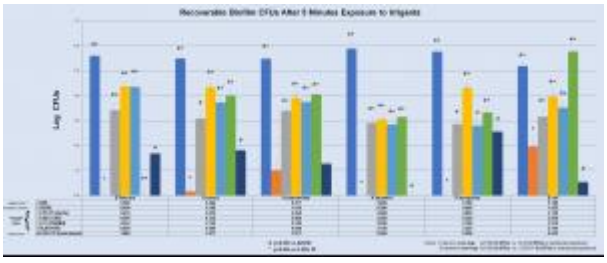


1085 Operating Room Air May Harbor Pathogens: The Role of An Ultraviolet Air Filtration Unit

Authors: **Diana Fernández-Rodríguez**, Nicolina Zappley, Javad Parvizi

Background And Rationale: Prevention of surgical site infections (SSIs) involves implementation of numerous steps including ultraclean air in the operating room (OR). Despite all efforts, particles in the room air may exist and some of these particles may be live pathogens that can potentially cause subsequent SSI. This prospective study aimed to determine and compare the nature and quantity of microbes in the operating room, as detected from the inlet flow of an ultraviolet filtration unit, and the efficacy of the unit to remove particles and creating clean room air (the outlet flow).

Study Question: Are pathogens present in the OR room air? Will a filtration unit with crystalline ultraviolet light be able to clean microorganisms and particles present in the OR room air during surgery?

Methods: This prospective study was conducted at a single institution. The OR was fitted with a positive ventilation system. In addition, a filtration unit with a crystalline ultraviolet unit (C-UVC) was placed in the OR. The inflow and outflow air from the unit was sampled using specialized swabs at the beginning and at conclusion of each procedure. Additional surgical-related variables were also recorded at each time of sampling. Swabs were processed for culture and Next-Generation Sequencing.

Results: The mean length of the surgical procedures sampled was 68 Â± 13 minutes. Overall, 19 out of 200 (9.5%) swabs isolated microorganisms. Inflow swabs were positive at a higher rate (16% vs. 3%; $p<0.01$).

Discussion: Our study demonstrated that microorganisms are present in the OR room air. The particles in the inflow air were inactivated by a C-UVC light. We confirmed that door opening was associated with an increase in the number of particles or microroganims in the OR room air. We did not find an association between total PPM and the detection of pathogens; however, the exposition to certain VOCs can cause serious health effects, as many of these compounds are carcinogenic.

Conclusion: Microorganisms are present in the operating room air. A specialized filtration unit with a C-UVC light was effective in filtering these microorganisms in the majority of cases.

1131 Chondrocyte Invasion is a Mechanism for Persistent Staphylococcus Aureus Infection

Authors: **Jerry Chang**, David Kerr, Thorsten Seyler

Background And Rationale: Staphylococcus aureus is a leading cause of bone and joint infections. Even with proper antibiotic treatment, there is a high rate of recurrent or chronic infection. S. aureus has been shown to invade osteoblasts and fibroblasts, but little is known about the mechanism of chondrocyte infection.

Study Question: The focus of this study was to identify whether chondrocytes provide an intracellular reservoir for S. aureus infection in vitro.

Methods: Equal numbers of human chondrocyte (C20A4), human osteoblast (MG63), and mouse fibroblast (NIH-3T3) cell lines were cultured in vitro and exposed to S. aureus at MOI 100 for 60 minutes. Cells were then washed and treated with high dose antibiotic containing media for 90 minutes, then replaced with maintenance dose antibiotic media. Each day, antibiotic media and washed cell lysate from each cell line were collected and individually plated on TSA agar plates and assessed for colony forming units (CFU). Maintenance antibiotic media was refreshed daily.

Results: Initial high dose antibiotic media yielded 0 CFU. C20A4 lysates yielded 5.3x103 CFU/mL up to 6 days post infection. MG63 lysates grew 2.4x103 CFU/mL up to 6 days post infection. 3T3 grew 3.6x103 CFU/mL up to 2 days post infection. Maintenance antibiotic cell media yielded no CFU each day for all cell lines.

Discussion: S. aureus readily invaded all tested cell lines as demonstrated by colony growth from cell lysates. No colonies grew from initial high dose or maintenance dose antibiotic media suggesting adequate killing of extracellular S. aureus. Even after one week of antibiotic treatment, S. aureus continued to grow from lysed C20A4 and MG63 cells. Our findings showed chondrocytes harbored a higher load of intracellular infection and for a longer duration compared to positive control osteoblast and fibroblast cell lines. This suggests chondrocyte invasion contributes to the recurrence of bone and joint infections even after thorough treatment with antibiotic therapy.

Conclusion: Human chondrocytes provide an intracellular reservoir for S. aureus infection, even in the setting of antibiotic treatment, providing a mechanism for persistent bone and joint S. aureus infection.

1199 Polymicrobial infection with Candida albicans and Staphylococcus aureus increases bacterial biofilm formation in a murine model of periprosthetic joint infection

Authors: **Zeinab Mamouei**, Aaron Kavanaugh, Christopher Hamad, Rahul Sobti, Jack Pearce, Adolfo Hernandez, Rene Chun, Fabrizio Billi, Nicholas Bernthal

Background And Rationale: Polymicrobial periprosthetic joint infections (PJI) are increasing in incidence, more recalcitrant to treatment, and portend worse clinical outcomes compared to monomicrobial PJI. It is unclear how various pathogens interact in polymicrobial biofilm infections. To address this gap, we developed a polymicrobial model of post-arthroplasty infection to study the most common bacterial and fungal combination in polymicrobial PJI, S. aureus (SA) and C. albicans (CA).

Study Question: How does co-infection of SA and CA impact infection burden in a murine model of PJI?

Methods: In vitro, SA (Xen36) and CA (SC5314) were co-incubated with 10 x .8mm titanium wires and SA implant colony forming units (CFUs) were calculated at 24 h. Some implants were taken for scanning electron microscopy (SEM) and compared to monomicrobial controls. In vivo experiments, a 6 x 0.8mm titanium wire was implanted into the distal femur of 10-week-old C57BL/6 mouse and inoculated with 1E3 CFUs of SA, 1E7 CFUs of CA, or a combination of the two. Longitudinal bacterial burden was quantified using an IVIS Spectrum. Animals were sacrificed on post-operative days (PODs) 7, 14, and 35 to collect implants and tissues for CFU analysis. Lastly, on POD35, microCT analysis was performed to compare the degree of femoral diaphysis widening.

Results: In vitro, SA CFUs were 1.5 logs higher on co-infected implants at 24hrs compared to monomicrobial controls. On SEM, SA biofilm densely formed where CA hyphae were adherent to the implant (Fig. 1). On longitudinal bioluminescence, SA burden was elevated in co-infected animals on PODs 3-14 compared to SA monomicrobial controls (Fig. 2A). In vivo, SA biofilm burden began to increase on co-infected implants on POD 14 ($p=0.19$), and this difference became significant on POD35 (p

Discussion: Polymicrobial infection with SA and CA significantly increases SA bacterial burden and bony remodeling in a murine model of PJI. This is driven by greater SA biofilm formation on implants, which was observed both in vitro and in vivo.

Conclusion: CA appears to facilitate the formation of SA biofilm in a murine model of PJI. Further investigation is required to understand the synergistic mechanisms between these pathogens.

1113 Systemic versus increasing intra-articular doses of vancomycin in a prosthetic joint infection rat model: Efficacy and Impact on Mitochondria

Authors: **Nour Bouji**, Elizabeth Stewart, John Hollander, Ethan Meadows, Dylan Shaver, Matthew Dietz

Background And Rationale: PJI treatment using systemic antibiotics remains unsatisfactory. Mitochondria are known as the cell's powerhouse, however, recent literature linked its dysfunction to infection-driven sepsis and bactericidal antibiotic treatment. No research examined the efficacy and mitochondrial effects of different antibiotic administration routes in PJI

Study Question: To compare the efficacy of systemic versus increasing intra-articular (IA) doses of vancomycin in PJI and its impact on mitochondria

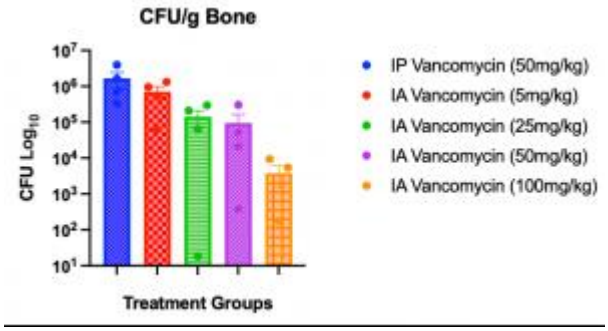
Methods: Using an MSSA associated in vivo model, rats were assigned to 10 day five treatment groups. Vancomycin was administered systematically via intraperitoneal (IP) (50mg/kg) injection or locally via IA injection as 1)5mg/kg 2)25/kg, 3)50mg/kg, and 4)100mg/kg. To assess efficacy, bone and tissues were harvested from surgical limb to quantify bacterial burden and to evaluate vancomycin concentration. To assess for mitochondrial function, coupling assays were used to measure oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) in IP versus IA group receiving same dose of 50mg/kg

Results: CFU/g bone revealed statistically significant differences between treatment group means (p=0.04), with the highest bacterial concentration observed in IP group and the lowest value observed in IA 100mg/kg group. CFU/g bone was decreasing as IA dose increased. The lowest concentration of vancomycin was observed in IP group while the highest concentration was observed in IA 100 mg/kg group as the concentration increased with the increased IA dose across the groups. As for mitochondrial outcomes, IP group showed a higher ECAR, a lower OCR, and a significantly decreased in maximal respiration and oxygen consumption due to ATP synthesis (P

Discussion: As for efficacy, increasing doses of IA Vancomycin demonstrated decreased bacterial count across IA groups and lower bacterial count when compared to IP vancomycin. Local tissues demonstrated increasing concentrations of vancomycin observed with higher IA dose and in comparison, to IP group. Comparing same doses of IP and IA vancomycin impact on mitochondria yielded more favorable results for mitochondrial respiration with IA route

Conclusion: IA vancomycin could be an effective and safe alternative to systemic vancomycin for PJI control and potentially avoid deleterious effects on mitochondria

Attachments:



1191 A refillable drug delivery device that sustains local, high dose antibiotic therapy manages biofilm implant-related infection in a sheep model of long bone open fracture.

Authors: Dustin Williams, Robert Falconer, **Nicholas Ashton**

Background And Rationale: Fractures represent the leading cause of injury hospitalization in the US, with an estimated 3 - 6 million patients suffering from bone fractures annually. Approximately 3-4% of fractures are open and are associated with high infection rates (upwards of 50%). Current therapies fail to effectively manage these infections. We are developing a refillable local drug delivery device (referred to as the Purgo Pouch) that sustains local, high dose antibiotic therapy.

Study Question: Does a refillable drug delivery device that sustains local, high dose antibiotic therapy manage biofilm implant-related infection in a sheep model of long bone open fracture more effectively than clinical standards of care?

Methods: We tested the Purgo Pouch in an established sheep model of long bone open fracture infection in which biofilms are used as initial inocula; monomicrobial or polymicrobial biofilms of S. aureus and P. aeruginosa were grown on simulated fracture fixation plates and secured to the proximal medial aspect of the right tibia. Purgo Pouch efficacy was tested for 10 and 20 days with four different antibiotic treatments. For comparison, data were collected with standards of care: systemic therapies, antibiotic-loaded calcium sulfate beads, and direct antibiotic powder. All sheep had a 21-day endpoint. Positive and negative controls were analyzed. Data were collected in n=8 sheep/treatment.

Results: The Purgo Pouch reduced biofilms by up to 7 log10 colony forming units (CFU; Figure 1). In all cases, the Purgo Pouch reduced more bioburden than any of the clinical standards; clinical standards reduced at most 4 log10 CFU. Histological data indicated that bone in those sheep treated with a Purgo Pouch was healthier than bone of sheep treated with a clinical standard or controls.

Discussion: Surgeons are desperate for a solution to address the persistent problem of open fracture infection. Local therapies are promising, but no product exists that can sustain high doses of antibiotic in a fracture site. The Purgo Pouch, currently under FDA review, addresses these limitations and animal data indicates that it can reduce biofilm burden to a far greater degree than current clinical standards.

Conclusion: A refillable local drug delivery device that sustains local, high doses of antibiotic may address a decades-long gap in healthcare.

Attachments:

1104 Gentamicin-loaded bone cement is effective against representative small colony variants: an in vitro study

Authors: **Jeongeun Cho**, Emanuele Chisari, Diana Fernández-Rodríguez, Javad Parvizi

Background And Rationale: Bacteria can lower their metabolic activity to escape antimicrobials. One of the forms that bacteria can take in clinical practice is called small colony variants (SCVs), named after the culture appearance of these bacteria. Antibiotic-loaded bone cement is widely used in revision arthroplasty to prevent or treat active periprosthetic joint infections (PJIs). The efficacy of antibiotic-loaded cement elution on SCV has not been reported in literature.

Study Question: Is antibiotic-laden bone cement (ALBC) effective against small colony variants (SCV) of common pathogenic bacteria in orthopaedic infections?

Methods: An in vitro model was built to simulate antibiotic elution within the joint, as previously reported. Two grams of bone cement (40g pack, 0.5 g gentamicin per pack) were immersed in 30 ml of PBS and incubated at 37 C. PBS with eluted gentamicin was drawn at 1h, 24h, and 1 week. Then, elution was used to perform a standard time-to-kill test using 1 h, 6 h, and 24h as contact time points. The appropriate neutralizer was selected and validated. The negative and positive control consisted of plain bone cement elution and 70% isopropyl alcohol solution, respectively. The primary endpoint was the log reduction difference between the reference strain, namely American Type Culture Collection (ATCC) strain, and the SCV strains of Staphylococcus aureus and Pseudomonas aeruginosa. Statistical analysis consisted of descriptive statistics.

Results: After 1 h of elution, the log reduction of ALBC was not different between ATCC and SCV strain, while S aureus showed a 1-log difference even at 24-hour contact time (ATCC 2.58 log reduction vs. SCV 1.27 log reduction)(Table 1) When the 24 hour elution and the 1-week elution were tested, SCV S. aures showed more than 2 logs of reduction, but still showed less killing compared to the ATCC reference strain. P. aeruginosa showed complete killing after 24 h of exposure (Table 1)

Discussion: Multiple reports have shown the relevance of SCV in periprosthetic joint infections and other orthopaedic infections. This is the first study to report data on ALBC elution on SCV killing. SCV are able to resist commonly used oral and intravenous antibiotics by lowering their metabolic activity, underlining the need of high local doses of the same agent.

Conclusion: Based on our study, ALBC could be a valuable allied against common bacteria like S. aureus and P.aeuroginosa.

Attachments:

Table 1

Log reduction		ATCC- Library		Small Colony Variant	
Length of incubation	Contact time	S. aureus	P.aeruginosa	S. aureus	P.aeruginosa
1H Elution	1hour	0.01	2.00	0.01	3.66
	6hour	0.77	3.80	0.00	7.44
	24hour	2.58	7.08	1.27	7.38
24H Elution	1hour	0.07	2.10	0.00	2.47
	6hour	0.64	4.77	0.03	7.54
	24hour	3.32	7.03	2.30	7.43
1 week Elution	1hour	0.00	4.60	0.00	3.38
	6hour	0.50	5.37	0.14	7.30
	24hour	5.86	6.11	2.50	7.04

Monitor 1

23-AEP-1122 Mature M2 MRSA Biofilm Inhibition On Metal Plates Using Combination Therapy of Very Low to Low Frequency Electro-Magnetic Fields (EMF) and Vancomycin
Gerhard Maale, Matthew Maale, Steve Dollery, Gregory Tobin

23-AEP-1138 nfluence of Staphylococcus epidermidis Biofilm on Collagen Crimp Patterns of Soft Tissue
Koral Blunt, Paul Stoodley, David Flanigan

23-AEP-1150 The Infected Marlex Mesh: Which Antiseptic Solution Most Effectively Removes Biofilm?
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23-AEP-1152 Chemical treatment of infected orthopedic surfaces decreases viable bacteria, but mechanical methods are needed to remove biofilm
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23-AEP-1188 Translation of a heavy-duty antibiotic wound protectant gel from benchtop to animal study
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23-AEP-1197 The potential of lactoferrin and ceftazidime powders to manage biofilm implant-related infection in a sheep model of long bone open fracture
Tyler Smith, Robert Falconer, Nicholas Ashton, Dustin Williams

23-AEP-1207 Monomicrobial and polymicrobial efficacy: Do surgical irrigants meaningfully reduce or eradicate infectious burden?
Christopher Hamad, William Sheppard, Rene Chun, Zeinab Mamouei, Adolfo Hernandez, Rahul Sobti, Jack Pearce, Matthew Dipane, Nicholas Bernthal, Edward McPherson

23-AEP-1214 Can the Use of Bacteriophage Derived Endolysin Reliably Prevent S. aureus Periprosthetic Infection in a Murine Model?
Christopher Hamad, Zeinab Mamouei, Adolfo Hernandez, Alan Li, Rahul Sobti, Jack Pearce, Nicholas Bernthal, Kevin Francis

1122 Mature M2 MRSA Biofilm Inhibition On Metal Plates Using Combination Therapy of Very Low to Low Frequency Electro-Magnetic Fields (EMF) and Vancomycin

Authors: Gerhard Maale, Matthew Maale, Steve Dollery, Gregory Tobin

Background And Rationale: Many types of pathogens, especially bacteria and fungi, can form biofilms which create a proteoglycan barrier that reduces the effectiveness of antimicrobial agents, such as antibiotics, and/or the immune system. In addition, many pathogens have developed genetic resistance mechanisms to antimicrobials. Today, the majority of infections seen in surgical implantations form biofilms that are resistant to front-line systemic antibiotic treatments because a thousand times MIC is necessary to destroy biofilm related infections. The phenotypic expression of biofilm organisms is different from their planktonic counterpart. Surgical removal of all implants is usually necessary for clinical treatment.

Study Question: Is mature biofilm disrupted with combination treatment using 1ug/ml of vancomycin and EMF?

Methods: 430 steel coupons (19 mm x 25.4 mm x 2 mm) were cultured with M2 MRSA under 1x tryptic soy broth (TSB) containing media for 1 week at 37Â°C. The media was changed every 3-4 days. Coupons were collected and washed four times in 25ml PBS by gentle inversion and placed in a 50 ml tube which was filled with 20 ml of TSB. If vancomycin was indicated for the particular sample, the vancomycin concentration was 1ug/ml. The samples were incubated at 37Â°C and exposed to EMF that generated heat on the plates at respectively 45, 55, and 65Â°C. The coupons were washed four times with PBS. Bacteria was removed from the coupons with a plastic cell scraper and titered on agar plates using 10-fold dilutions.

Results: At 45Â°C there is a log-3 reduction in the biofilm measuring the CFUs. At 55Â°C there was a 100% reduction of the biofilm CFUs. This was attributed to a rapid temperature heating curve generated from EMF on the metal plate. In a separate experiment, EMF on plastic plates generated no inhibitory effect with vancomycin on biofilm. In another experiment, without EMF a metal coupon was submerged at 60Â°C with a log-3 reduction for the equivalent amount of time.

Discussion: Very Low/Low EMF combined with vancomycin on metal plates at 55Â°C completely destroyed biofilm. This may be useful in clinical application for retention in prosthesis in biofilm related infection and in it's prevention.

Conclusion: EMF generated temperature increase on metal plates at 55Â°C in the presence of vancomycin completely destroyed the M2 MRSA biofilm. At 45Â°C biofilm showing log 3 reduction in CFU.

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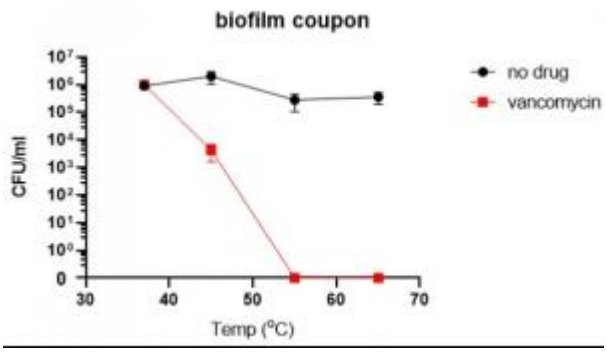

1138 Influence of Staphylococcus epidermidis Biofilm on Collagen Crimp Patterns of Soft Tissue Allograft

Authors: Koral Blunt, Paul Stoodley, David Flanigan

Background And Rationale: Postoperative infections, commonly from Staphylococcus epidermidis, may result in anterior cruciate ligament (ACL) graft failure and necessitate revision surgery. In biomechanical studies, S. epidermidis has been shown to establish biofilms on tendons and reduce graft strength. We hypothesized that an increase in S. epidermidis biofilm will compromise tendon crimp, a pattern necessary for mechanical integrity, of soft tissue allografts.

Study Question: The goal of this study was to determine the impact of S. epidermidis bioburden on the collagen crimp structure of tendon allografts.

Methods: Cultures of S. epidermidis were inoculated on tibialis anterior cadaveric tendons. Conditions assessed included 5 x 105 CFUs (colony-forming units) or concentrated spent media from culture (no living bacteria). Incubation times of 30 minutes, 3 hours, 6 hours, and 24 hours were utilized. Second-harmonic generation microscopy allowed for visualization of collagen autofluorescence. Crimp lengths were determined with ImageJ and compared based on incubation time.

Results: Incubation time positively correlated with increasing S. epidermidis bioburden. Additionally, macroscopic changes in projected tendon surface area were observed significantly following 6 hours of incubation. Both fine and coarse crimp patterns lengthened with increasing incubation time. Significant coarse crimp changes were observed after only 30-minute incubations (p=

Discussion: The results of this study demonstrate that S. epidermidis biofilms negatively impact collagen crimp structure and that crimp waveform patterns lengthen with increasing bioburden. In the presence of S. epidermidis biofilm, structural alterations at the collagen fiber level occur quickly and before gross changes can be appreciated, which highlights the need for antimicrobial precautions to prevent graft colonization and maximize graft mechanical strength.

Conclusion: This study demonstrates that exposure to S. epidermidis biofilms compromises collagen crimp structure in tendon allografts. Structural alterations at the collagen fiber level occur within 30 minutes of exposure to media containing S. epidermidis.

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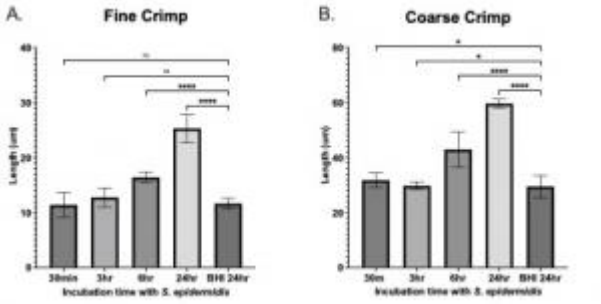

1150 The Infected Marlex Mesh: Which Antiseptic Solution Most Effectively Removes Biofilm?

Authors: Suenghwan Jo, Christina Chao, Tyler Khilnani, Mathias Bostrom, Alberto Carli

Background And Rationale: Polypropylene (PPE) synthetic mesh is increasingly used in knee arthroplasty surgery to salvage a disrupted extensor mechanism. Despite its clinical success, it is associated with a high rate of periprosthetic joint infection (PJI), which is hypothesized to be caused by bacterial biofilm.

Study Question: 1)Describe the progression of PPE-based biofilm formation over time. 2)Determine the effect of intraoperative antiseptic solutions when treating PJI associated with Marlex mesh.

Methods: Surgical PPE mesh (Marlex Bard, BD) was cut and cultured individually with methicillin-sensitive staphylococcus aureus for 10 days to elucidate the biofilm grown on the mesh over time. At every 24 hours, biofilm on the mesh was sonicated using low-frequency ultrasound, and dislodged bacteria were quantitated by counting colony-forming units (CFUs) after overnight growth. The biofilm formation was also verified using scanning electron microscopy (SEM). The effect of saline and antiseptic solutions was verified by exposing prepared mesh to 1) Irrisept (0.05% chlorohexidine gluconate, Irrimax corp, FL), 2) Bactisure (acetic acid based formulation; Zimmer-Biomet, Warsaw IN), 3) diluted povidone-iodine (P-I, 0.35%), 4) undiluted P-I (10%), and 5) 1:1 combination of 10% P-I & 3% hydrogen peroxide on immature and mature biofilms for 3 minutes, created by culturing with bacteria for 24 hours and 72 hours respectively. All experiments were performed in quintuples and repeated. Antiseptic treatments produced a three-log reduction in CFU counts compared to controls were considered clinically significant.

Results: PPE-mesh produced a reliable CFU count at 24 hours which reached a peak at 72 hours and the biofilm formation was confirmed through SEM. All formulations of P-I produced clinically significant reductions of immature biofilm while formulations based on P-I and Bactisure produced significant reductions of mature biofilm.

Discussion: Based on these findings, we recommend that surgeons consider using an antiseptic solution, preferably P-I based, in addition to regular saline lavage when attempting to salvage a PPE mesh in the setting of PJI. Further work is needed to determine how antiseptic solution efficacy is affected once fibroblast incorporation into the mesh has commenced.

Conclusion: Biofilm may form on mesh as early as 24 hours after bacterial exposure. P-I formulations were consistently the most effective in removing biofilm on mesh surface.

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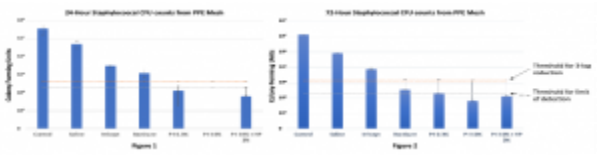

1152 Chemical treatment of infected orthopedic surfaces decreases viable bacteria, but mechanical methods are needed to remove biofilm

Authors: Christina A Chao, Tyler Khilnani, Suenghwan Jo, Mathias Bostrom, Alberto V Carli

Background And Rationale: The optimal method to remove biofilm from orthopedic surfaces remains unknown. Although surgeons utilize antiseptic solutions and intrawound antibiotics to eradicate bacteria, treatment failure rates remain high especially when infected implants are retained in the setting of periprosthetic joint infection (PJI). Consequently, there has been a renewed interest in optimizing mechanical methods of removing biofilm intraoperatively.

Study Question: Does the application of sonication brushing work synergistically with antiseptic solutions when treating mature methicillin-sensitive staphylococcus aureus (MSSA) biofilm that is formed on orthopedic surfaces?

Methods: MSSA (Xen36) was grown on porous Ti-6Al-4V screw caps (G7; Zimmer-Biomet), cobalt chrome coupons (Smith & Nephew), and polymethylmethacrylate coupons for 72 hours to establish mature biofilm. Surfaces were then treated for 3 minutes with either an antiseptic solution (1:1 ratio of 10% povidone iodine and hydrogen peroxide, PI+HP; diluted 0.35% povidone iodine, dPI; or Bactisure (Zimmer-Biomet)) or a saline control. Half of the antiseptic treated surfaces were randomly allocated to also receive mechanical treatment involving a 20-second direct contact exposure to a sonication brush (minimum 40,000 movements/minute). All treated surfaces were then sonicated in tryptic soy broth and plated to count colony forming units (CFUs) to quantify viable bacteria. Experiments were performed in triplicate and repeated.

Results: On porous titanium, brushing produced an additional 1.5 log reduction in CFU counts when combined with all antiseptic solutions tested. On smooth cobalt chrome (CC), an additional 3 log reduction was observed when the method was utilized with dPI but the effect in combination with Bactisure and PI+HP was limited. No additional benefit was observed with brushing applied on the PMMA surface.
Discussion: The sonication brushing works synergistically with antiseptic solutions in removing biofilm from textured orthopedic implants while limited efficacy was noted when combined with high-efficacy antiseptic solutions on smooth orthopedic surfaces or on PMMA. Further work to determine optimal protocol based on surface and brush settings is needed.

Conclusion: Surgeons should consider employing mechanical cleaning methods such as brushing when attempting to clean porous cementless implants.

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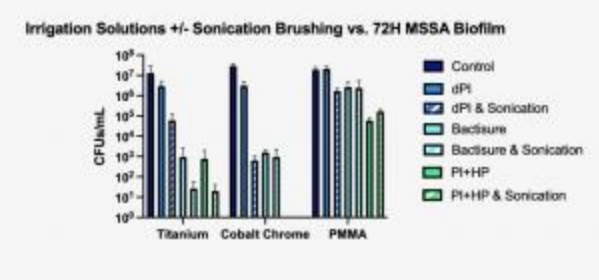

1172 Small colony variants causing Prosthetic joint infection depict a different gene expression profile.

Authors: Diana Fernández-Rodríguez, Luis Esau Lopez Jacome, Rafael Franco-Cendejas

Background And Rationale: Prosthetic joint infection (PJI) is an infectious complication after total joint arthroplasty (TJA) with a high socioeconomic impact. Staphylococcus species attain for more than half of PJI cases. Biofilm formation and the development of small colony variants (SCV) have proven to enhance chronic and/or relapsing bacterial infections. In this regard, a better understanding of these factors can help overcome PJI and other device-associated infections. Thus, we aimed to analyze the clinical and microbiological differences between common/wild type (WT) and SCV Staphylococcus epidermidis strains.

Study Question: Are SCVs frequent among patients with prosthetic joint infection? Is gene expression equal between WT and SCV bacteria?

Methods: We analyzed a monomicrobial cohort of PJI patients affected by S. epidermidis. The bacterial isolates of patients with more than one-year of follow-up were examined for SCV detection. Then, we determined the genetic relatedness between strains with a pulsed field gel electrophoresis (PFGE). Finally, we selected 4 representative strains (2 WT and 2 SCV strains) to perform a differential expression analysis by RNA-seq. We performed a multiple test correction by controlling the false discovery rate (FDR) at 10%.

Results: S. epidermidis SCV affected 16 (37.6%) patients with monomicrobial PJI. The DNA fingerprints showed a high similarity, according to the Dice coefficient, between SCV strains and their WT counterparts. Nevertheless, further experiments demonstrated 22 genes with a significant differential expression profile: 12 were associated to metabolic pathways (carbon, amino acids, nucleotide, purines) and biosynthesis of secondary metabolites and cofactors, 3 with transmembrane transportation, 2 with redox balance, 1 with pH balance, 1 with integral components of the membrane and cell adhesion. Function was not identified for 3 of these genes

Discussion: SCV are common in device-related infections like PJI. S. epidermidis SCV and their WT counterparts showed an extremely similar genetic background: still, SCV strains have a different gene expression profile. These genes may be promising therapeutic targets for combating chronic and/or relapsing bacterial infections.

Conclusion: Our findings explain some phenotypic variations (growth rate, biofilm properties, antimicrobial susceptibility profiles) found in clinical SCV strains.

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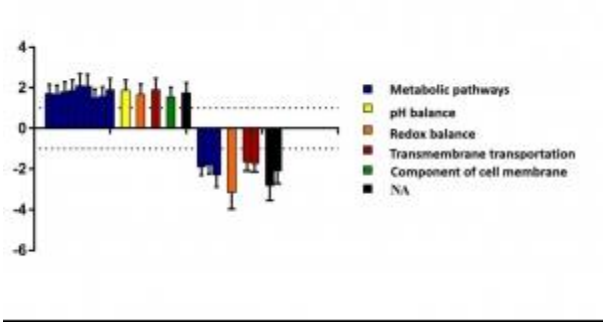

1187 Development of an Ovine Model of Implant-Associated Spine Infection Using Biofilm Inocula

Authors: Nicholas Ashton, Darrel Brodke, Dustin Williams

Background And Rationale: Postoperative implant-associated spine infection remains poorly understood, with no large animal model available, and no model that specifically uses biofilm inocula, to study this challenging entity. The purpose of the present study was to develop a sheep model for implant-associated spine infection using more-relevant biofilm inocula and to assess the in vivo utility of methylene blue (MB) for visualizing infected tissues and guiding debridement.

Study Question: To determine if biofilm inocula could be used to rapidly produce robust clinically-relevant infection in a large-animal ovine spinal fusion model.

Methods: This 28-day study used five adult female Rambouillet sheep, each with two non-contiguous surgical sites -in the lumbar and thoracic regions- comprising randomized positive and negative infection control sites. A standard mini-open approach to the spine was performed to place sterile pedicle screws and Staphylococcus aureus (ATCC 6538) biofilm-covered (positive sites), or sterile (negative sites) 75 mm long spinal fusion rods. Bacterial quantification of representative rods was performed prior to implantation and after explantation at necropsy. Soft tissue bioburden was quantified from three tissue biopsies in each surgical site. Negative and positive sites were stained with MB and photographed under controlled lighting. Vertebrae were analyzed with x-ray, micro-CT and histologically.

Results: Inoculation rods contained ~2.74x1010 colony forming units (CFU)/rod. Biofilm inocula persisted on positive-control rod explants with ~1.62x106 CFU/rod. There was ~8.37x106 CFU/gram of tissue in the positive controls versus no identifiable bioburden in the negative controls. Positive controls displayed hallmarks of deep spine infection and osteomyelitis, with robust local tissue response, bone resorption, and demineralization. MB staining was more intense in infected, positive control sites.

Discussion: At positive control sites, there was reliable creation of deep spine infection with robust local tissue response and evidence of osteomyelitis with bone resorption and demineralization typical of clinical infections. There was no cross contamination between infected and uninfected surgical sites within the same animal.

Conclusion: This work presents an animal-efficient sheep model displaying clinically relevant implant-associated deep spine infection and shows that MB has potential as a guide for surgical debridement.

1188 Translation of a heavy-duty antibiotic wound protectant gel from benchtop to animal study

Authors: Annika Hylen, Charles Florek, Korinna Hylen, David Armbruster, David Rothberg, Dustin Williams

Background And Rationale: Military service members are likely to experience traumatic battlefield-related injuries often contaminated by biofilms, which lead to difficult-to-treat infections that delay healing and decrease quality of life. Currently, there is a lack of products specifically designed to eradicate biofilm and stabilize a wound microbiologically following injury. We are developing an easy-to-apply antibacterial wound protectant for administration into a wound site at the time of injury to eradicate biofilm-dwelling bacteria.

Study Question: Can an antibiotic-loaded wound protectant gel that is formulated to withstand austere environments effectively reduce biofilms that contaminate a wound site in a sheep model of traumatic injury?

Methods: An antibacterial gel was formulated to maintain structure and activity up to 70Â° C. In vitro and ex vivo antibiofilm analyses were performed using a unique glass bead biofilm reactor. The right hind limb of sheep was traumatized using an air cannon, the femur was exposed, the periosteum roughened, and biofilm-ridden glass beads were inoculated. The gel was mixed with antibiotic and applied into the site. The sheep was monitored for seven days, then euthanized. Tissue samples were evaluated microbiologically, and a portion of the leg was left minimally disturbed for histological analysis. Three animal groups were studied: 1) a positive infection control that received formulation without antibiotic, 2) a negative control that did not receive formulation or antibiotics, and 3) treatment that received biofilm and antibiotic-loaded gel. Data were repeated in n=6 sheep/test.

Results: Increasing the ratio of solids in the gel product correlated with greater stability in extreme temperatures. In vitro elution kinetics of antibiotic release correlated biofilm reduction ex vivo and could be controlled by altering material ratios. No bacterial burden has been detected in the treated or negative control animal tissues. In the positive infection animals, swelling, edemas, and necrosis are visible during gross necropsy. Positive control animals had between log 10^5 to 10^7 colony-forming units in the infection site.

Discussion: Direct inoculation of biofilm provided a repeatable animal infection model. Localized delivery of high concentrations of antibiotic from the gel is effective at eliminating bioburden.

Conclusion: Our antibiotic-loaded gel manages biofilm in a large animal model to below-detectable levels.

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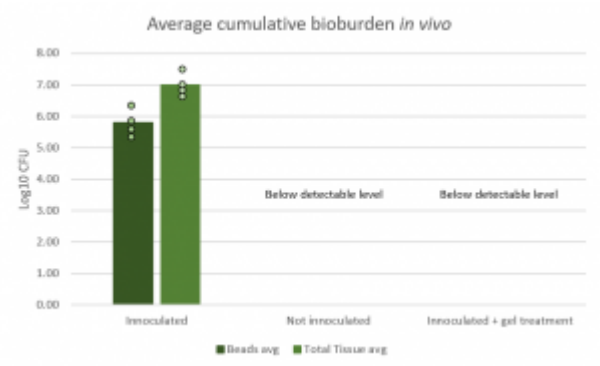

1197 The potential of lactoferrin and ceftazidime powders to manage biofilm implant-related infection in a sheep model of long bone open fracture

Authors: Tyler Smith, Robert Falconer, Nicholas Ashton, Dustin Williams

Background And Rationale: Fractures are a leading cause of injury hospitalization in the US, with an estimated 3 - 6 million patients suffering from bone fractures annually. Approximately 3-4% of fractures are open and are associated with high infection rates (upwards of 50%). Current therapies fail to effectively manage these infections. We are working with the University of Auckland to assess the antibiofilm potential of an adjunct protein, lactoferrin, combined with ceftazidime used as a combination powder in a sheep model of long bone open fracture infection.

Study Question: Does a locally sprinkled powder containing lactoferrin and ceftazidime reduce biofilm inocula in a sheep model of long bone open fracture infection better than ceftazidime alone?

Methods: We tested ceftazidime alone and ceftazidime plus lactoferrin in an established sheep model of long bone open fracture infection in which biofilms are used as initial inocula; biofilms of Staphylococcus aureus Xen36 were grown on simulated fracture fixation plates and secured to the proximal medial aspect of the right tibia. Powders were sprinkled into the surgical site prior to closure. Sheep were monitored for 21 days after which they were euthanized and microbiological and histological data collected. Positive and negative controls were also analyzed. Data were collected with n=7 sheep/group.

Results: Data indicated that a combination powder with lactoferrin and ceftazidime reduced biofilm burden by ~1.5 log10 units compared to ceftazidime only.

Discussion: The biofilm reduction was fairly minimal, yet the outcomes lead to important considerations for future work. For example, 1) The combination powder may be more effective when used with systemic antibiotics, 2) Lactoferrin and ceftazidime could be administered longer using a local drug delivery device and have increased efficacy, 3) Other antibiotics used in conjunction with lactoferrin could be more effective.

Conclusion: Lactoferrin and ceftazidime powders have some effect against biofilms of S. aureus Xen36, but additional work is needed to determine if such a combination would be clinically beneficial.

1207 Monomicrobial and polymicrobial efficacy: Do surgical irrigants meaningfully reduce or eradicate infectious burden?

Authors: Christopher Hamad, William Sheppard, Rene Chun, Zeinab Mamouei, Adolfo Hernandez, Rahul Sobti, Jack Pearce, Matthew Dipane, Nicholas Bernthal, Edward McPherson

Background And Rationale: There is no clear consensus regarding the ideal surgical irrigant to be utilized in orthopaedic hardware infections and surgeon or institutional preference often determines which irrigant is used. Most studies influencing decision making rely on data comparing single agents to normal saline and there is a paucity of evidence to dictate surgical decision making. This study compares the efficacy of commercial and non-commercial irrigants in vitro against S. aureus (Xen36) (SA) and C. albicans (CA) in both planktonic and biofilm states.

Study Question: Which surgical irrigants have the most efficacy against monomicrobial and polymicrobial infections in vitro?

Methods: Commercially sold irrigants tested include Irrisept, XPERIENCE, Bactisure, and Dakins (0.5%). Non-commercial irrigants tested include povidone iodine (.35%) (PI), PI (10%), hydrogen peroxide (3%) (HP), 1:1 PI (10%) + HP (PI + HP), and normal saline (NS). For planktonic testing, 1E6 colony forming units (CFUs) of SA, CA, or both were utilized and biofilms were grown in these aforementioned conditions on 0.8mm x 10mm titanium implants for 48hrs. All killing assays were performed using 5-minute contact times, representing the average surgical dwell time. Success was defined by complete eradication of planktonic or biofilm CFUs.

Results: HP, PI + HP, and Bactisure were the only irrigants capable of eliminating planktonic SA (Figure 1A). In addition, only PI (.35%), PI (10%), HP, PI + HP, and Bactisure eradicated SA biofilms (Figure 1B). PI + HP and Bactisure were the only irrigants capable of eliminating SA in both planktonic and biofilm states and were tested against polymicrobial infection. Only PI + HP was able to eradicated polymicrobial SA + CA infections in both planktonic and biofilm states (Figures 1C & 1D).

Discussion: PI + HP and Bactisure appear to be superior irrigants against SA as they are able to eliminate this bacterium in both planktonic and biofilm states. However, only PI + HP was able to eradicate polymicrobial biofilm and planktonic infections.

Conclusion: Our in vitro data demonstrates that irrigants have variable killing efficacy against microbes depending on their state. Future studies are needed to confirm these findings in vivo.

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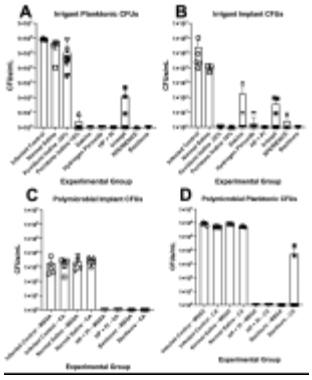

1214 Can the Use of Bacteriophage Derived Endolysin Reliably Prevent S. aureus Periprosthetic Infection in a Murine Model?

Authors: Christopher Hamad, Zeinab Mamouei, Adolfo Hernandez, Alan Li, Rahul Sobti, Jack Pearce, Nicholas Bernthal, Kevin Francis

Background And Rationale: Despite implementation of multi-modal preventative strategies, there has been little improvement in clinical periprosthetic joint infection (PJI) outcomes and breakthrough infections still occur. Hence, there is a need to develop novel antimicrobials. Bacteriophage derived endolysins are a potential candidate and function by potently digesting the bacterial cell wall. Endolysins have multiple advantages over antibiotics as they function specifically against pathogens and do not disturb host flora, have the ability to kill antibiotic resistant bacteria, and rarely induce bacterial endolysin resistance. We will test the ability of two endolysins, M23 and CHAP, to prevent S. aureus PJI a murine model of post-arthroplasty infection.

Study Question: Can endolysin therapy prevent PJI in murine model of post-arthroplasty infection?

Methods: A 6 x 0.8mm titanium Kirschner wire was implanted retrograde into the distal femur of 10-week-old C57BL/6 mouse and inoculated with 1E3 colony forming units (CFUs) of bioluminescent S. aureus (Xen36) or sterile saline. There were three mice per experimental group. Shortly after surgical closure, mice were administered intraarticular lysin injections (20mg/kg). Mice received subsequent once daily injections for four days. Bacterial burden was longitudinally measured in vivo by quantifying bacterial bioluminescence using an IVIS Spectrum. Animals were sacrificed on post-operative day (POD) 14 to collect implants and harvest tissue for CFU analyses.

Results: As compared to infected control implant and tissue CFUs, M23 was able to prevent infection in all three animals, while CHAP was able to prevent infection in one of three animals.

Discussion: Two S. aureus specific endolysins, M23 and CHAP, with differing biologic activity, were tested in a validated murine model of post-arthroplasty infection. While CHAP only prevented the establishment of PJI in one of three animals, M23 successfully prevented infection in all three animals.

Conclusion: M23 and similar endolysins could be helpful in conjunction with current multi-modal strategies to help prevent PJI caused by microbial contamination at the time of surgery. Future tests should study the therapeutic efficacy of M23 endolysin against established PJI.

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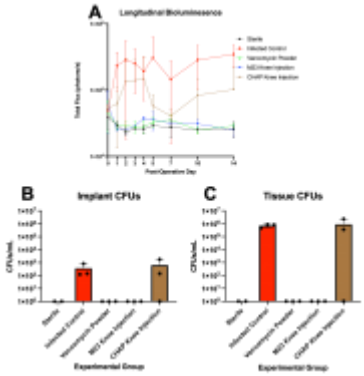

Monitor 2

23-AEP-1076 Dalbavancin is Thermally Stable at Clinically Relevant Temperatures Against Methicillin-Sensitive Staphylococcus Aureus
Aaron Hoyt, Patrick Lawler, Alberto Carli, Mathias Bostrom, Ashley Levack

23-AEP-1087 Multiplex Molecular Panel as a Supplement to Routine Culture for Tissue Infection
Christina Cox, Kristin Weghorn, Federico Palacio, Eleanor Powell, Margaret Powers-Fletcher

23-AEP-1098 The Results of 16S DNA-NexGen Sequencing (NGS) in Culture-Negative Periprosthetic Joint Infections
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Christopher Hamad, Joseph Kendal, Rene Chun, Zeinab Mamouei, John Adams, Nicholas Bernthal, Aaron Meyer, Jackson Chin

1076 Dalbavancin is Thermally Stable at Clinically Relevant Temperatures Against Methicillin-Sensitive Staphylococcus Aureus

Authors: Aaron Hoyt, Patrick Lawler, Alberto Carli, Mathias Bostrom, Ashley Levack

Background And Rationale: While the rate of orthopaedic infections has remained constant over the years, the burden on healthcare systems continues to rise with the aging population. Antibiotics must be thermally stable to be delivered locally in different conditions such as during polymethymethacrylate (PMMA) cement polymerization or extended periods at human core body temperature for long-term carriers such as hydrogels and calcium sulfate. Dalbavancin is a novel lipoglycopeptide antibiotic shown efficacy against gram-positive organisms when used systemically but has not been investigated as a local antibiotic.

Study Question: This study aims to assess the thermal stability of dalbavancin through modeling two clinically relevant scenarios: 1) within PMMA bone cement as a bead or as part of an articulating knee spacer, and 2) within a long-term antibiotic carrier such as hydrogels or calcium sulfate.

Methods: Stock solutions of dalbavancin were prepared and heated using a polymerase chain reaction machine-based models of curing temperatures in two clinically relevant models: a 10-mm polymethylmethacrylate bead and a polymethylmethacrylate articulating knee spacer model. Aliquots of heated dalbavancin were then transferred to incubate at core body temperature (37ËšC) and analyzed at various time points up to 28 days. The minimum inhibitory concentration at which 90% of colonies were inhibited (MIC90) of each heated sample was determined against methicillin-sensitive Staphylococcus aureus (ATCC 0173K) using a standard microbroth dilution assay.

Results: The average MIC90 of unheated control dalbavancin was 1.63Âµg/mL Â± 0.49 against 0173K S. aureus. There were no significant differences in MIC90 values after heating dalbavancin in both PMMA models with 28-days of incubation at human core body temperature compared to control.

Discussion: Overall, our study results demonstrate that dalbavancin is thermally stable during exothermic reactions in two clinically relevant models of PMMA cement in addition to being stable over an extended period at human core body temperature suggesting it may be used in long-term carriers. This study is foundational in establishing which local antibiotic carriers may be used for local delivery of dalbavancin prior to its clinical use.

Conclusion: Dalbavancin is thermally stable at clinically relevant curing temperatures of polymethylmethacrylate cement and at human core body temperature over 28-days.

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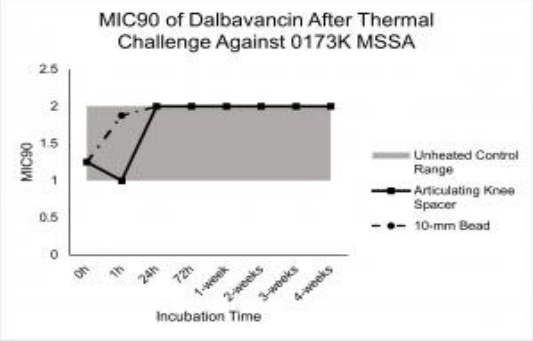

1087 Multiplex Molecular Panel as a Supplement to Routine Culture for Tissue Infection

Authors: Christina Cox, Kristin Weghorn, Federico Palacio, Eleanor Powell, Margaret Powers-Fletcher

Background And Rationale: Rapid and accurate diagnosis of fracture-related infections is essential for patient management. Limitations in routine culture sensitivity have been overcome for many types of infection via the application of molecular-based techniques, but these methods have not been broadly applied to tissue infections.

Study Question: What is the performance of the Unyvero ITI G2 multiplex PCR panel compared to routine culture for the identification of potential pathogens in bone and soft tissue?

Methods: Multiplex molecular testing was performed using the Unyvero ITI G2 panel (OpGenÂ®, Rockville, Maryland). Remnant tissue homogenate previously submitted for standard clinical microbiology testing was used for analysis. Following homogenate concentration, the pellet was resuspended in 200 Î¼L of Unyvero ITI G2 buffer for lysis and analysis. Each sample was tested according to manufacturer's recommendations and results were compared to organism identification from routine cultures performed by the clinical laboratory as part of standard patient care.

Results: In the 47 tested specimens, there were 108 microorganism analytes detected by multiplex PCR or isolated in culture. Almost 54% (n = 58) of all detected analytes correlated between multiplex PCR and culture. Only 20 microorganisms were isolated in culture but not detected by multiplex PCR (but are included on the panel) and 30 targets were detected by multiplex PCR but not isolated in culture. Considering all results (either multiplex PCR or culture) as true positives, multiplex PCR performed with a sensitivity of 81.5% (88 targets detected out of 108 total), while culture performed with a sensitivity of 72.2% (78 microorganisms isolated out of 108 total detected).

Discussion: We have demonstrated that a concentrated tissue homogenate specimen can be used with the Unyvero ITI G2 panel. Importantly, use of the Unyvero ITI G2 multiplex PCR assay resulted in detection of targets for microorganisms not isolated in culture, suggesting a potential for increased analytical sensitivity for some scenarios.

Conclusion: Although lack of comparison to patient outcomes in our study makes determining the clinical performance of this approach difficult, these results suggest that multiplex PCR assays may play an important role in supplementing routine laboratory testing and improving the diagnostic yield for tissue infections for culture-negative results.

1098 The Results of 16S DNA-NexGen Sequencing (NGS) in Culture-Negative Periprosthetic Joint Infections

Authors: Gerhard Maale, Nikitha Adari, Aniruth Srinivasaraghavan, Suhas Nalla, Ibrahim Khalilullah

Background And Rationale: Traditional culture methods have long been used to identify the presence of organisms in periprosthetic joint infections (PJI). Culture retrieval is at best 50-60% recovery for one organism alone. With preoperative treatment of PJI with antibiotics, the rate is anticipated to be much lower. 16S DNA-NexGen sequencing is thought to have a much higher recovery rate for patients pretreated with antibiotics.

Study Question: The questions asked are whether 16S DNA-NexGen sequencing can recover more than one organism from draining sinus tracts and is it more effective than classic culture and sensitivity and does pre-op use of antibiotics alter this?

Methods: 97 patients were identified with open draining sinus tracts around PJI, including 69 knees, 20 hips, 5 shoulders, and 3 elbows. All patients had an average of 5-7 operations (historically) prior to referral. All wounds were open and culture-negative. Each open wound was swabbed and underwent 16S DNA-NexGen sequencing by Microgen.

Results: None of this patient population had a positive culture of their draining sinus wound. Of these 97 patients, 58 of the open wounds were monomicrobial, and the other 39 were found to be polymicrobial PJI, with an average of 1.67 bacteria/fungal species per patient. Of the patients with polymicrobial infections, 21 were identified to have both gram-positive and gram-negative bacteria on 16S DNA-NexGen sequencing. 90 patients had preoperative treatment with antibiotics. 33 patients were treated with oral agents and 57 patients with IV antibiotics prior to referral

Discussion: Our findings indicated better identification of organisms in PJI with 16S DNA-NexGen sequencing over classic culture. The majority of patient in this cohort have preoperative use of antibiotics secondary to doing a one-stage surgical procedure for treatment and to calm the wound down. Additionally, preoperative antibiotics coverage did not seem to alter the recovery of the organisms with 16S DNA-NexGen sequencing. Furthermore, it identified resistant genomes in the organisms recovered and it recovered multiple organisms in 40% of the cases.

Conclusion: 16S DNA-NexGen sequencing with a mega-genomic library was better than culture and sensitivity. The pre-operative use of antibiotics did not alter the rate of recovery of the organisms and 40% were poly-microbial and 22% were both gram positive and negative.

1137 The clinical difference between Minimum Inhibitory Concentration and Minimum Biofilm Eradication Concentration

Authors: Paris Taylor, Elizabeth Stewart, Jacob Herriott, Matthew Dietz

Background And Rationale: Dosing of antimicrobials in the treatment of Prosthetic Joint Infection (PJI) is guided by the Minimum Inhibitory Concentration (MIC) of identified pathogens, determined using planktonic bacteria. However, most PJIs are caused by bacteria within biofilm, which can have up to a 50,000-fold increase in the antimicrobial tolerance when calculated using the Minimum Biofilm Eradication Concentration (MBEC). The purpose of this study is to quantify the MBEC of Staphylococcus aureus biofilms from clinical isolates and compare it to the reported MIC.

Study Question: Can the MBEC of clinical S. aureus isolates be quantified and will it be greater than the MIC. We hypothesized that the MBEC will be higher than the MIC.

Methods: With IRB approval (#2203550953) clinical isolates of S. aureus from revision arthroplasty cases collected over two years were identified from the clinical microbiology registry. The MIC of each isolate was determined using the Vitek 2 Susceptibility Panel. To quantify the MBEC, four clinically relevant antimicrobials were tested: Daptomycin (Dpt), Doxycycline (Dox), Oxacillin (Ox), and Vancomycin (V). Inoculums of each isolate were standardized and introduced into a 96-well MBEC Assay device, in which pegs remain immersed in the inoculum to form a biofilm. Pegs were then submerged in the antibiotics challenge plate for 20h. The remaining biofilm was determined via sonication and CFU quantification. Concentrations at which no viable bacteria remained were identified as the MBEC.

Results: To date, the MBEC of 5 clinical isolates has been determined using this method. The MIC values for Dpt (0.25 Î¼g/mL), Dox (27,500 Î¼g/mL for Dpt, 0-8 and 10-100 Î¼g/mL for Dox, 1000-5000 and >27,000 Î¼g/mL for Ox, and 650-1,250 and 4,500-5,000 Î¼g/mL for V.

Discussion: For the isolates tested, antibiotic concentrations much higher than the MIC were needed to eradicate viable bacteria in biofilms, highlighting the inability of MIC values alone to treat infections caused by biofilm. When selecting an optimal antibiotic treatment, both MIC and MBEC values should be considered.

Conclusion: The Minimum Biofilm Eradication Concentration (MBEC) for these clinical isolates was higher than the Minimum Inhibitory Concentration (MIC) for each antibiotic tested. Continued evaluation of the difference between these values should be explored.

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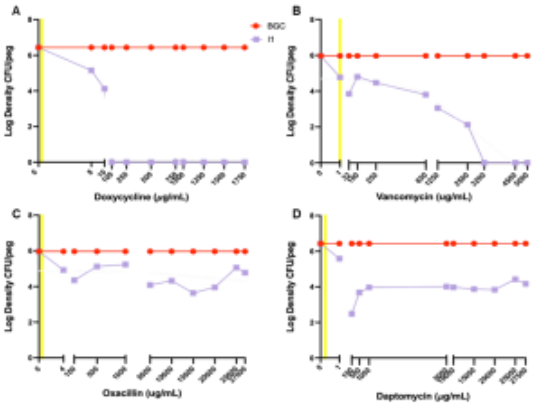

Figure 1: Biofilm Density per Antibiotic Treatment Log density remaining on peg after treatment with (A) Doxycycline, (B) Vancomycin, (C) Oxacillin, and (D) Daptomycin for one MSSA Isolate. The MIC for each antibiotic is shown in yellow. The Biofilm Growth Control (BGC) is shown in red, and the clinical Isolate (I1) is shown in purple.

1163 The Antibiotic Tolerance of Synovial Fluid Induced Aggregates of Staphylococcus aureus

Authors: Peter Burback, Amelia Staats, Paul Stoodley

Background And Rationale: When a patient undergoes an arthroplasty, a periprosthetic joint infection can develop. A major causative agent is S. aureus which rapidly aggregates in synovial fluid (SF) and can form biofilms. These aggregates provide bacterial protection from antibiotics, and this warrants an investigation into the mechanisms behind it.

Study Question: Is the protective effect from these aggregates long-lived enough to allow biofilm formation? Is there a size threshold for protection? Does the digestion of aggregates return them to their native susceptibility?

Methods: Bioluminescent S. aureus was aggregated in SF or left planktonic and exposed to gentamicin. Metabolic activity- luminescence- was captured using an IVIS and quantified. Aggregates were then stimulated in SF for varying times and subsequent viability was determined with plating. The pre-formed aggregates were then exposed to vancomycin and plated for CFUs. The aggregates were digested with trypsin prior to the addition of gentamicin and the resulting solutions were plated.

Results: Following a 21-hour challenge with gentamicin, the aggregated bacteria were still metabolically active. In contrast, the planktonic cells were killed within 6 hours. Within 15 minutes of exposure to SF, there were aggregates large enough to provide protection from gentamicin. After a size threshold was reached, there was no correlation between aggregate size and bacterial protection. Finally, the disruption of the aggregates with trypsin prior to treatment resulted in the bacteria returning to their native susceptibility.

Discussion: Since S. aureus can develop a biofilm within 24 hours, we show that aggregation likely provides protection until this crucial juncture. The rapid aggregation of S. aureus in SF is mirrored by the swift protective effect of the aggregates. Further, our work suggests that gentamicin may be better than vancomycin to as a prophylactic. Finally, by showing that trypsin can return aggregated bacteria to their native susceptibility, we report positively on the future of aggregate disruptors as potential therapeutics.

Conclusion: We show here that rapid aggregation of S. aureus in SF provides protection from antibiotic challenge, theoretically enabling the bacteria to develop a biofilm. This protective aggregate phenotype can be achieved in 15 minutes following exposure to SF. By disrupting the aggregates, we can return the bacteria to their native susceptible state in vitro.

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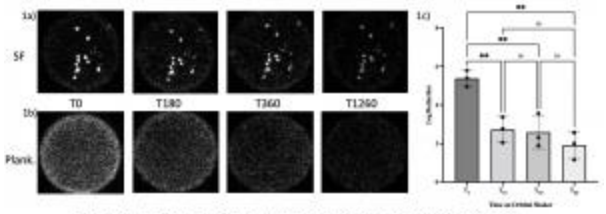

Figure 1: Large synovial fluid induced staphylococcal aggregates provide protection from antibiotics. Macroscopic aggregates of bioluminescent *S. aureus*, stimulated with 10% synovial fluid under flow (1a) or planktonic cells (1b) were treated with gentamicin and imaged with an IVIS system. Following a 1-hour gentamicin challenge, viability of intra-aggregate *S. aureus* cells were determined with CFU plating (1c).

1178 Biofilm Growth on Orthopaedic Cerclage Materials: Nonmetallic Polymers Are Less Resistant to Bacterial Adhesion

Authors: Kyle Cichos, Matthew Christie, Brent Ponce, Elie Ghanem

Background And Rationale: No studies have directly compared orthopaedic cerclage materials for bacterial adherence as a precursor to biofilm formation. We aimed to compare 5 of the most common cerclage products for MRSA attachment as indication of future biofilm formation.

Study Question: Are nonmetallic polymer cables more resistant to bacterial adhesion than common metallic wires/cables?

Methods: 5 cerclage products were compared: 1) monofilament stainless steel sternal/cerclage wires, 2) multifilament stainless steel cables, 3) multifilament Co-Cr cables, 4) multifilament Dall-Miles Vitallium (Co-Cr-Mo) cables, and 5) multifilament non-metallic polymer-based SuperCables. Each was cut in sterile fashion into 2 cm lengths and placed into 12-well plates. 5 wells were wire/cables in TSB with MRSA (1x104 CFU/mL) with remaining wells being appropriate controls. All plates were incubated for 24 h at 37C and 5% CO2 with shaking. Media was replaced for another 18 h incubation. Wires/cables were prepared and randomly imaged via SEM in middle section and cut end of each wire/cable with counts performed on 3 images x 3 different wires/cables per study group. SEM technician and counter were blinded. Additionally, SS wire and polymer cable were analyzed by microcalorimetry.

Results: Bacterial attachment differed significantly between study groups in the middle section ($p=0.0003$) (Figure 1). Post-hoc comparison showed no difference between groups individually (all $p>0.05$) apart from polymer cables (median 551 bacteria) having significantly increased attached bacteria compared to the Dall-Miles cable (157, $p=0.0004$), SS cable (101, $p=0.0004$), and SS wire (211, $p=0.0004$). There was no difference between polymer and CoCr cables (133, $p=0.056$). Microcalorimetry supported these results as polymer cables had shorter time to max heat flow (6.2 vs 7.5 h, $p=0.006$) and increased max heat flow (117 vs 64 uW, $p=0.045$), indicating increased bacterial load.

Discussion: This in-vitro study demonstrates that polymer cables have increased bacterial attachment of MRSA compared to common metallic wires/cables. For all groups except SS wires, cut ends were increased in bacterial attachment compared to the middle.

Conclusion: Non-metallic polymer cables are less resistant to bacterial adhesion than metallic wires/cables in-vitro. Given the reported clinical benefits of these polymer cables, clinical studies are necessary to confirm the translation of these findings.

1203 Histological Changes in Cortical Bone Due to the Presence of Various Biofilms

Authors: Richard T Epperson, Brooke Kawaguchi, Winston Rudisin, Nicholas Ashton, Dustin Williams

Background And Rationale: Bone infection due to biofilms can cause extreme damage due to significant bone loss and continued reinfection resulting in chronic osteomyelitis. However the literature is lacking in regards to a standard histological way to identify biofilm infected bone with biomaterials. In this study we set out to identify the initial cortical bone response to various biofilms with hard plastic histological imaging.

Study Question: Does the bacterial strain of a biofilm change the cortical bone response or do all biofilm bone infections react similar.

Methods: For bacteria inoculations, various biofilms were grown on the surface of 2 x 2 cm titanium plate for 48h utilizing a modified CDC biofilm reactor. Animal work was performed at the University of Utah utilizing a simulated Type IIIB open fracture infection model with a timepoint of 21 days. The groups consisted of the following with an n=5 sheep/group: Negative control (No Biofilm), Methicillin-resistant Staphylococcus aureus (MRSA), Staphylococcus aureus 6538 (Staph), Pseudomonas aeruginosa (Pseudo), Staph + Pseudo (Polymicrobial) Micro-CT scans were captured directly under the plate to observe any bone resorption due to the presence of biofilm. Next, the specimens were embedded in polymethyl methacrylate and sectioned for histological analysis by way of Scanning Electron Microscopy and florescent/light microscopy to determine the various bone responses (Figure 1).

Results: The analysis demonstrated distinct features indicating a biofilm infection (Fig 1). When comparing the biofilm response of MRSA to Staph, no differences were observed in regards to screw track osteomyelitis, periosteal reaction and/or new woven bone growth under the plate. However, notable differences were observed in osteoclast activity, with the Staph specimens containing 28.5Â±8.2 osteoclast per mm2 compared to the MRSA specimens 17.6Â±5.8. This resulted in a greater loss of bone/higher porosity in the Staph (72.5Â±15.4%) compared to the MRSA (56.3Â±21.5%) specimens. The analysis also revealed that the MRSA specimens had a much higher percentage of reactive bone (28.8Â±8.2%) compared to the Staph (13.7Â±12.1%) resulting in a larger amount of endosteal growth.

Discussion: The effects of Pseudo and the polymicrobial groups are currently being analyzed and will be ready by the meeting.

Conclusion: The preliminary analysis has demonstrated that the infection response in cortical bone may differ depending on bacterial stain.

1213 Can We Uncover Immunologic Mechanisms Promoting the Development of Chronic Periprosthetic Joint Infections?

Authors: Christopher Hamad, Joseph Kendal, Rene Chun, Zeinab Mamouei, John Adams, Nicholas Bernthal, Aaron Meyer, Jackson Chin

Background And Rationale: Periprosthetic joint infection (PJI) is a devastating outcome of total joint arthroplasty. The formation of a local immunosuppressive immune microenvironment (IME) may promote chronic infection. We aim to characterize the molecular and cellular changes that occur temporally in a murine model of PJI with the intention of identifying candidate immunotherapeutics.

Study Question: Can we temporally characterize the peri-implant IME in a murine model of post-arthroplasty infection utilizing Luminex, flow cytometry, and single cell sequencing (CITE-Seq)?

Methods: A murine model of S. aureus PJI was utilized. On post-operative days (PODs) 1, 3, 7, 14, 21, and 35, periarticular tissue was homogenized and peri-implant IME cells were isolated by centrifugation for 32-plex cytokine array and flow cytometry analyses, respectively. Tensor Method Analysis was used to analyze data. CITE-seq was performed on pooled (N=4) sterile and infected samples on PODs 1 and 7. Lastly, an in vivo efficacy pilot was performed utilizing FDA approved immunotherapies (PD-L1 and CSF-1R).

Results: Tensor analysis identified three distinct components that represent patterns in the data (Figure 1A & B). Component 1 represents sterile animals characterized by the recruitment of macrophages and myeloid derived suppressor cells (MDSCs) that co-express immunosuppressive markers and are recruited by M-CSF (Figure 1C). Component 2 represents the acute inflammatory response in infected animals characterized by cytokines that promote the NF-kB and STAT3 pathways (Figure 1D). Component 3 represents sub-acute and chronically infected samples typified by STAT1 signaling and alternatively activated macrophages and MDSCs (Figure 1E). CSF-1R immunotherapy reliable reduced tissue bacterial burden by 1.5 logs.

Discussion: Sterile hardware placement (surgery itself) appeared to induce immunosuppression via the recruitment of pro-phagocytic and poor antigen presenting phagocytes driven by M-CSF. There was an early recruitment of pro-inflammatory cells via NF-kB and STAT3 pathways, which lead to Th17 T-cell polarization. As inflammation persisted, STAT1 signaling began and induced the recruitment of Th1 polarized T-cells and immunosuppressive macrophages and MDSCS.

Conclusion: The native host immune response consisting of early Th17 and delayed Th1 responses failed to eradicate infection. Immunosuppressive polarization may be driven by both surgery and infection.

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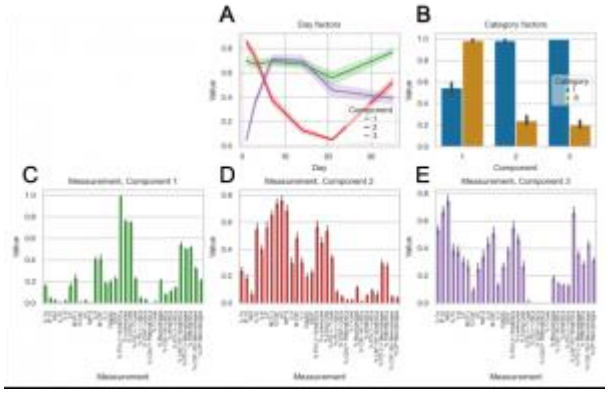

Monitor 3

23-AEP-1083 Characterizing the Native Microbiome Using Next Generation Sequencing of Bilateral 'Aseptic' Knees Undergoing Total Knee Arthroplasty
Tracy Borsinger, Michael Torchia, Bethany Malskis, Benjamin Levy, Paul Werth, Wayne Moschetti,

23-AEP-1102 Racial Disparities in Treatment and Outcomes of Patients with Hepatitis C Undergoing Total Joint Arthroplasty
Cole Howie, Kyle Cichos, Eric Jordan, Kian Niknam, Antonia Chen, Erik Hansen, Elie Ghanem

23-AEP-1116 Static Versus Articulating Spacer: Outcomes Not Associated with Infectious Organism
Caitlin Grant, Jerry Chang, Emily Poehlein, Cindy Green, Jessica Seidelman, William A Jiranek

23-AEP-1117 Clinical Success with Antibiotic Suppression Therapy in Patients with Prosthetic Joint Infection and Retained Hardware
Anne Spichler, Moffarah, Jane O'Bryan, Lidia Ani, Matthew Davis, Lee Rubin, Marjorie Golden

23-AEP-1128 Patients with periprosthetic joint infection have an elevated omega-6: omega-3 ratio in blood
Laura Y Lu, Joshua Davis, Antonia Chen

23-AEP-1130 Inferior Outcomes for Patients Transferred Between Surgical Stages for Knee Periprosthetic Joint Infection
Jerry Chang, Jonathan Florance, Patrick Kelly, Denise Smith, Michael Bolognesi, Thorsten Seyler, Sean Ryan

23-AEP-1136 Next Generation Sequencing Test for Diagnosing Periprosthetic Joint Infection Is Not Affected by Premature Antibiotic Administration
Alisina Shahi

23-AEP-1177 The Use of Irrigation in Total Knee and Hip Arthroplasty to Prevent Periprosthetic Joint Infection: A Systematic Review and Meta-Analysis
Sandhya Ganesan, Zachary Coles, Gwo-Chin Lee

23-AEP-1179 The Synovial Fluid Alpha-Defensin, Cell Count, PMN%, and CRP are Non-redundant Biomarkers
Krista Tiler, Pearl Paranjape, Van Thai-Paquette, Greg Deirmengian, Alex McLaren, Carl Deirmengian

23-AEP-1185 Development of Diagnostic Quality Metrics for Prosthetic Joint Infection
Andy Miller, Alberto Carli, Diana Chee, Sam Simon, Catherine Maclean, Amy Chin

1083 Characterizing the Native Microbiome Using Next Generation Sequencing of Bilateral 'Aseptic' Knees Undergoing Total Knee Arthroplasty

Authors: Tracy Borsinger, Michael Torchia, Bethany Malskis, Benjamin Levy, Paul Werth, Wayne Moschetti,

Background And Rationale: Next generation sequencing (NGS) has proven ability to identify organisms beyond those identified through traditional culture-based techniques. However, there is concern that some microorganisms identified may represent the natural joint microbiome rather than pathogenic agents. Appropriate use of NGS will be predicated on accurate interpretation of these organisms to avoid both under- and over-diagnosis.

Study Question: This work sought to use NGS to analyze the potential microbiome of bilateral knee joints in patients undergoing TKA. In doing so we sought to add to prior literature regarding potential for presumed 'aseptic' native knees to have microorganisms present on NGS analysis.

Methods: Forty patients undergoing primary unilateral (30) or bilateral (10) TKA were prospectively enrolled. During surgery, samples of both fluid and tissue were obtained on operative knees and joint fluid was obtained from non-operative knees. Samples were sent for NGS analysis and processed according to manufacturer protocols. Patient age, BMI, comorbidities, prior history of injections, and Kellgren-Lawrence (KL) grade of arthritis were evaluated for association with positive NGS results.

Results: Three of the 80 samples (3.8%) demonstrated positive NGS. Two of these had multiple microorganisms identified (one knee with 4 microorganisms; one knee with 2 microorganisms). An additional two samples had positive NGS results below the manufacturer's reporting threshold. No patients were found to have positive NGS results in their bilateral knees. All of the knees with microorganism(s) identified with NGS (3/3) in the present study had advanced arthritis (KL Grade IV), while 60% of those without positive NGS results had advanced arthritis. No patient baseline characteristics were associated with positive NGS results.

Discussion: To our knowledge, this is the first study to evaluate NGS results in bilateral native knees. The present findings support the previously established premise of a native knee microbiome and should be taken into consideration in appropriate application of NGS specifically for diagnosis and treatment of infection.

Conclusion: The findings of this work align with that of prior studies demonstrating positive NGS results in presumed 'aseptic' native joints, however the relative prevalence of this was lower in the present study.

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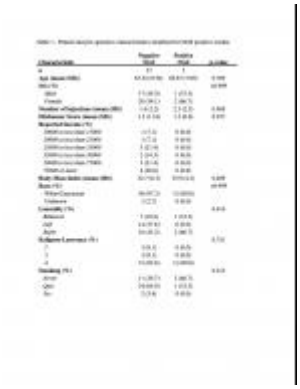

1102 Racial Disparities in Treatment and Outcomes of Patients with Hepatitis C Undergoing Total Joint Arthroplasty

Authors: Cole Howie, Kyle Cichos, Eric Jordan, Kian Niknam, Antonia Chen, Erik Hansen, Elie Ghanem

Background And Rationale: African Americans have the highest prevalence of chronic Hepatitis C virus (HCV) infection compared to any other ethnic group in the United States with greater complications and different treatment responses to HCV. These disparities are also observed after total joint arthroplasty (TJA) where black patients have greater surgical complications, readmissions, and longer lengths of stays.

Study Question: What health disparities exist between black and white patients with HCV prior to elective TJA, and the subsequent effects on postoperative outcomes?

Methods: A retrospective review of all patients with HCV undergoing TJA at three academic tertiary care centers was conducted. A total of 270 TJAs performed from 2005-2019 were included for analysis. Patient demographics, comorbidities, HCV characteristics, perioperative variables, in-hospital outcomes, and postoperative complications at 1-year follow-up were collected and compared between the two races.

Results: AST, ALT, and MELD levels were all higher in black patients ($p=0.001$; $p=0.04$; p

Discussion: HCV treatment prior to TJA with UVL has been shown to be a key factor in mitigating postoperative complications including PJI. This disparity in patients' management can have deleterious effects on postoperative outcome and complications. Improving access to HCV treatment and targeted education for African American patients may be effective strategies to address these disparities.

Conclusion: Despite overall improvements in PVL rates over time, disparities persist, with higher rates among black patients. These findings underscore the urgent need for targeted interventions to address these disparities and improve outcomes for all patients undergoing TJA.

1116 Static Versus Articulating Spacer: Outcomes Not Associated with Infectious Organism

Authors: Caitlin Grant, Jerry Chang, Emily Poehlein, Cindy Green, Jessica Seidelman, William A Jiranek

Background And Rationale: Treatment with an antibiotic spacer prior to prosthesis reimplantation is a common strategy for treating prosthetic joint infections (PJI). Yet, many patients have persistent infection after spacer treatment. While previous studies have compared efficacy of static and articulating spacer at treating PJI, few have examined their efficacy stratified by organism type.

Study Question: The purpose of this study is to determine whether the association between spacer type and patient outcomes differ by infectious pathogen species.

Methods: 246 patients who were treated for a PJI with spacer insertion at a single institution between January 1 2014 and January 1 2022 were included. Organism type was defined as staph versus non-staph and resistant versus non-resistant organisms. Other variables collected included sex, age, ASA, BMI, Elixhauser score. Treatment failure was defined as reoperation, reinfection, chronic antibiotic use at 1 year, or death. Cox proportional hazards models were used to assess the relationship between spacer type and treatment failure, including an interaction between spacer type and organism to identify differences in the association by organism type. Statistical significance was assessed at alpha = 0.05.

Results: Of 246 patients included in this study, 61 had static spacers and 185 had articulating spacers. Treatment failure occurred in 47.2% of patients. When averaged over covariates, failure-free survival probability (95% CI) at 1 year was 50.1% (39.3-63.8%) for static and 58.5% (51.8%-66.0%) for articulating spacers (p=0.02). However, there was no significant difference in overall hazard of failure over time for static versus articulating spacer. Additionally, there was no significant difference in the relationship between spacer type and hazard of failure by organism type (p-value for staph interaction: 0.10, p-value for resistant organisms interaction: 0.26).

Discussion: Our results of no relationship between spacer type and resistant organisms are consistent with previous literature demonstrating similar reinfection rates for resistant and non-resistant organisms.

Conclusion: This study demonstrates that at 1-year, articulating spacers may have improved survival when compared to static spacers, but there was no evidence of an overall difference in the hazard of failure over time. Additionally, there was no evidence of a difference in the association between spacer type and treatment failure by organism type.

1117 Clinical Success with Antibiotic Suppression Therapy in Patients with Prosthetic Joint Infection and Retained Hardware

Authors: Anne Spichler, Moffarah, Jane O'Bryan, Lidia Ani, Matthew Davis, Lee Rubin, Marjorie Golden

Background And Rationale: Antibiotic continuation for long-term suppression has been proposed as a mechanism to prevent treatment failure after periprosthetic joint infection (PJI) with retained hardware. Suppression carries potential risks of C. difficile colitis, medication-related adverse events, issues with tolerability, and emergence of resistance. Furthermore, few studies have assessed optimal duration of suppression. Our primary objective was to evaluate the role of suppression and suppression duration in the prevention of treatment failure during the 2-year period post-PJI.

Study Question: What are the 2 year rates of treatment failure for patients with prosthetic joint infection who receive oral antibiotic suppression?

Methods: We conducted a retrospective review of patients admitted to a tertiary medical center from September 2017-December 2020 with first time PJI of the hip or knee and retention of hardware. Demographic and clinical characteristics of the sample, medical and surgical management of PJI, and outcomes during the 2-year period post-PJI were assessed. Suppression was defined as antibiotic administration after completion of a 6-week primary course. Treatment failure was defined as recurrence of PJI, re-operation for PJI, or death secondary to PJI. Cure tiers at 2 years post-PJI were assigned based on the 2019 Musculoskeletal Infection Society guidelines

Results: N=60 patients met inclusion criteria (mean age 70.3 Â± 12.7 years, 56.7% female, 80.0% white/Caucasian). Most patients underwent DAIR (80.0%) or one-stage procedures (16.7%). Methicillin-susceptible S. aureus (MSSA) (33.3%) and coagulase-negative staphylococcus (18.3%) were the most common pathogens. Seventy-five percent of patients received antibiotic suppression, most often with doxycycline (44.4%) or cefadroxil (15.6%). Patients who were not suppressed accounted for nearly two-thirds of all treatment failures (Figure 1). Prevalence of failure during 2-year follow-up differed significantly by suppression status (p

Discussion: Failure rates for patients with PJI are not well defined. We found that patients not on suppressive antibiotics accounted for 64.3% failures.

Conclusion: Suppressive therapy may be beneficial to prevent treatment failure after PJI. Optimal duration remains unknown

Attachments:

Figure 1. Failure During 2-Year Period Post-PJI

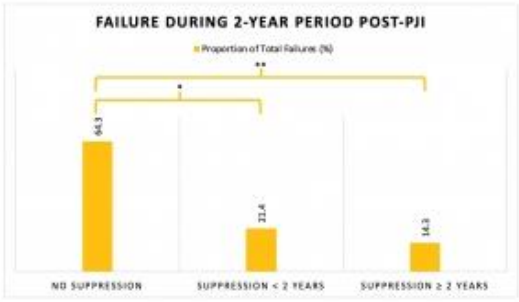

Figure 1 Caption: A total of n=14 patients (23.3%) experienced treatment failure during the 2-year period post-PJI due to recurrence (n=10), re-operation (n=2), or death (n=2). Deaths occurred in 1 patient who was not suppressed and 1 patient who was suppressed for <3 months. Patients who were not suppressed accounted for nearly two-thirds of failures (64.3%). Prevalence of failure during the 2-year period post-PJI differed significantly by degree of suppression (p<0.001; p-value for Fisher's Exact Test). Within-groups comparisons revealed statistically significant differences in prevalence of failure between Group 1 (No Suppression) vs Group 2 (Suppression < 2 Years) (p=0.029), and between Group 1 (No Suppression) vs Group 3 (Suppression ≥ 2 years) (p<0.001), but not between Groups 2 and 3 (p=0.330), indicating that the presence or absence of suppressive therapy was associated with prevalence of failure, but the duration of suppression (< 2 years vs ≥ 2 years) was not. * p<0.05; ** p<0.001

1128 Patients with periprosthetic joint infection have an elevated omega-6: omega-3 ratio in blood

Authors: Laura Y Lu, Joshua Davis, Antonia Chen

Background And Rationale: Omega-3 fatty acids (FA) have anti-inflammatory properties and have been shown to have antibacterial and anti-biofilm forming properties in cultures obtained from patients with PJI. Omega-6 FA promote a pro-inflammatory state. The omega-6: omega-3 ratio and the arachidonic acid (AA): eicosapentaenoic acid (EPA) ratio (AA:EPA) have been suggested to be better metrics for inflammation in several disease processes.

Study Question: Do patients with PJI have elevated omega-6: omega-3 and AA:EPA ratios in blood?

Methods: Laboratory values including erythrocyte sedimentation rate (ESR), C-Reactive Protein (CRP), and a full fatty acid profile (Omega Quant Omega-3 Index Complete Test) were obtained from 8 patients with PJI (per IDM 2013 guidelines) prior to secondary surgery. Additional clinical data was obtained from electronic medical record review.

Results: We enrolled 5 males (62.5%) and 3 females (37.5%) with a mean age of 67.4 Â± 8.3 years. Mean ASA was 2.9 Â± 0.6. One patient had a total hip arthroplasty (12.5%) and seven had total knee arthroplasty (87.5%). Mean number of days from the index surgery was 492 Â± 371 days. Joint aspiration and preoperative laboratory values are summarized in Table 1. The omega-3 index is the proportion of two long chain omega-3s, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), to all fatty acids in red blood cell membranes reflective of the last 4 months (desired range 8-12%). The omega-6: omega-3 ratio is the sum of 7 omega-6 FA divided by the sum of 4 omega-3 FA (desired range 3:1-5:1). The desired range for AA:EPA is 2.5:1- 11:1. All patients had omega-3 indices that were below the desired range (mean 4.2% Â± 1.0%). For the omega-6: omega-3 ratio, 7 patients had high ratios (87.5%), and 1 was within the desired range (12.5%). For the AA:EPA ratio, 1 patient was below the desired range (12.5%), 1 was within the range (12.5%), and 6 were above the desired range (75.0%).

Discussion: We found that 7 out of 8 (87.5%) of patients had elevated omega-6: omega-3 ratios, and 6 out of 8 patients (75.0%) had elevated AA:EPA ratios. All the patients in our cohort had omega-3 indices below the desired range. Future work will be done to determine if this is a significant association that can be used to assist with PJI diagnosis, management, and prevention.

Conclusion: In our pilot study, we found that many patients with PJI have elevated omega-6: omega-3 and AA:EPA ratios in blood.

1130 Inferior Outcomes for Patients Transferred Between Surgical Stages for Knee Periprosthetic Joint Infection

Authors: Jerry Chang, Jonathan Florance, Patrick Kelly, Denise Smith, Michael Bolognesi, Thorsten Seyler, Sean Ryan,

Background And Rationale: Periprosthetic joint infection (PJI) in total knee arthroplasty (TKA) may result in 2-stage revision surgery. There is limited data describing outcomes when the first stage is completed at an outside hospital and the patient is referred to a tertiary center. We hypothesize that patients have greater success when both surgeries occur at a single center.

Study Question: What are the outcomes for patients transferred to a tertiary center between surgical stages for knee PJI treatment?

Methods: 25 knee PJI patients who presented with an antibiotic spacer and had a minimum 2-year follow-up were retrospectively identified at a single tertiary referral center from 2014-2021. A cohort matched for age, gender, BMI, Elixhauser comorbidity measure, spacer type, infectious organism, and year of surgery was established with patients who had both stages completed at the investigating institution. Modified Delphi success criteria of no subsequent surgery or reinfection with any species was compared.

Results: The transferred group demonstrated a treatment success of 40% compared to 84% in the continuous group ($p < 0.01$). The transferred group was more likely to have an additional procedure between stages (44% vs 8%, $p < 0.01$), with a higher number of surgeries after primary TKA (4.8 vs 3.0, $p < 0.01$), between stages (1.4 vs 0.2, $p < 0.01$), and after second stage (0.8 vs 0.2, $p = 0.03$). The transferred group had longer durations between stages (20.1 vs 7.0 weeks, $p < 0.01$).

Discussion: PJI patients transferred between stages demonstrated higher treatment failure than those receiving continuous management at a tertiary center, consistent with prior literature. Additional studies with larger sample sizes are warranted.

Conclusion: PJI treatment success is low in patients transferred between surgical stages. Surgeons should consider early transfer with a goal of continuous management by a single tertiary institution.

Attachments:

1136 Next Generation Sequencing Test for Diagnosing Periprosthetic Joint Infection Is Not Affected by Premature Antibiotic Administration

Authors: Alisina Shahi

Background And Rationale: Administration of antibiotics prior to diagnostic testing for periprosthetic joint infection (PJI) can impede the accuracy of standard diagnostic tests, namely cultures results. Next generation sequencing (NGS) has shown promising results when cultures failed to detect the infecting organism.

Study Question: To assess the impact of administration of premature antibiotics prior to performing diagnostic workup for PJI on serum ESR and CRP, synovial WBC and PMN%, synovial culture and NGS results.

Methods: A retrospective analysis of 132 patients who underwent revision hip or knee arthroplasty due to MSIS confirmed PJI. All patients underwent synovial NGS testing for detecting the infecting organism in addition to serum ESR and CRP, synovial WBC and PMN% and synovial cultures. Among the patients, 46% received antibiotic therapy before the diagnostic workup, while the rest did not. The patients were categorized into two groups depending on whether or not they received antibiotics and the sensitivity of the mentioned diagnostic tests were compared.

Results: Patients in the antibiotic group had lower median in serum ESR (87 vs 62 mm/hr; p = 0.007), CRP (17.8 vs 11.2 mg/L; p=0.0042) synovial WBC (48,252 vs 8,788; p=0.002) and PMN% (95% vs 84.2%; p=0.004). Administration of antibiotics negatively impacted the sensitivity of all the diagnostic tests ESR (75.2% vs 91.5% [relative risk (RR) for false-negative results, 2.4; p = 0.04]), CRP (65.4% vs 82.5% [RR, 2.1; p = 0.03]), synovial WBC (70.2% vs 94.4% [RR, 5.2; p = 0.001]), PMN% (75.8% vs 93.5% [RR, 3.4; p = 0.01]). The rate of negative cultures were higher in the antibiotics group at 36.0% compared to the no-antibiotics group at 18.3% (p = 0.029). NGS was overall significantly more sensitive than cultures 96.2% vs. 73.5% [RR, 5.3; p = 0.001]. Administration of antibiotics did not impact the NGS results 95.1% in the antibiotic group vs 97.2%.

Discussion: Administration of antibiotics prematurely can have negative consequences on the accuracy of standard diagnostic tests for periprosthetic joint infection, leading to a significant increase in false-negative results. However, the NGS test was found to maintain its effectiveness even when antibiotics had been administered prior to diagnostic workups.

Conclusion: NGS test can still be used as a reliable diagnostic marker, even when premature antibiotics are administered.

1177 The Use of Irrigation in Total Knee and Hip Arthroplasty to Prevent Periprosthetic Joint Infection: A Systematic Review and Meta-Analysis

Authors: Sandhya Ganesan, Zachary Coles, Gwo-Chin Lee

Background And Rationale: Periprosthetic joint infection is a serious complication of total joint arthroplasty and is the cause of over 25% of revision TJA procedures. The use of antiseptic irrigation solutions intra-operatively is an increasingly common, low-cost practice to eradicate contaminants and bacteria from the surgical wound prior to closure; however, there is a lack of consensus on the use of antiseptic irrigation solutions in primary and aseptic revision TJA.

Study Question: The purpose of this study was to determine the efficacy of various antiseptic irrigation solutions (PI, CHG, vancomycin) in preventing PJI after primary/aseptic revision TJA as compared to normal saline through a systematic review and meta-analysis of current literature.

Methods: Queries were run in PubMed, Cochrane Library, Embase, and Web of Science using search terms related to knee or hip arthroplasty, irrigation, and infection. Abstract screening and full-text review were completed by two independent reviewers. 13 studies were identified through systematic review, and the occurrence of PJI in antiseptic and normal saline groups was extracted for meta-analysis. Odds ratios were calculated to assess differences in the rate of PJI between antiseptic and normal saline groups.

Results: Pooled data from 13 studies show a significant benefit of using an antiseptic irrigation solution as compared to normal saline in preventing PJI (OR=0.58, [0.37;0.90]). This finding is significant in primary TJA (OR=0.57, [0.41; 0.80]) but not in aseptic revision TJA (OR=0.50, [0.09; 2.79]). The current study did not identify a significant benefit of using a specific irrigation solution (CHG: OR=0.60, [0.40; 0.90]; PI: OR=0.62, [0.35; 1.10]; Vancomycin: OR=0.32, [0.10; 1.00]).

Discussion: Subanalyses showed a significant benefit of antiseptic irrigation in primary but not aseptic revision procedures, which may be explained by the complexity of revision procedures, patient comorbidities, and infections unrelated to intraoperative contamination. Despite a large sample size, the heterogeneity and lack of high-quality randomized controlled trials preclude definitive conclusions regarding the efficacy of any of these agents individually.

Conclusion: This study shows that the addition of an antiseptic to the surgical protocol in hip and knee arthroplasty procedures had a positive effect in preventing subsequent PJI compared to normal saline alone.

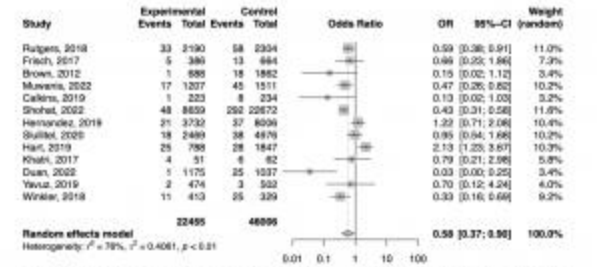

Figure 2. Forest plot including all 13 studies to determine the efficacy of irrigation in general to prevent PJI. A random effects model was used in this meta-analysis to compare the risk of infection following the use of antiseptic irrigation versus normal saline. Results are reported as odds ratios (ORs) with 95% confidence intervals (CI). Heterogeneity was calculated to be 78% (p<0.01) with a pooled OR of 0.58 and 95% CI of [0.37;0.90].

1179 The Synovial Fluid Alpha-Defensin, Cell Count, PMN%, and CRP are Non-redundant Biomarkers

Authors: Krista Tiler, Pearl Paranjape, Van Thai-Paquette, Greg Deirmengian, Alex McLaren, Carl Deirmengian

Background And Rationale: Periprosthetic joint infection (PJI) has various formal definitions involving multiple synovial fluid (SF) biomarkers. The 2018 International Consensus Meeting placed the alpha-defensin (SF-AD) test and the SF white blood cell (SF-WBC) count in the same category, assuming a strong correlation. However a strong correlation has never been demonstrated.

Study Question: This study examined the correlation between SF biomarkers for PJI and in the context of culture-positive rate.

Methods: 143,168 synovial fluid samples from hip and knee arthroplasties were submitted by 2,974 institutions to a single clinical laboratory for PJI diagnosis. Samples met integrity requirements and included SF-CRP, SF-AD, SF-WBC, and SF-PMN% results. Spearman correlations were calculated for each biomarker pair after scaling by percentile rank. Logistical regression and eigensystem analysis evaluated biomarker collinearity. The relative contribution of biomarker combinations to positive culture likelihood was assessed.

Results: No strong correlations were found between biomarker pairs, with all [r] < 0.7. Correlations between SF-AD, SF-WBC, and SF-PMN% ranged from 0.65-0.67, while all SF-CRP correlations ranged from 0.44-0.55. Multiple logistic regression showed all variance inflation factors < 2.5, and eigensystem analysis yielded a condition number = 8.5, both indicating low biomarker collinearity. SF culture-positive rates increased incrementally with each additional positive biomarker (0.4%, 1.9%, 8.3%, 37.1% and 70.2%; all p<0.001). Each biomarker was evaluated for its ability to enhance culture-positivity stratification based on all possible combinations of the other three biomarkers' results. SF-AD had the most significant impact on culture-positivity stratification (9.4-fold), followed by SF-PMN% (4.5-fold), SF-WBCs (2.4-fold), and SF-CRP (1.7-fold).

Discussion: This large study found no strong correlations or collinearity between SF-CRP, SF-AD, SF-WBCs, or SF-PMN%. The AD/WBC pair did not demonstrate excess redundancy when compared to other biomarker pairs and yielded quite different impacts on the prediction of culture-positivity.

Conclusion: The biomarkers SF-CRP, SF-AD, SF-WBC, and SF-PMN% failed to demonstrate a strong correlation. Notably, the SF-AD and SF-WBC did not stand out as having excess redundancy. Future formal systems defining PJI should consider assessments of collinearity before grouping biomarkers.

Figure 1 – Culture-positivity of cohorts representing all possible combinations of biomarkers (AD, WBC, PMN%, CRP). All N=143,168. Colors green through red represent a heat map as cohort culture positivity varies from 0% to 70%. Alpha-defensin (AD) is the primary driver of predicting culture-positivity of a sample.

1185 Development of Diagnostic Quality Metrics for Prosthetic Joint Infection

Authors: Andy Miller, Alberto Carli, Diana Chee, Sam Simon, Catherine Maclean, Amy Chin

Background And Rationale: Clinical practice guidelines (CPGLs) exist for the diagnosis of prosthetic joint infection (PJI), but little is known about the quality of PJI diagnosis in actual practice. Understanding the gaps between recommendations and reality would allow the development of processes which could improve PJI diagnosis and lessen its burden.

Study Question: We attempted to define (1) a discrete set of minimum necessary steps to diagnose with PJI; (2) discrete populations at highest risk for PJI; (3) specific steps that should be performed for patients who are high risk for PJI; and (4) valid clinical quality measures to improve the timeliness, accuracy and care for patients with PJI.

Methods: Using CPGLs, literature review, and the clinical judgement of the research team, we defined a minimum set of care processes that should be performed in patients with (or at risk for) PJI, and we proposed six quality measures. We convened a nine-member multidisciplinary panel of national PJI experts including orthopedic surgeons and infectious disease specialists to assess the validity of the proposed measures. We used a modified RAND-UCLA appropriateness method which has demonstrated content, construct, and predictive validity.

Results: 57 permutations of 6 proposed measures were rated. 7 of 11 care processes for PJI diagnosis were necessary to establish a diagnosis of PJI (preoperative ESR & CRP, arthrocentesis including cell count, differential, and culture, as well as â‰¥ 3 intraoperative tissue cultures). High-risk populations included revision arthroplasty, loosening or resorption, local pain, or at least 2 of the following: swelling, erythema or warmth. The panel rated 5 measures as valid: (1) preoperative and (2) intraoperative testing among PJI patients, (3) diagnostic workup for PJI among high-risk patients, (4) evaluation for PJI among revision arthroplasty candidates, and (5) infectious disease consultation.

Discussion: A critical subset of the recommendations detailed in CPGLs were considered necessary to establish a diagnosis of PJI, among populations with (or at high risk of) PJI.

Conclusion: This minimum necessary set of processes establishes the foundation for five novel clinical quality measures which could improve our understanding of care gaps, and improve quality, in the diagnosis of PJI.

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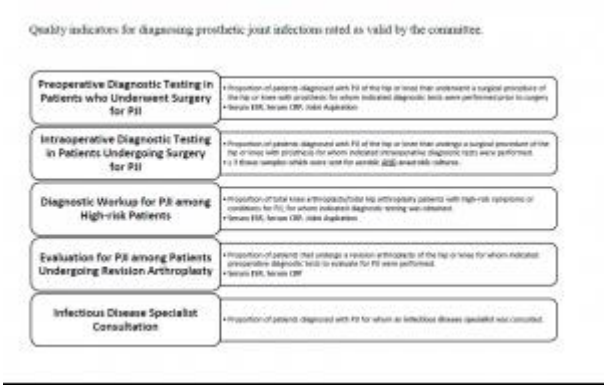

Monitor 4

23-AEP-1097 Metal-ion Allergies Associated with Higher Risk of Infection at the Time of Revision of Total Knee Arthroplasty (TKA)
Gerhard E Maale, Aniruth Srinivasaraghavan, Ibrahim Khalilullah, Suhas Nalla

23-AEP-1099 Multi-directional Instability and Arthrofibrosis Associated with Metal-ion Allergies Mimicking Periprosthetic Joint Infections
Gerhard Maale, Ibrahim Khalilullah, Suhas Nalla, Aniruth Srinivasaraghavan

23-AEP-1161 Are patients who are candidates for extended oral antibiotic prophylaxis at higher risk for PJI after aseptic revision TJA?
Mia Fowler, Allina Nocon, Yu-Fen Chiu, Kathleen Tam, Alberto Carli

23-AEP-1170 Time to Positive Growth of Synovial Fluid Cultures for Periprosthetic Joint Infection: A Benchmark Study
Carl Deirmengian, Alex McLaren, Julia Hatfield, John Miamidian

23-AEP-1174 The Cost of Delayed Referral for Prosthetic Joint Infection
Josef Jolissaint, Samuel Posey, Rory Metcalf, Taylor Rowe, Kayla Hietpas, Thomas Fehring

23-AEP-1175 Treatment at a Specialized Prosthetic Joint Infection Center improves Mortality Rates
Samuel Posey, Josef Jolissaint, Alexander Dombrowsky, Rory Metcalf, Taylor Rowe, Susan Odum, Thomas Fehring

23-AEP-1194 Automated Knee Implant Identification Using Deep Learning
Douglas Chonko, Vineet Batta

23-AEP-1200 Are Real Component Articulating Spacers a Safe and Effective Option Compared to All Cement Spacers for the Treatment of Prosthetic Joint infection in Total Knee Arthroplasty?
Brandt Buckner, Brandon Staple, Annemarie Leonard, Philip Holubeck, Jamal Salaymeh, Curtis Hartman, Beau Kildow, Angela Hewlett, Nicolas Cortes-Penfield

23-AEP-1202 Periprosthetic Joint Infection Risk after Primary Total Knee Arthroplasty: Are All Pre-operative Corticosteroid Injections the Same?
Brian Muffly, Ayomide Ayeni, Kevin Heo, Ajay Premkumar, George Guild

23-AEP-1211 Patient sex does not affect outcome following 2-stage revision for periprosthetic joint infection in total joint arthroplasty
Rory Metcalf, Taylor Rowe, Megan Tersteeg, Susan Odum, Jesse Otero

1097 Metal-ion Allergies Associated with Higher Risk of Infection at the Time of Revision of Total Knee Arthroplasty (TKA)

Authors: Gerhard E Maale, Aniruth Srinivasaraghavan, Ibrahim Khalilullah, Suhas Nalla

Background And Rationale: Multidirectional instability (MDI) associated with metal ion allergies presents with arthrofibrosis and mimics infection as a cause of failures following 1.5% of primary total knee arthroplasty (PTKA) patients. As part of the patient workup in the 276-patient MDI cohort, Lymphocyte Transformation Tests (LTT) were done, and 82.5% had metal ion allergies, with the most common being Nickel (72.5%). Vascular flow phase imagery with tri-phase bone scans demonstrate increased vascular flow to the surrounding capsular areas and thickened synovium on CT scans. This is a probable source for infection risk.

Study Question: In this cohort, is the infection rate higher at the time of replacement compared to historical values?

Methods: All patients with known metal ion allergies by LTT were reviewed for infection. The organisms recovered were noted. All patients were diagnosed by the Consensus definition of Periprosthetic Joint Infections (PJI).

Results: Out of the 200 patients experiencing nickel allergies, 21 (10.5%) experienced PJI following a PTKA, all of which required subsequent revisions. For the 21 PJI patients, 12 were female and 9 were male. The average age was 66 with a range 44 -79. Comparing this rate with historical rates of infection of PTKAs that ranged from 0.4 to 4.5%, Fisher's exact test demonstrated significant increases in infection rates with people with metal-ion allergies, with the p-value of 0.005.

Discussion: Infection is a major cause of concern in PTKA. Rates are usually 0.4 to 4.5% for acute problems associated with PJI. Infection rates among patients with MDI associated with metal allergies are significantly greater after PTKA compared to the general population. The underlying cause of this increased rate of infection is unknown but thought to be associated with the increase in vascularity of the joint capsule as demonstrated by the vascular flow phase imagery in MDI patients due to the metal allergy.

Conclusion: There is a higher infection rate in patients undergoing revision of PTKAs in patients with metal ion allergies.

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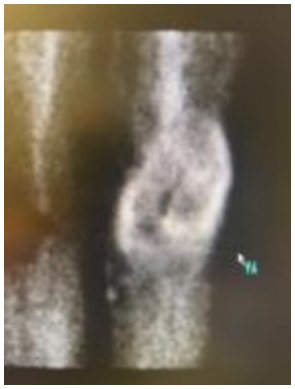


1099 Multi-directional Instability and Arthrofibrosis Associated with Metal-ion Allergies Mimicking Periprosthetic Joint Infections

Authors: Gerhard Maale, Ibrahim Khalilullah, Suhas Nalla, Aniruth Srinivasaraghavan

Background And Rationale: Patients can experience multiple problems following a primary Total Knee Arthroplasty (PTKA). These problems include infection, component loosening, multi-directional instability (MDI), and arthrofibrosis. MDI following a PTKA is a clinical syndrome characterized by global ligament laxity, pain while getting up from a seated position, audible clunking of the implant in varus-valgus stressing, instability in gait, and a warm knee effusion. These patients present with restricted range of motion (arthrofibrosis). This syndrome occurs in roughly 1.5% of primary total knees secondary only to infection as an acute acute cause of failures.

Study Question: Is MDI associated with arthrofibrosis commonly seen with metal-ion allergies in failed PTKA patients?

Methods: In this cohort, patients presenting with clinical MDI and restricted ROM following a PTKA were subject to a Metal-Lymphocyte Transformation Test (LTT). These studies were done prior to revision TKA. Specific metal-ion allergies were reviewed retrospectively. All patients had pre-op imagery including WBC, CT, and Tri-phase bone scans. Biopsies and cultures were performed at the time of revision.

Results: Of the 277 patients experiencing MDI with arthrofibrosis, 200 patients (72.2%) tested positive for nickel hypersensitivity and 228 (82.3%) were allergic to some metal and/or cement in the implant. Of the 200 patients with nickel allergy, 67 had multiple metal-ion allergies. When comparing metal-ion allergies seen in the normal population of total knees 1.5 to 14.5% reported the metal-ion allergy rate in patients with MDI and arthrofibrosis was 82.3%. This is clinically significant when using Fischer's exact study for this cohort with a $p<0.001$).

Discussion: MDI associated with arthrofibrosis accounts for 1.5% of failures in PTKAs. It is associated with metal-ion allergies in 82.3% of the cases. Nickel is the most common metal allergy (72.2% of the MDIs). It is gender-specific 2:1 female to male. MDI with arthrofibrosis is the second most common cause of failure in PTKAs, only second to infection.

Conclusion: Patients presenting with MDI and arthrofibrosis after PTKAs mimic infections. With LTT testing, 82.3% have metal-ion allergies which is significantly greater than the expected 1.5-14.5%. It occurs more frequently in females.

1161 Are patients who are candidates for extended oral antibiotic prophylaxis at higher risk for PJI after aseptic revision TJA?

Authors: Mia Fowler, Allina Nocon, Yu-Fen Chiu, Kathleen Tam, Alberto Carli

Background And Rationale: Prosthetic joint infection (PJI) is a devastating complication of total joint arthroplasty (TJA). Extended oral antibiotic prophylaxis (EOAP) has become increasingly popular following a highly publicized study (Inabathula et al) from a single center demonstrating protection (81% reduction) against PJI in 'high-risk' patients. However, these results have not been reproduced, and EOAP use conflicts with antibiotic stewardship efforts. In order to study EOAP in PJI prevention, consensus is needed to define 'high-risk' patients. The revision TJA (rTJA) population is appropriate to study, due to a higher PJI risk.

Study Question: We aimed to determine which comorbidities described by Inabathula et al. (referred to as Inabathula criteria (IBC)) confer a higher rate of PJI following aseptic rTJA.

Methods: 2,256 patients that underwent aseptic rTJA at a single high-volume institution from 2016 to 2022 were reviewed. Patient comorbidities were recorded to determine presence of IBC, a list of conditions including autoimmune diseases, active smoking, body mass index (BMI)>35, diabetes mellitus, and chronic kidney disease (CKD). Reoperation for PJI at 90-days and 1-year was recorded. Chi-squared or Fischer's exact tests were calculated to determine the association between presence/absence of IBC and PJI. Multivariable logistic regressions were conducted to determine if specific IBC conferred an increased PJI risk.

Results: 1223 patients (54.2%) had at least one IBC. IBC-positive patients were more likely to be female, have an increased ASA score, and higher BMI. IBC-positive patients had a significant increase in PJI at 90-days (relative risk (RR)=2.32, p<0.0001) and 1-year (RR=2.14, p=0.002) versus IBC-negative patients. Within IBC-positive patients, each additional IBC conferred a 1.8x odds increase for 90-day PJI (p<0.0001), and 1.76x odds increase in 1-year PJI (p<0.0001). Multivariable logistic regression identified active smoking, BMI>35, CKD, and diabetes mellitus as independently associated with PJI (p<0.05)(Table 1).

Discussion: Over half of rTJA patients meet IBC and could be eligible to receive EOAP. However, the specific presence of active smoking, BMI>35, CKD, and diabetes mellitus appear to be responsible for this increased PJI risk.

Conclusion: Prospective studies investigating EOAP use for patients with these specific conditions are urgently needed to prevent unnecessary antibiotic use.

Attachments:

1170 Time to Positive Growth of Synovial Fluid Cultures for Periprosthetic Joint Infection: A Benchmark Study

Authors: Carl Deirmengian, Alex McLaren, Julia Hatfield, John Miamidian

Background And Rationale: Anticipating time to positive (TTP) growth of microbiological culture and understanding differences between organisms and laboratories may be useful for setting expectations and determining how long to hold cultures. To date, no study has created or confirmed these benchmarks for periprosthetic joint infection (PJI) in synovial fluid (SF).

Study Question: The purpose of this study was to define the synovial fluid culture TTP benchmarks for microorganisms commonly associated with PJI.

Methods: From 2016 to 2022, 18,931 SF samples from 1,933 US institutions were tested for PJI at a centralized CLIA laboratory and rendered a positive culture result. Samples underwent comprehensive testing, and the TTP was recorded for positive cultures. Samples were classified by 2018 ICM criteria as Not Infected (2.5%), Inconclusive (2.1%), or Infected (95.4%). Synovial fluid culture was performed using aerobic and anaerobic automated culture bottle technique. Samples were held for 7 days (standard) or 14 days (shoulder). The relationship between median TTP and microorganism type was examined within the Infected group.

Results: The median TTP, in hours, for all 18,931 positive cultures was 19.8 (IQR 13.6 - 26.8). Over 94% of Infected samples had TTP < 48 hrs. Median TTP was 28.3, 30.7, and 19.5 hours for Not Infected, Inconclusive, and Infected samples, respectively. The fastest growing organism was S. aureus followed by Gram-Negative spp., Streptococcus spp., other Gram-Positive spp., S. epidermidis, Candida spp., and C. Acnes (Table 1).

Discussion: The current study establishes a benchmark for the incubation time required for synovial fluid culture to yield a positive result, with species-level analysis. Clear differences between the median time to positivity were identified when comparing various species. Surprisingly, more than half of all samples yielding a positive culture result did so within 20 hours of culture initiation. The median TTP in this study was 59% faster than that of a recent study reporting on SF culture timing, indicating the potential impact of methodologic differences between laboratories.

Conclusion: The current study establishes a benchmark for the incubation time required for SF culture to yield a positive result, with species-level analysis, demonstrating that over 94% of Infected samples had TTP < 48 hrs.

Attachments:

Table 1. 2016-2022 PJI ICM(+) samples – Median TTP

Microorganism	Median	IQR	n
All Samples	**19.5**	13.4 - 26.3	18,058
Staphylococcus aureus	12.6	10.3 - 16.1	3,946
Gram Negative	13.0	10.7 - 17.0	2,098
Streptococcus spp.	15.6	11.6 - 22.2	2,127
Other Gram Positive	22.3	18.0 - 29.7	4,449
S. Epidermidis	24.5	20.7 - 28.8	4,766
Candida spp.	31.9	27.0 - 38.2	612
C. Acnes	155.9	122.4 - 200.2	60

1174 The Cost of Delayed Referral for Prosthetic Joint Infection

Authors: Josef Jolissaint, Samuel Posey, Rory Metcalf, Taylor Rowe, Kayla Hietpas, Thomas Fehring

Background And Rationale: Periprosthetic joint infection (PJI) is a rare yet devastating complication occurring in 1-2% of all total joint arthroplasties. Revision rates of total hip (THA) and knee (TKA) arthroplasty for PJI are expected to increase approximately 176% for THA's and 170% TKA's by 2030. As the frequency of revision TJA for PJI increases many patients will be referred to tertiary PJI centers after multiple failed procedures for infection.

Study Question: What is the projected local and national cost of delayed referral for prosthetic joint infection?

Methods: A review of our PJI registry was performed to identify patients treated from 2017-2021 with a chronic PJI defined by MSIS criteria. All patients were treated with 2-stage exchange. Patients not referred from an external location were excluded. The number of previous surgeries for infection and 6-week courses of intravenous antibiotics were recorded. The estimated cost was calculated using established PJI literature and the Mariner dataset within PearlDiver.

Results: 182 patients referred during this timeframe met inclusion criteria. A majority of these patients were referred >3 months after diagnosis of PJI. 104 patients underwent an infection-related procedure prior to referral. The overall estimated cost of treatment in this cohort of patients prior to referral was $7,070,162 (Table 1), $2,196,691 for infected THA's (Table 2) and $4,873,471 for infected TKA's (Table 3). The average cost per patient who underwent a procedure for infection prior to referral was $69,540. A PearlDiver query identified 12,613 THA and 8,189 TKA resection procedures performed for PJI in the US in 2019.

Discussion: Assuming patients referred to our center were reflective of the national patient population, an estimated projected cost of $832,141,972 in one year alone was incurred by the US healthcare system when treatment was delayed, and ineffective treatment modalities attempted prior to referral and definitive resection.

Conclusion: Delayed referral following the diagnosis of prosthetic joint infection leads to a significant economic burden to the healthcare system.

Attachments:

Table 1: Overall Estimated Costs of Surgical Procedures Prior to Referral (THA & TKA)

Estimated Overall Cost of Previous Infection-Related Procedures Prior to Referral					
Group	N	Mean Hospital Cost	Mean Antibiotic Cost	Mean Total Cost	Sum of total costs
2 Stage	7	$54,991.00	$8,917.71	[illegible]	[illegible]
I&D & 2 Stage	6	$101,120.67	$14,123.67	$115,244.33	$691,466.00
I&D & Resection	4	$87,012.25	$18,159.00	$105,172.25	$420,689.00
I&D, 2 Stage, & Re-Resection	6	$142,004.17	$22,194.33	$164,198.50	$985,191.00
Isolated I&D	62	$38,987.87	$6,130.83	$45,118.20	$2,798,587.69
Multiple I&D	11	$88,390.09	$12,738.82	$101,128.91	$1,114,082.00
Resection	5	$49,525.20	$8,474.20	$57,997.40	$289,987.00
Resection & 2 Stage	1	$95,825.00	$16,141.33	$112,066.33	$108,199.00
					$7,070,162.69

1175 Treatment at a Specialized Prosthetic Joint Infection Center improves Mortality Rates

Authors: Samuel Posey, Josef Jolissaint, Alexander Dombrowsky, Rory Metcalf, Taylor Rowe, Susan Odum, Thomas Fehring

Background And Rationale: Mortality following treatment for prosthetic joint infection (PJI) remains a significant concern and rivals some cancers. The 90-day mortality rate in patients with PJI is as high as 9% and this increases to 12.6% at 1-year. Mortality rate in PJI increases to 41% and 43% at 5 and 10 years, respectively. Improvement in mortality 4.7-fold has been demonstrated when patients are treated at high volume centers. Whether treatment at a specialized PJI Center can improve these outcomes remains to be determined. The purpose of this study is to determine if the mortality rate at a specialized PJI center is improved compared to large data mortality rates.

Study Question: What is the mortality rate at a specialized prosthetic joint infection center?

Methods: A retrospective review of our institution's PJI registry was performed to identify patients treated at our PJI Center from 2017-2021 with a chronic PJI defined as symptoms >6 weeks and meeting the Musculoskeletal Infection Society (MSIS) criteria. All patients who were treated with a 2-stage exchange were included. Patients not referred from an external location were excluded. Mortality, or lack thereof as well as time to death was recorded. 182 patients met final eligibility criteria and were included in final analysis. 15 patients were excluded due to the definitive diagnosis of infection occurring after referral to the Center.

Results: Of the 182 patients included in analysis, 2 (1.1%) patients were deceased within 90 days following resection arthroplasty. One patient was deceased within 1 year (3/182; 1.65%). The remaining 179 patients had at least 1 year follow up and were not deceased.

Discussion: The 1.1% 90-day mortality rate of PJI patients treated at a PJI Center compares favorably with the large data 90-day mortality rate of 7%. The 1.65% 1-year mortality of PJI patients treated at a PJI Center is dramatically better than the 12.6% mortality rate reported in large data studies.

Conclusion: The mortality rate at a specialized center for prosthetic joint infection with more experience and access to medical consultants, may lead to a lower mortality rate following treatment for PJI.

1194 Automated Knee Implant Identification Using Deep Learning

Authors: Douglas Chonko, Vineet Batta

Background And Rationale: Implant Identification is an area of concern, a very important and significant step before planning a revision surgery for an infection. Failure to identify an implant can lead to delayed surgeries and can increase the spread of infection. This also leads to increased healthcare costs. The study aims to automate the implant identification process without any manual interventions quickly and effectively.

Study Question: The study aims to identify the make and model of 4 different total knee replacement implants from plain X ray images without any manual or human inputs. Deep learning techniques are used extensively in the domain of medical image analysis for various applications. Data augmentation, which is the first step to increase the number of images for training are explored in this study. Combined efficiency of data augmentation and deep learning to identify make and model of knee prosthesis are experimented through this study.

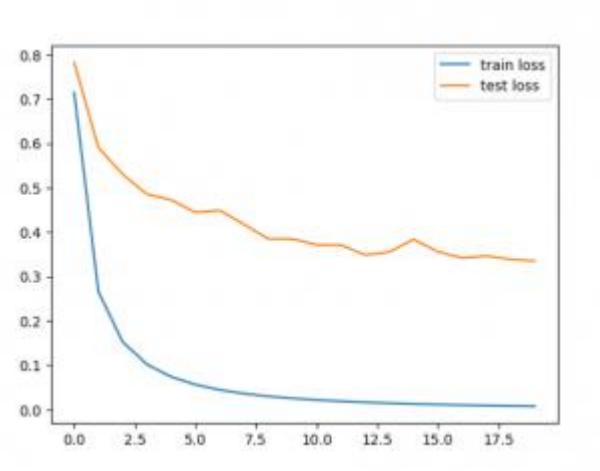
Methods: Augmentation techniques such as Contrast Adjustments, Zoom In, Zoom Out and Rotations at various angles are used in this study. These techniques resemble the real world X Ray images of the patients and thus will help make precise identification quickly. Deep learning based pretrained models such as VGG16 and VGG19 are used in this study. These are well established models in the domain of image classification and thus were helpful in rapid and accurate identification of implants from plain radiographic images.

Results: Overall system archives an accuracy of 84% in classification of 4 different knee implant types.

Discussion: Training was performed with 8,155 radiographic images after augmentation and the model was tested with 227 unseen and unaugmented images. The image shows the plot of loss and accuracy for train and test images. This indicates that the model is learning well and does not underperform or overperform. While Accuracy indicates the level of good training and subsequent predictions, loss indicates number of samples misclassified under each epoch/ iteration. Further training will increase accuracy with estimates of >98%.

Conclusion: The study shows the use of deep learning techniques in automated implant identification. Efficiency was obtained in the classification of implants. The methods accurately determine the make and model of a total knee prosthesis from its X Ray images , promising the technology has much higher scope and potential.

Attachments:



1200 Are Real Component Articulating Spacers a Safe and Effective Option Compared to All Cement Spacers for the Treatment of Prosthetic Joint infection in Total Knee Arthroplasty?

Authors: Brandt Buckner, Brandon Staple, Annemarie Leonard, Philip Holubeck, Jamal Salaymeh, Curtis Hartman, Beau Kildow, Angela Hewlett, Nicolas Cortes-Penfield

Background And Rationale: Articulating spacers, used in two-stage treatment of prosthetic joint infection (PJI) following total knee replacement (TKA), have historically been all cement. Recently, real femoral components and polyethylene tibial components have been implanted with antibiotic cement to serve as an articulating spacer. There is limited data comparing the effectiveness of all-cement (AC) and real-component (RC) spacers.

Study Question: Are real-component spacers a safe, effective alternative to all-cement spacers in two-stage treatment of TKA PJI?

Methods: This ongoing retrospective review examines all patients at our institution who underwent AC or RC spacer placement from March 2019 and April 2023. Data on demographics, baseline health status, surgical information at the time of first and second-stage procedures and final outcomes are being collected.

Results: To date, 29 patients have been identified: 20 with RC spacers, and 9 with AC spacers. There were similar demographics, baseline health status, and Charlson Comorbidity Index scores between groups. During first stage procedures, mean surgical time was higher in the RC group (203 vs 108 minutes; P=0.0003). Eight patients in the AC group and 11 in the RC group went on to reimplantation. For replant procedures, mean surgical time was higher in the RC group (191 vs 140 min, p=0.0056) and mean length of stay was shorter for the RC group (1.45 vs 2.15 days) although not statistically significant (p=0.12). Based on the MSIS successful infection management guidelines, 8 patients in the AC group had controlled infections with no chronic suppression (Tier 1), and one had a retained spacer (Tier 3). In the RC group 9 patients were Tier 1, and 4 required reoperation or retained spacer (Tier 3). Of the remaining 8 RC patients, 5 are awaiting second stage surgery and 3 have elected to forgo second stage as they are satisfied with their prosthesis.

Discussion: There was a statistically significant difference of longer mean surgical time during placement of RC spacers and RC replantation procedures. Patients with RC spacers were less likely to go on to replant, since they were content with their prosthesis.

Conclusion: Based on preliminary data, RC spacers appear to be a safe, effective alternative to AC spacers in patients with TKA PJI, and may allow patients the option of forgoing second-stage procedure.

1202 Periprosthetic Joint Infection Risk after Primary Total Knee Arthroplasty: Are All Pre-operative Corticosteroid Injections the Same?

Authors: Brian Muffly, Ayomide Ayeni, Kevin Heo, Ajay Premkumar, George Guild

Background And Rationale: Previous evidence has demonstrated an increased risk of periprosthetic joint infection (PJI) following primary total knee arthroplasty (TKA) in patients receiving corticosteroid injection (CSI) in the preoperative period.

Study Question: This study sought to compare the risk of PJI development following primary TKA between different corticosteroid agents.

Methods: 79,606 patients undergoing primary TKA between 2009 and 2019 were identified from the IBM Marketscan database. Of these, 3,445 (4.3%) had intra-articular CSI in the ipsilateral knee. Patients receiving CSI within 90 days of arthroplasty were compared to the control group using Fisher exact tests, with PJI development as the primary outcome.

Results: Compared to the control group, the 1,092 patients receiving an ipsilateral injection within 90 days of primary TKA had significantly higher PJI rate (95% CI [0.9%-2.5%] versus [0.19% - 0.26%], OR 4.2). This risk normalized when CSI was administered greater than 90 days prior to surgery (95% CI [0.26% - 0.89%] versus [0.33% - 0.42%]). Patients given methylprednisolone acetate (n=543) or betamethasone (n=153) were significantly more likely to develop PJI, with prevalence rates of 1.7% and 2.61%, respectively (95% CI [0.8% - 3.1%] and [0.7% - 6.7%], respectively). PJI risk following methylprednisolone or betamethasone injection normalized to control levels when given greater than 90 days before surgery. No significant increase in PJI was observed for patients receiving triamcinolone (n=342) or dexamethasone (n=54) at any time point, including within 90 days of primary TKA.

Discussion: These results suggest that PJI risk after CSI may differ depending on the type of corticosteroid administered. In this large database study, only patients given methylprednisolone acetate or betamethasone injections within 90 days of surgery had significantly higher PJI rates compared to those not receiving CSI.

Conclusion: This study offers significant insights into the association between, specific corticosteroids, and the risk of PJI in primary TKA. The findings emphasize the importance of carefully considering the timing of corticosteroid administration to mitigate the risk of PJI and improve patient outcomes. Further research will contribute to a deeper understanding of this complex relationship and aid in refining perioperative protocols for corticosteroid use in TKA.

1211 Patient sex does not affect outcome following 2-stage revision for periprosthetic joint infection in total joint arthroplasty

Authors: Rory Metcalf, Taylor Rowe, Megan Tersteeg, Susan Odum, Jesse Otero

Background And Rationale: Although the rate of total joint arthroplasty is greater in women than men, several studies have shown males to be at greater risk for PJI following primary TJA. However, the literature lacks studies examining the relationship between sex and outcomes following single and 2-stage exchange for PJI. The purpose of this study was to examine the effect of sex on disease-free survival at 1-year follow-up.

Study Question: What is the relationship between sex and disease-free survival at 1-year follow-up after single or 2-stage exchange for PJI?

Methods: A retrospective cohort registry study which reviewed patients who presented to our center following a diagnosis of PJI and were indicated for a 1 or 2-stage exchange for treatment between January 2010-January 2021. Eligible patients were at least 18 years of age, had confirmed PJI following TJA, had a known infecting organism or confirmed culture negative infection, and underwent first stage resection as part of a planned single or 2-stage exchange. Comorbidity and infection details were collected for each patient. Incidence of primary and aseptic revision arthroplasty cases were included between sexes. Success was defined as disease-free survivorship at 1 year following reimplantation.

Results: 476 patients met final eligibility criteria for inclusion. 250 male patients and 226 female patients were analyzed. 200 males (80.0%) and 180 females (79.6%) were found to be disease-free at 1 year follow up. There was no statistically significant difference between male and female patients' success at 1 year ($p = >0.99$).

Discussion: During the time frame of January 2010-January 2021 at our institution, more female patients underwent a primary TJA than males although more males went on to require a revision for PJI. The effect of patient sex on the outcomes following these revision procedures is not currently known. In our study, we found that sex was not significantly associated with re-revision at 1 year following revision for PJI.

Conclusion: Our study lends evidence which supports the assertion that males are treated with revision for PJI more commonly than females. However, sex did not affect the ultimate outcome of surgery, and we were unable to detect characteristics in males and females that differentiated the two populations.

Monitor 5

23-AEP-1064 Vancomycin Resistance Enterococcus and Implications to Trauma and Orthopedic Care.
Owain Davies, Parag Panwalkar, Karunakar Veravalli, Mehdi Tofighi,, Brendan Healy, Ali Mofidi

23-AEP-1126 Arthroscopy versus Arthrotomy in the Treatment of Hip and Knee Septic Arthritis
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23-AEP-1157 Angiotensin Converting Enzyme Inhibition as a Potential Risk Factor for Periprosthetic Joint Infection following Total Knee Arthroplasty
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23-AEP-1168 Delayed Referral for Prosthetic Joint Infection Leads to Inferior Outcomes
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Jesus M Villa, Katherine Rajschmir, Vivek Singh, Jorge Manrique, Carlos Higuera

23-AEP-1180 Synovial Fluid Culture Performance and Its Relationship to Inflammation
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23-AEP-1184 Comparison of 14 versus 5-day culture duration in total hip periprosthetic joint infection
Catalina Baez, Robert Macdonell, Abtahi Tishad, Edvinas Sipavicius, Jonathan Kass, Justin Deen, Chancellor Gray, Hari Parvataneni, Hernan Prieto, Luis Pulido

23-AEP-1205 Patellar Tendon Disruption Following Total Knee Arthroplasty, A Novel Orthoplastic Reconstruction Method
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23-AEP-1215 Racial disparities in periprosthetic joint infections: A retrospective study
Joshua Davis, Saundra Nelson, Matthew Jamison, Adrianna Liimakka, Jodi Pinkney, Antonia Chen

1064 Vancomycin Resistance Enterococcus and Implications to Trauma and Orthopedic Care.

Authors: Owain Davies, Parag Panwalkar, Karunakar Veravalli, Mehdi Tofighi,, Brendan Healy, Ali Mofidi

Background And Rationale: VRE is a devastating nosocomial infection commonly in intensive care units and long term residence facilities but not in orthopaedic patients. We studied a VRE outbreak in the orthopaedic unit in Morriston hospital.

Study Question: We studied this cohort to identify risk factors and outcome of VRE infection.

Methods: 24 cases of VRE infection and 34 cases of VRE colonization were identified in patients who were treated for orthopedic care in a 15-month period. Cases were reviewed to identify predisposing-factors specifically looking at patient characteristics, risk-factors, VRE risk and clearance (PREVENT) scores, and impact on outcome and institution. The presenting condition, treatment, presence of postoperative infection and VRE-scores, was compared between colonized and the infected cohort.

Results: Predominant VRE type was Van A, Enterococcus Faecium. Diabetes, old age, high ASA score, and perifemoral surgery was associated with VRE infestation. All VRE infected patients had an infected complication of their fracture fixation or arthroplasty requiring reoperation and prolonged antibiotic therapy. The infected group had an average VRE risk score of 8.5 versus 2 in the colonized group ($p<0.05$).

Discussion: VRE positivity is associated with old age, diabetes and long-stay in infested ward. VRE infection was associated with high VRE score specifically long-term antibiotic care over the last 12 months, chronic renal failure. VRE colonization is how the bacteria gets in. Literally all infection with VRE are superinfections in patients who are treated with an orthopedic infection with other bacteria. The colonized group will clear VRE but not the infected group.

Conclusion: We advise surveillance, prompt therapy and discharge of patients with perifemoral surgery, especially avoidance of infected metalwork, infective complications, antibiotic stewardship and radical surgery beyond infective precautions.

1126 Arthroscopy versus Arthrotomy in the Treatment of Hip and Knee Septic Arthritis

Authors: Vineet Desai, Jared Alswang, Gabriel Linden, Sophie Lipson, Scott Ryan, Matthew Salzler, Antonia Chen

Background And Rationale: Septic arthritis is a surgical emergency that often requires treatment with both irrigation and debridement (I&D) and antibiotics. There is currently no consensus on whether treating hip and knee native septic arthritis with arthrotomy or arthroscopy is more effective. Therefore, the purpose of this study was to evaluate whether undergoing arthrotomy or arthroscopy affected the outcomes of patients with hip and knee native septic arthritis.

Study Question: Does undergoing arthrotomy versus arthroscopy affect clinical outcomes in hip and knee septic arthritis patients?

Methods: A retrospective analysis was conducted at two separate hospital systems on 135 patients with hip or knee septic arthritis admitted from 3/2016-11/2018 (system 1) and 6/2014-9/2018 (system 2). Patients with periprosthetic joint infections, tuberculous or fungal infections, or no outcomes data recorded were excluded. If patients had multiple septic joints, each joint was analyzed individually. We analyzed a total of 147 joints (hip=51, knee=96). Statistical analysis was performed using Pearson's Chi-squared test for independence, Fisher's Exact Test, and independent samples t-test with an alpha of 0.05.

Results: 72 joints underwent arthroscopy and 75 joints underwent arthrotomy. Patients in the two cohorts did not differ significantly in gender (p=0.15), age (p=0.82), immunocompromised status (p=0.20), smoking status (p=0.45), serum C-reactive protein (CRP, p=0.39) and serum white blood cell (WBC, p=0.21) when presenting to the emergency department. No significant difference was observed between the groups in regard to undergoing a second I&D, overall readmission at 30 days, readmission at 30 days for septic arthritis, overall readmission at 90 days, readmission at 90 days for septic arthritis, death at 30 days, death at 90 days, or amputation at 90 days (Table 1). There was no significant difference in serum CRP (p=0.87) or serum WBC (p=0.62) after the first I&D.

Discussion: Clinical outcomes after I&D for hip and knee septic arthritis were similar between arthrotomy and arthroscopy cohorts. Arthroscopy may be an effective and less invasive treatment option for hip and knee septic arthritis compared to arthrotomy.

Conclusion: Treating hip and knee septic arthritis with arthroscopy or arthrotomy was not associated with differences in patient clinical outcomes.

Attachments:

Table 1. Post-operative outcomes based on type of irrigation and debridement (I&D) in hip and knee native septic arthritis (SA)

	Arthroscopy N=72		Arthrotomy N=75		
	n	(%)	n	(%)	p-value
Underwent a second I&D	20	(28%)	16	(21%)	0.34
30 day readmission overall	11	(15%)	15	(20%)	0.45
30 day readmission due to SA	7	(10%)	12	(16%)	0.26
90 day readmission overall	20	(28%)	29	(39%)	0.16
90 day readmission related to SA	13	(18%)	21	(28%)	0.15
30 day death	0	(0%)	2	(3%)	0.50
90 day death	0	(0%)	5	(7%)	0.06
90 day amputation	0	(0%)	1	(1%)	1.00

P-values < 0.05 considered significant

1157 Angiotensin Converting Enzyme Inhibition as a Potential Risk Factor for Periprosthetic Joint Infection following Total Knee Arthroplasty

Authors: Nicolas Cevallos, Rishi Trikha, Alan Zhang, Alexandra Stavrakis, Nicholas M Bernthal

Background And Rationale: There is growing evidence suggesting angiotensin-converting enzyme (ACE) has an immunomodulatory role. Prior in-vitro studies and in-vivo surgical animal models show ACE inhibitors may have an immunosuppressive effect. ACE inhibition (ACEi) may be a risk factor for surgical site infection.

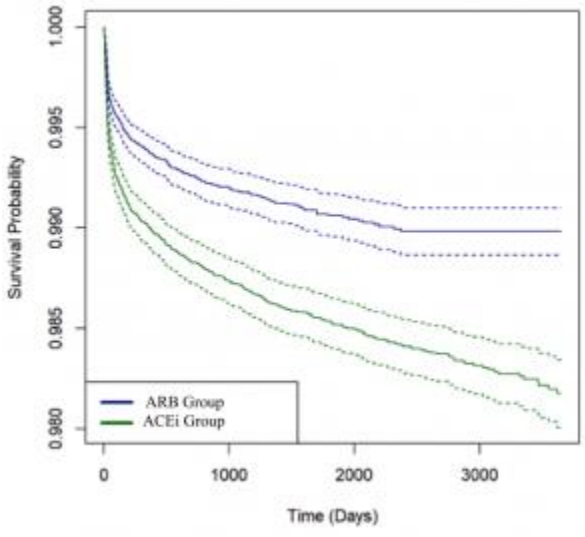
Study Question: Do patients taking ACEi for at least 1 year prior to surgery have higher rates of periprosthetic joint infection compared to ARB?

Methods: A retrospective review of the PearlDiver database was performed. Patients were divided into two groups; those taking an ACEi or an ARB for at least 1 year prior to primary TKA. Current Procedural Terminology codes were used to identify which patients underwent an irrigation and debridement procedure as a surrogate for infection following surgery at 6 months, 1 year, 2 years, 5 years, and 10 years. Propensity matching was used to match and control for age, gender, insurance plan, Charlson Comorbidity Index (CCI), and medical comorbidities. Kaplan Meier survival (KMS) curves and log-rank test calculated survival differences. Odds ratios (ORs) and 95% confidence interval (CI) were analyzed with $p < .05$ as significant.

Results: 77831 patients were identified in the ACEi group, 39105 in ARB. After propensity score matching, 39105 patients were included in each group. ACEi had statistically significant higher rates of infection in the KMS compared to ARB, $p < .0001$. At 6 months ACEi had a 95% CI of [2.10, 3.57], 1 year [2.06, 3.36], 2 years [2.06, 3.26], and 5 years [2.12, 3.19] all p values <.0001.

Discussion: Periprosthetic joint infection is a devastating complication. After controlling for demographic factors and comorbidities, the ACEi group had significantly higher rates of irrigation and debridement procedures. Given the increasing age, rates of diabetes, and hypertension, ACEi and ARB use have subsequently increased. The impact to optimize surgical candidates is critical to patients and the healthcare system.

Conclusion: The sequelae of periprosthetic joint infection are devastating, thus any strategy to optimize the host immune system is paramount. Given the possible interchangeability of ACEis and ARB, this study suggests that switching from an ACEi to an ARB preoperatively may potentially decrease postoperative infectious burden.



1159 Systemic symptoms of prosthetic joint infection are not associated with worse DAIR outcomes.

Authors: Mia Fowler, Elshaday Belay, Yu-Fen Chiu, Daniel Devine, Alberto V Carli

Background And Rationale: Prosthetic Joint Infection (PJI) is a devastating complication of total joint arthroplasty (TJA), often presenting with a prolonged course of joint dysfunction and pain. However, patients can present with acute systemic symptoms of infection that can be life threatening, resulting in systemic inflammatory response syndrome (SIRS) or even sepsis. This necessitates urgent surgical debridement, antibiotics, and implant retention (DAIR). Previous studies of small patient cohorts have determined that sepsis is associated with poor DAIR outcomes.

Study Question: The purpose of the current study was to evaluate the effect of blood cultures, SIRS, and sepsis on DAIR outcomes in the largest related patient cohort collected to date.

Methods: 275 patients underwent DAIR for PJI at a single institution from 2017 to 2021. SIRS was defined as at least two of: body temperature <36â„ƒ or >38â„ƒ, heart rate >90 beats/minute, respiratory rate >20 breaths/min, and serum leukocyte count >12000 or <4000/ÂµL. Sepsis was defined as SIRS plus a positive blood culture. DAIR success was defined at 1-year postoperatively according to the 2019 Musculoskeletal Infection Society (MSIS) working group tiers1. Multivariable logistic regressions were used to investigate the association between SIRS, blood culture, sepsis, and treatment success, adjusting for PJI chronicity, C-reactive protein, white blood cell (WBC) count, positive tissue culture, body mass index (BMI), sex, and Charlson Comorbidity Index (CCI).

Results: 47 (17.1%) PJI patients had SIRS on admission, 18 (6.5%) had a positive blood cultures, and 6 (2.2%) had sepsis. DAIR treatment success at 1-year (MSIS Tiers 1 and 2) was achieved in 174 (63.3%) patients. In regression analysis, patients with BMI>40 (OR 3.1 95% CI (1.1-9.0), p=0.049) were more likely to present with SIRS. SIRS, positive blood culture, and sepsis had no significant association with DAIR treatment success. CCI â‰¥ 3, diabetes, and synovial WBC>10,000 were significantly associated with DAIR treatment failure.

Discussion: This is the largest study to date to investigate the association between systemic PJI and DAIR outcomes. We found that over 1 in 6 patients undergoing DAIR presented with SIRS, and 1 in 50 with sepsis. The presence of SIRS, positive blood culture, and sepsis on admission were not associated with poorer infection control.

Conclusion: This suggests that DAIR is an appropriate treatment for urgent clinical situations.

1168 Delayed Referral for Prosthetic Joint Infection Leads to Inferior Outcomes

Authors: Thomas Fehring, Josef Jolissaint, Alexander Dombrowsky, Rory Metcalf, Samuel Posey, Susan Odum, Taylor Rowe

Background And Rationale: Prosthetic Joint Infection (PJI) is an uncommon event. Intuitively, the time to accurate diagnosis and treatment could affect results. Delays in appropriate treatment permit the offending organism to become more deeply entrenched in the bone, soft tissue, or on the implant for biofilm maturation. Although tertiary PJI centers with more experience and access to medical consultants exist, many patients are referred to such centers after prolonged inadequate treatment with open wound management, oral antibiotics, or multiple debridements without explantation. We asked if the time from diagnosis of a PJI to referral to a tertiary PJI center affects treatment outcomes.

Study Question: Does the time from diagnosis to referral to a tertiary prosthetic joint infection center affect treatment outcomes in Hip & Knee PJI?

Methods: A retrospective review of our institution's PJI registry was performed to identify patients treated at our PJI Center from 2017-2021 with a chronic PJI defined as symptoms >6 weeks and meeting the Musculoskeletal Infection Society (MSIS) criteria. All patients who were treated with a 2-stage exchange were included. Patients not referred from an external location were excluded. The time from the initial date of infection diagnosis until the date of referral was recorded. Outcomes were documented as failure of treatment at final clinical follow up. The number and type of prior surgical procedures as well as the amount of intravenous antibiotics was documented for each patient.

Results: 182 patients met inclusion criteria during this timeframe. 18/182 (9.9%) failed two-stage exchange due to further surgical intervention for infection or persistent infection. Of the 18 failures, the majority were referred greater than 3 months following their initial diagnosis of PJI (Table 1). Of the 104 patients referred within 3 months, 8 failed (7.7%). Of the 78 patients referred greater than 3 months after diagnosis, 10 failed (12.8%).

Discussion: Delayed referral following the diagnosis of prosthetic joint infection leads to inferior patient outcomes.

Conclusion: Such delays in definitive resection can cause a significant clinical burden for patients.
Attachments:

Table 1: Timing of PJI Referral

Timing of Referral (from initial PJI diagnosis)		
	Referral Timing (N)	Failure Rate (x/x, %)
Referred <= 90 days	104	8/104 (7.7%)
Referred > 90 days	78	10/78 (12.8%)
Overall	182	18/182 (9.9%)

1171 Patient Survivorship Is Strikingly Decreased Among Those Who Undergo Revision Total Hip or Knee Arthroplasty for Periprosthetic Joint Infection

Authors: Jesus M Villa, Katherine Rajschmir, Vivek Singh, Jorge Manrique, Carlos Higuera

Background And Rationale: Periprosthetic joint infection (PJI) is a potentially deadly and catastrophic complication.

Study Question: This study was designed to determine the contemporary impact on mortality of revision total hip (THA) or knee (TKA) arthroplasty performed for PJI diagnosis when compared to revision(s) performed exclusively for aseptic indications.

Methods: Retrospective electronic medical records review of a consecutive series of 978 patients who underwent revision THA/TKA from January 2015 to November 2020 in a single institution. All revisions performed in our institution at any point in time were evaluated for each patient and it was determined whether patients had a revision(s) for PJI or not. The cohort was split in two groups: (1) patients who had revision(s) for PJI diagnosis at any point in time (n=350) and (2) patients who only underwent revision(s) for aseptic indications (n=628). A complete chart review was performed for all patients to assess demographics, the number of revisions underwent by each patient, and mortality status at latest follow-up (mean 3 years, range 0-18 years, from the first revision performed in our institution).

Results: In the entire series, a total of 65 patients (6.6%) were deceased at latest follow-up. Demographics were not significantly different between both groups (PJI vs. aseptic) with exception of sex and American-Society-of-Anesthesiologist (ASA) status. There were more males (56.6%) in the PJI group when compared to the aseptic group (41.9%) ($p<0.0001$). Likewise, there were more patients with ASA-IV status in the PJI cohort (4.3% vs. 0.8%, respectively, $p<0.0001$). Remaining demographics were not significantly different (Table 1). The mean number of revisions underwent by patients with PJI diagnosis was 2.7 while it was 1.2 for patients who only underwent aseptic revision(s) ($p<0.0001$). The mortality rate for PJI patients was more than twice the one of patients who only had revision(s) for aseptic indications (10.9% vs. 4.3%, respectively, $p<0.0001$). However, among patients with PJI, the frequency of revisions within 90 days (only 1-revision [n=187] vs. 2 or more revisions [n=163]) was not associated with higher mortality rates: 13.5% vs. 8.6%, respectively, $p=0.168$.

Discussion: PJI diagnosis is significantly associated with higher mortality.

Conclusion: PJI revision patients have 2.5 times the mortality rate of patients who only undergo aseptic revision(s). More research on the mortality causes is warranted.

Attachments:

1180 Synovial Fluid Culture Performance and Its Relationship to Inflammation

Authors: Krista Toler, Pearl Paranjape, Van Thai-Paquette, Greg Deirmengian, Alex McLaren, Carl Deirmengian

Background And Rationale: Prior assessments of synovial fluid (SF) culture diagnostic performance for prosthetic joint infection (PJI) mainly involved smaller studies predating current culture methods, biomarkers, and infection definitions.

Study Question: This study evaluates SF culture's diagnostic performance in a contemporary laboratory and investigates the relationship between culture-positivity and host inflammation.

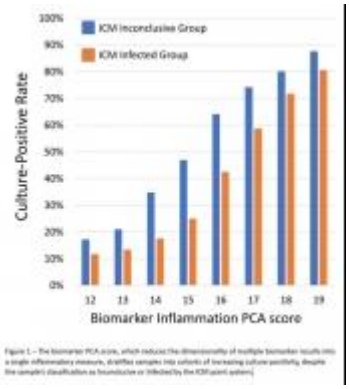
Methods: SF samples from 143,168 painful hip and knee arthroplasties, submitted by 2,974 institutions to a single lab between January 2016 and April 2023, were analyzed. Each sample included completely annotated diagnostic SF tests. SF cultures were performed with aerobic and anaerobic culture bottles. Diagnostic performance was assessed using the 2018 ICM's point system. Principal component analysis (PCA) condensed five host inflammation biomarkers into a single PCA score, categorizing samples by inflammation degree from -21 to 21.

Results: SF-culture sensitivity and specificity, compared to the 2018 ICM classification, were 67.7% and 99.6% with a 0.4% false-positive rate. Culture-positivity rates were examined in relation to the biomarker PCA score, revealing associations with host inflammation. False-positive culture rate was 0.3% in samples with the lowest scores (-21 to -4). Culture-positivity increased exponentially with higher inflammatory PCA scores, reaching 86.4% sensitivity for samples with a PCA score of 21. Cohorts with different ICM classifications but similar biomarker PCA scores displayed comparable culture-positivity. ICM Inconclusive and Infected samples showed rising culture-positivity with biomarker PCA scores from 12 to 19, starting at 17.2% and 11.7%, and reaching 87.7% and 80.6%, respectively (Figure 1). Organism species proportions remained relatively stable with increasing inflammatory PCA scores.

Discussion: Current SF culture techniques offer sensitivity in line with prior literature and a substantially lower false-positive rate (0.4%) than earlier reports. We found a robust link between SF culture positivity and host inflammation, surpassing relationships with modern scoring systems.

Conclusion: Modern SF culture demonstrates a false-positive rate below 1% and identifies an organism in about 70% of Infected samples. A new association between SF culture and host inflammation is described, further stratifying samples within 2018 ICM diagnostic categories.

Attachments:



1184 Comparison of 14 versus 5-day culture duration in total hip periprosthetic joint infection

Authors: Catalina Baez, Robert Macdonell, Abtahi Tishad, Edvinas Sipavicius, Jonathan Kass, Justin Deen, Chancellor Gray, Hari Parvataneni, Hernan Prieto, Luis Pulido

Background And Rationale: Periprosthetic joint infections (PJI) are one of the deadliest complications in total hip arthroplasty (THA). One of the major diagnostic criteria for PJI is the identification of an organism in two positive tissue cultures. However, common PJI pathogens have varied growth times, and it is still unclear if a longer culture time will aid in identifying these.

Study Question: Is there a difference in bacterial culture outcomes between 5-day and 14-day cultures? Is there a difference between infection types among different organisms?

Methods: A total of 102 consecutive THA PJI cases were included over a 7-year period. Demographic data, culture, and surgical data were obtained and compared between 5 and 14-day cultures.

Results: A total of 150 cultures were collected from 102 patients (57.8% females, 42.2% males) made up of 99 5-day cultures (66%) and 51 14-day cultures (34%) with an overall culture-negative rate of 33%. Culture positive rate was 64% for 5 days and 36% for 14 days, though not significant (p=0.236). 14-day cultures had a higher rate of polymicrobial growth (27.8% vs 9.4%, p=0.016) and fungi cultures (5.6% vs 0%, p=0.01), and a lower rate of gram-negative cultures (2.8% vs 12.5%, p=0.01) than 5-day. MRSA and MSSA were the two most common pathogens for monomicrobial infections, at 13.3% each. Time to positive culture was longer in 14 than in 5-day cultures (mean 5.50d vs. 3.34d, p=0.002). There was no difference between 5 and 14-day cultures in organism subgroup analysis for time to positive culture or infection type.

Discussion: There was no difference in rate of culture positivity between the 14 and 5-day cultures, but there was a higher rate of polymicrobial positivity and increased time to positivity for 14-day cultures. Although no difference between groups was found for known slow-culture pathogens, these all had higher rates in the 14-day group. Unsurprisingly, MRSA and MSSA were the most common monomicrobial infection pathogens.

Conclusion: Holding cultures for 14 days did not increase the rate of culture positivity compared to a 5-day hold but did appear to show a higher rate of polymicrobial growth and known slow-culture pathogens. Our study supports the use of longer culture holds for PJI to aim at a more thorough identification of organisms. Future efforts can be directed toward evaluating whether these differences represent contamination or microbes that would otherwise be missed in shorter culture times.

1205 Patellar Tendon Disruption Following Total Knee Arthroplasty, A Novel Orthoplastic Reconstruction Method

Authors: Douglas Chonko, Anne Sullivan, Rajiv Chandawarkar

Background And Rationale: Patellar tendon disruption after total knee arthroplasty (TKA) with/without infection leads to significant functional loss. In patients with a rupture alone, traditional repair techniques require placement of anchors, non-absorbable sutures,, autograft, tendon allograft, or synthetic biologic mesh reconstruction and have been described with mixed results. In patients with a PJI, these options becomes even less desirable since they introduce a foreign body into an infected field. Complication rates with these reconstructive methods are >18%, and include extension lag of 30Â° or greater, re-rupture and infection.

Study Question: Will a medial Achilles tendon and gastrocnemius muscle flap for patellar tendon reconstruction demonstrate improved function, lower infection rates and faster healing rates than traditional reconstruction techniques.

Methods: Pre-operative planning begins with identification of the missing elements and defining the length of tendon loss/disruption. The length is measured with the knee in full extension. Subsequently, the medial gastrocnemius muscle is harvested along with the required length of the medial half of the achilles tendon. Care is taken to not disrupt the achilles tendon and cause donor site morbidity. The vascularized tendon is used to either buttress the partially disrupted patellar tendon or, replace its entire length in patients where the patellar tendon is completely sacrificed. In patients with additional skin and soft tissue loss, the gastrocnemius muscle belly provides excellent soft tissue coverage of the knee.

Results: 8 patients underwent reconstruction of the patellar tendon. 7 of 8 patients went on to have an extensor lag of less than 10 degrees, mean flexion to 88 degrees. One patient had recurrence of PJI with healing of the tendon. All patients had excellent healing of the skin and incision. One patient experienced a repeat rupture.

Discussion: The small number of patients in our study limit statistical analysis however the technique demonstrated promise. Additional patients and longer term outcomes are needed.

Conclusion: This myotendinous flap presents an effective reconstructive option in patients with complicated tendon disruption and soft tissue loss.

1215 Racial disparities in periprosthetic joint infections: A retrospective study

Authors: Joshua Davis, Saundra Nelson, Matthew Jamison, Adrianna Liimakka, Jodi Pinkney, Antonia Chen

Background And Rationale: Total joint arthroplasty (TJA) is one of the most common surgical operations performed in the US. Periprosthetic joint infection (PJI) is a daunting complication of TJA and is associated with high morbidity. Previous studies have shown that racial disparities exist in postoperative complications of TJAs, including readmissions and mortality. However, it is unclear if such disparities also exist for PJI.

Study Question: Does PJI incidence vary between Black and non-Black patient populations

Methods: A single large hospital system database was used to identify all patients who underwent either primary total knee arthroplasty (TKA) or total hip arthroplasty (THA) between January 2018 and December 2021. Patients were stratified by self-identified racial categories. PJI was defined by ICD-9/10 coding. We present descriptive data as frequencies and percentages for categorical variables and means and standard deviations for continuous variables. We used chi-square tests to estimate crude risk ratios (cRR) and 95% confidence intervals (CIs) for PJI by race.

Results: A total of 11,818 patients were included in the final analysis. The majority (96.6%) of patients identified as non-Black (Table 1). The mean age was 69.4 (Â±10.3) years for non-Black patients and 65.5 (Â±11.5) years for Black patients. Females represented the majority of non-Black and Black patients who underwent TJA (54.1% and 66.9%, respectively). The majority of TJAs were TKAs for both non-Black and Black patients (54.6% and 56.1%, respectively). The incidence of PJIs was 1.6% among non-Black patients compared to 3.3% among Black patients (cRR (95% CI): 1.99 (1.17 - 3.39); p=0.0112). The majority of PJIs occurred post TKA (Table 1).

Discussion: Black patients have a significantly higher PJI incidence than non-Black patients. These findings were not adjusted for possible confounding factors such as age, sex, and comorbidities. Future studies are needed to determine if such disparities persist when other factors are considered.

Conclusion: Preliminary findings show that Black patient populations have a greater incidence of PJIs than Non-Black patient populations.

Attachments:

Table 1: Study population characteristics stratified by race.

Characteristic	Non-Black (n=11,422) n (%)	Black (n=396) n (%)
Age- years, mean (±SD)	69.4 (±10.3)	65.5 (±11.5)
Sex		
Male	5,245 (45.9)	131 (33.1)
Female	6,177 (54.1)	265 (66.9)
THA	5,183 (45.4)	174 (43.9)
PJI post THA	6 (0.05)	2 (0.5)
TKA	6,239 (54.6)	222 (56.1)
PJI post TKA	179 (1.6)	11 (2.8)
Total PJI	185 (1.6)	13 (3.3)

Abbreviations: THA - Total Hip Arthroplasty; PJI - Periprosthetic Joint Infection; TKA- Total Knee Arthroplasty

Monitor 6

23-AEP-1125 Arthroscopy versus Arthrotomy in the Treatment of Upper Extremity Septic Arthritis
Vineet Desai, Jared Alswang, Gabriel Linden, Sophie Lipson, Scott Ryan, Matthew Salzler, Antonia Chen

23-AEP-1127 Native Joint Septic Arthritis Management in Patients with Intravenous Drug Use
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23-AEP-1140 Early versus Late Periprosthetic Joint Infection after Total Knee Arthroplasty: Do Patient Differences Exist?
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23-AEP-1143 Cefazolin Alone versus Cefazolin with Tobramycin or Gentamicin as Intraoperative Antibiotic Prophylaxis for Total Joint Arthroplasty
Meera Dhodapkar, Scott Halperin, Zachary Radford, Lee Rubin, Jonathan Grauer, Mengnai Li

23-AEP-1144 Reliability of a classification for the quality of debridement for first stage revision of primary total knee arthroplasty prosthetic joint infection
Wayne Hoskins, Kelly Vince

23-AEP-1153 A Multicenter Study of 621 Patients Investigating the Antimicrobial Properties of 45S5 Bioglass Graft and Decreased Surgical Site Infection after Posterior Lumbar TLIF Reconstruction
Sohrab Vatsia, Derek Thomas, Kyle Cichos, Erik Westerlund

23-AEP-1167 Double Debridement and Rapid Sequence Reimplantation (DD-RSR) To Treat Periprosthetic Knee Infection: A Preliminary Report
Jesus Villa, Katherine Rajschmir, Vivek Singh, Carlos Higuera, Aldo Riesgo

23-AEP-1183 Psychosocial implications of prosthetic joint infection in hip and knee arthroplasty
Taylor Stauffer, Sharrieff Shah, Emily Poehlein, Cindy Green, William Jiranek, Thorsten Seyler, Jessica Seidelman

1125 Arthroscopy versus Arthrotomy in the Treatment of Upper Extremity Septic Arthritis

Authors: Vineet Desai, Jared Alswang, Gabriel Linden, Sophie Lipson, Scott Ryan, Matthew Salzler, Antonia Chen

Background And Rationale: Septic arthritis of the shoulder, elbow, and wrist, while not as common as lower extremity joint infections, is nonetheless a surgical emergency that may require treatment with irrigation and debridement (I&D) and antibiotics. There is currently no consensus on whether treating septic arthritis of the upper extremity with arthrotomy or arthroscopy is more effective. Therefore, the purpose of this study was to investigate whether undergoing arthrotomy or arthroscopy affected the outcomes of patients with upper extremity native septic arthritis.

Study Question: Does undergoing arthrotomy versus arthroscopy affect clinical outcomes in shoulder, elbow, and wrist native septic arthritis patients?

Methods: A retrospective analysis was conducted at two separate hospital systems on 37 patients with shoulder, elbow, or wrist septic arthritis admitted from 2015-2019. Patients with periprosthetic joint infections were excluded. If patients had multiple septic joints, each joint was analyzed individually. Patients were defined as being septic based on the SIRS criteria. We analyzed a total of 44 joints (shoulder=32, elbow=6,wrist=6). Statistical analysis was performed using a Fisher's Exact Test and independent samples t-test with an alpha of 0.05.

Results: 32 joints underwent arthroscopy and 12 joints underwent arthrotomy. Patients in the two cohorts did not differ significantly in gender (p=0.29), age (p=0.97), immunocompromised status (p=0.13), steroid use (p=0.12), serum CRP on admission (p=0.20), serum WBC on admission (p=0.14), and being septic on admission to the ED (p=0.12). No significant difference was observed between groups in regard to undergoing a second I&D, overall readmission at 30 days, readmission at 30 days for septic arthritis, overall readmission at 90 days, readmission at 90 days for septic arthritis, and death at 90 days (Table 1). No patient died at 30 days or had an amputation at 90 days. There was no significant difference in serum CRP (p=0.06) or serum WBC (p=0.14) after the first I&D.

Discussion: Clinical outcomes after I&D for shoulder, elbow, and wrist native septic arthritis were similar between arthrotomy and arthroscopy cohorts. Arthroscopy may be an effective and less invasive treatment option for upper extremity native septic arthritis compared to arthrotomy.

Conclusion: Treating upper extremity septic arthritis with arthroscopy or arthrotomy was not associated with differences in patient clinical outcomes.

Attachments:

Table 1. Post-operative outcomes based on type of irrigation and debridement (I&D) of shoulder, elbow, and wrist native septic arthritis (SA)

	Arthroscopy N=32		Arthrotomy N=12		
	n	(%)	n	(%)	p-value
Required a second I&D	5	(16%)	5	(42%)	0.11
30 day readmission overall	7	(22%)	2	(17%)	1.00
30 day readmission due to SA	5	(16%)	2	(17%)	1.00
90 day readmission overall	10	(31%)	3	(25%)	1.00
90 day readmission related to SA	5	(16%)	3	(25%)	0.66
90 day death	0	(0%)	1	(8%)	0.27

P-values < 0.05 considered significant

1127 Native Joint Septic Arthritis Management in Patients with Intravenous Drug Use

Authors: Gabriel Linden, Vineet Desai, Jared Alswang, Scott Ryan, Antonia Chen, Matthew Salzler

Background And Rationale: Native joint septic arthritis occurs more in patients with a history of intravenous drug use (IVDU) than the general population. Management of septic arthritis requires timely initiation of antibiotics and irrigation and debridement (I&D). Though IVDU patients have a higher prevalence of septic arthritis, there is a lack of information regarding their risk for worsened outcomes following septic arthritis treatment.

Study Question: This study compared IVDU to non-IVDU with regards to I&Ds, readmission, and mortality after initial I&D for septic arthritis.

Methods: Adult patients from two urban level one trauma centers with native joint septic arthritis from 2015-2019 were retrospectively identified via ICD codes. Patients were included if they had a clinical presentation consistent with septic arthritis, with isolation of a pathogen in synovial fluid or another source, or turbid synovial fluid without crystals. Independent-sample T-tests, Fisher's Exact Tests, and multivariate analysis were performed to determine whether IVDU was associated with changes in postoperative outcomes.

Results: 192 patients diagnosed with septic arthritis were identified (70 (36%) female; 122 (64%) male). 231 joints were included in the analysis (knee, n=115; hip, n=53; shoulder, n=37; elbow, n=7; wrist, n=7; other, n=12). 67 joints were from IVDU patients, and IVDU patients underwent 1.70 I&Ds on average compared to 1.32 I&Ds in those with no history of IVDU (p=0.005). IVDU was significantly associated with increased rates of 30-day readmission related to septic arthritis, 90-day readmission, 30-day mortality, and 90-day mortality (Table 1). These associations remained significant when controlling for smoking history, diabetes, HIV status, immunocompromised status, rheumatoid arthritis, and steroid use. There was no significant difference in mean synovial WBC, synovial PMN%, serum ESR, serum CRP, or time from aspiration to first I&D between groups.

Discussion: IVDU patients were associated with a greater number of I&Ds, higher readmission rates at 30 and 90 days, and elevated mortality rates at 30 and 90 days after initial septic arthritis I&D treatment. Clinicians who treat septic arthritis patients with concomitant IVDU should proceed with caution, by setting proper patient expectations and taking extra care to prevent worsened outcomes after initial I&D.

Conclusion: IVDU patients were associated with more I&Ds, readmission, and postoperative mortality.

Attachments:

Table 1. Postoperative outcomes by intravenous drug use (IVDU) status

	Non-IVDU Joints N=164		IVDU Joints N=67		
	n	(%)	n	(%)	p-value
30 day readmission related to SA (n=221)	17	(12%)	17	(35%)	**0.008***
30 day readmission unrelated to SA (n=95)	16	(30%)	4	(20%)	0.58
30 day death (n=204)	5	(0.03%)	12	(22%)	**<0.001***
90 day readmission related to SA (n=169)	2	(21%)	25	(61%)	**0.002***
90 day readmission unrelated to SA (n=95)	30	(75%)	10	(67%)	1.00
90 day amputation (n=219)	0	(0%)	1	(0.02%)	0.30
90 day death (n=221)	13	(0.09%)	17	(35%)	**0.001***

SA, septic arthritis
* statistically significant

1140 Early versus Late Periprosthetic Joint Infection after Total Knee Arthroplasty: Do Patient Differences Exist?

Authors: Brian T Muffly, Ayomide Ayeni, Kevin Heo, Janice Bonsu, Ajay Premkumar, George Guild

Background And Rationale: Periprosthetic joint infection (PJI) is a devastating complication following total knee arthroplasty (TKA). Significant psychosocial implications for the patient as well as financial burden on the healthcare system accompany this diagnosis. Little evidence exists comparing those diagnosed with early versus late PJI.

Study Question: Are there demographic and/or comorbidity profile differences between patients with early and late periprosthetic joint infection (PJI) following total knee arthroplasty (TKA)?

Methods: 72,659 patients undergoing primary TKA from 2009-2021 were identified from the IBM MarketScan database. Subjects diagnosed with PJI were categorized as either “early” (within 90 days of index procedure) or “late” (>2 years after index arthroplasty). Non-infected patients within these same enrollment periods served as control groups following 1:4 propensity score matching on other extraneous variables. Demographics and comorbidities between groups were compared, including with univariate and multivariable logistic regression analyses.

Results: The late infection group was found to be significantly younger than the early infection group (58.1 vs. 62.4 years, P = <0.001). When comparing late to early PJI, patients with chronic kidney disease (13.3% vs. 4.1%; OR 5.17, P = 0.002), malignancy (20.4% vs. 10.5%; OR 2.53, P = 0.009), uncomplicated diabetes (40.8% vs. 30.6%; OR 2.00, P = 0.01), and rheumatoid arthritis (9.2% vs. 3.3%; OR 5.17, P = 0.046) were all significant predictors of developing a late PJI.

Discussion: When compared to patients diagnosed with early PJI following primary TKA, the presence of chronic kidney disease, malignancy, uncomplicated diabetes, and rheumatoid arthritis were found to be independent risk factors for the development of late PJI. Those with late PJI were significantly younger. Younger patients with these comorbidities may be targets for preoperative optimization interventions that minimize this risk.

Conclusion: Overall, this study provides valuable insights into the demographic and comorbidity differences between patients with early and late periprosthetic joint infection (PJI) after primary total knee arthroplasty (TKA). By optimizing patient selection and management, healthcare providers can work towards reducing the psychosocial and financial burden associated with PJI, ultimately improving the overall success of TKA procedures.

1143 Cefazolin Alone versus Cefazolin with Tobramycin or Gentamicin as Intraoperative Antibiotic Prophylaxis for Total Joint Arthroplasty

Authors: Meera Dhodapkar, Scott Halperin, Zachary Radford, Lee Rubin, Jonathan Grauer, Mengnai Li

Background And Rationale: Prosthetic joint infection (PJI), is a serious complication of total knee arthroplasty (TKA) and total hip arthroplasty (THA). Determining optimal antibiotic prophylaxis regimen to minimize the incidence of PJI is of importance.

Study Question: Does the addition of gentamicin/tobramycin to cefazolin for antibiotic prophylaxis for THA and TKA reduce surgical site infection (SSI), PJI or 5-year revision rates?

Methods: Adult primary THA and TKA patients were identified from 2010-2021 Q1 PearlDiver M151 database. Inclusion criteria were: activity in the database â‰¥90 days postoperative, no infectious, neoplastic, or traumatic diagnoses within 90 days preoperative. Intraoperative antibiotic prophylaxis regimens were determined utilizing CPT codes for intravenous cefazolin, gentamicin, or tobramycin administration. For both THA and TKA, two sub-cohorts were created: 1) Patients who received cefazolin alone, 2) Patients who received cefazolin and tobramycin/gentamicin. Differences in age, sex and Elixhauser Comorbidity Index (ECI), 90-day postoperative adverse outcomes (specifically PJI (or SSI), sepsis, wound dehiscence, pneumonia, urinary tract infection, acute kidney injury, and emergency department visits) were assessed with multivariable logistic regression controlling for patient age, sex and ECI. Five-year implant survival was assessed utilizing Kaplan-Meier analysis and compared with log-rank tests.

Results: For THA, 32,882 patients were identified, of which prophylactic cefazolin alone was given to 30,527 (92.8%) and cefazolin+gentamicin/tobramycin was given to 2,355 (7.2%). For TKA, 119,611 patients were identified, of which prophylactic cefazolin alone was given to 110,469 (92.4%) and cefazolin+gentamicin/tobramycin was given to 9,142 (9.6%). Overall SSI rate was 1.1% for THA and 0.8% for TKA. For both THA and TKA, antibiotic subgroups were clinically similar with regard to age, sex, and ECI. On univariable and multivariable analysis, none of the examined 90-day outcomes varied significantly. Five-year implant survivals were not significantly different.

Discussion: For THA and TKA, addition of cefazolin+gentamicin/tobramycin did reduce odds of 90-day perioperative adverse outcomes (including SSI/PJI) or five-year revision rates.

Conclusion: For primary THA/TKA, the addition of gentamicin/tobramycin is not associated with reduced 90-day adverse events, or 5-year revisions.

1144 Reliability of a classification for the quality of debridement for first stage revision of primary total knee arthroplasty prosthetic joint infection

Authors: Wayne Hoskins, Kelly Vince

Background And Rationale: Total knee arthroplasty (TKA) prosthetic joint infection (PJI) is a potentially devastating complication, with high rates of recurrent infection, cost and resource usage. Many factors may be associated with the ability to clear infection, with the quality of debridement considered an important parameter, on the premise that it removes devascularized tissues and biofilm, which is carried by soft tissues, bone and implants. No standardized method exists for grading the quality of debridement in TKA PJI. We hypothesize that the quality (thoroughness) of debridement should correlate with outcome in the surgical treatment of PJI. This study proposes a classification for the thoroughness of radiological debridement at first stage revision of primary TKA PJI and assesses its reliability.

Study Question: We asked whether an internally developed classification system would show high intraobserver and interobserver reliabilities when assessing the quality of debridement at first stage revision of primary TKA PJI. We therefore determined the interobserver and intraobserve reliabilities of the classification scheme.

Methods: A classification system for the quality of radiological debridement of first stage revision of primary TKA PJI was developed. There are nine grades in the heirachy of debridement. Twenty examples of first stage revisions of primary TKA PJI, with pre and post radiographic assessments were identified. Two surgeons graded the quality of debridement at two different times. Fleiss' and Cohen's K statistics were performed for interobserver and intraobserver reliabilities, respectively.

Results: The overall Fleiss'K value for interobserver reliability and Cohen's K value for intraobserver reliability were both considered excellent (>0.80).

Discussion: The quality of debridement at the time of first stage revision of primary TKA PJI may be variable. This classification system may facilitate standardization of reporting and make outcome studies more comparable.

Conclusion: This study identified a reliable classification system for the quality of debridement at the time of first stage revision of primary TKA PJI. Future research will identify the variance in the quality of debridement performed in a multicentre study design, and identify the association of the quality of debridement in the ability to reduce re-revision rates for recurrent infection.

1153 A Multicenter Study of 621 Patients Investigating the Antimicrobial Properties of 45S5 Bioglass Graft and Decreased Surgical Site Infection after Posterior Lumbar TLIF Reconstruction

Authors: Sohrab Vatsia, Derek Thomas, Kyle Cichos, Erik Westerlund

Background And Rationale: 45S5 bioglass synthetic bone graft has known intrinsic antimicrobial material properties in the in vitro setting but has not been studied clinically for surgical site infection (SSI) risk. Strategies to minimize SSI rates in posterior lumbar spine surgery and posterior lumbar interbody fusion (TLIF), in particular, are of particular importance and represent an ideal group to assess bioglass clinically given its increasing use in that area.

Study Question: Does the utilization of 3rd-generation 45S5 bioglass synthetic bone graft in posterior lumbar spine surgery afford the potential for attenuated SSI complication rates?

Methods: Retrospective data was collected and compiled in the course of a sequential multi-center surgical case series from two surgeons at two separate institutions using 45S5 synthetic bioglass bone graft along with standardized instrumentation and TLIF surgical implants for posterior lumbar fusion. The minimum follow-up period for SSI as a primary endpoint was six months. Standard peri-operative and patient metrics/comorbidities were obtained. Data were then statistically analyzed and referenced against a published, matched historical dataset while data for internal control group is finalized.

Results: 621 patients meeting all inclusion criteria from January 2016 to September 2022 were identified, all of whom underwent posterior lumbar TLIF reconstruction with 45S5 bioglass graft. All 621 patients had documented minimum clinical follow up at six months, demonstrating an SSI rate of 0.48% (3/621 patients). A historical cohort from a prior published study was used as a baseline for comparison of expected SSI rate after posterior lumbar TLIF of 3.4% (43/1269 patients), with the study group demonstrating significantly decreased SSI rate ($p = 0.0001$). There were no late-term or delayed SSI events (at six months or beyond) observed in any patient included within this study.

Discussion: Results of this multicenter retrospective analysis strongly support the established intrinsic antimicrobial properties of 45S5 bioglass graft and, more importantly, clinically translate to a significantly decreased SSI rate in the setting of posterior lumbar TLIF surgery.

Conclusion: 45S5 bioglass synthetic bone graft decreases SSI risk in posterior lumbar TLIF, supporting current clinical use and guiding potential future prospective studies.

1167 Double Debridement and Rapid Sequence Reimplantation (DD-RSR) To Treat Periprosthetic Knee Infection: A Preliminary Report

Authors: Jesus Villa, Katherine Rajschmir, Vivek Singh, Carlos Higuera, Aldo Riesgo

Background And Rationale: Two-stage exchange arthroplasty is widely used to treat periprosthetic joint infection (PJI), but prolonged inter-stage time may be overwhelming and several patients are never reimplanted. After failed two-stage, the proposition of going through the same experience is quite daunting for patients. Additionally, single-stage exchange remains controversial and may be contraindicated in patients at high-risk for PJI failure. Aware that majority of antibiotic elution from spacers occurs in the first week, we started offering patients an alternative called double-debridement and rapid-sequence-reimplantation (DD-RSR); comprising debridement and explantation with placement of a static spacer followed by subsequent debridement and reimplantation, all within 1-2 weeks and single hospitalization.

Study Question: This report describes our early experience with it. We sought to determine (1) DD-RSR survivorship rate and (2) radiographic status at latest follow-up.

Methods: Retrospective chart review of 11 consecutive DD-RSRs to treat PJI after total knee arthroplasty (TKA) performed by a single surgeon in a single institution (Sep/2020-Dec/2022). One patient died during hospitalization due to medical complications and was excluded, leaving 10 patients for follow-up. Patients presented at explantation as follows: 1 after primary TKA, 2 after revision-TKA, 3 after antibiotic spacers, and 4 after failed two-stage exchange. Mean number of days between stages was 9 (range, 6-12) and average hospital stay was 13 days (range, 7-20). Mean age: 73 years (range, 61-86). Average BMI and Charlson Comorbidity Index were 31 Kg/m2 (range, 24-37) and 4 (range, 2-6), respectively. Eighty percent were males and 80% were classified as ASA-3 (20% as ASA-2) (Table 1). Mean follow-up: 375 days (range, 84-911).

Results: At latest follow-up, we observed that 3/10 DD-RSRs (30%) were revised: 1 for aseptic loosening of the femoral component, 1 for periprosthetic fracture (delayed fall), and 1 for recurrent PJI. The revision for PJI had positive intraoperative cultures (staphylococcus epidermidis); aseptic loosening and periprosthetic fracture revisions were culture negative. Surviving implants (n=7) showed no signs of loosening at latest follow-up. There were no wound-related complications or reoperations.

Discussion: DD-RSR may be a reasonable option for patients who have already failed PJI treatment, particularly two-stage.

Conclusion: Further investigation is needed to assess the long-term results of this new treatment.

Attachments:

1183 Psychosocial implications of prosthetic joint infection in hip and knee arthroplasty

Authors: Taylor Stauffer, Sharrieff Shah, Emily Poehlein, Cindy Green, William Jiranek, Thorsten Seyler, Jessica Seidelman

Background And Rationale: Prosthetic joint infection (PJI) following joint arthroplasty is a devastating complication associated with an increased risk of new mental health diagnoses and a 4x higher prevalence of preoperative depression. There are a paucity of studies exploring the psychosocial impact of PJI utilizing Patient Reported Outcome Measures (PROMs).

Study Question: We aimed to compare psychosocial outcomes, as measured by PHQ-9 and PROMIS depression scores, among patients treated for hip or knee PJI, aseptic revisions, and primary arthroplasties. We also compared psychosocial clinical course as measured by new mood disorder diagnoses, medication changes, and referrals.

Methods: A retrospective review of 29 patients undergoing treatment for hip or knee PJI with PHQ-9 or PROMIS scores 3 months before and at least 3 months after was conducted. These patients were matched, 1:2, to primary arthroplasty patients by age, ASA, BMI, sex, and joint. Aseptic revisions (n= 40) were selected based on availability of PHQ-9 and PROMIS scores. Patients with less than 6 months follow up or no PROM scores within 3 months preoperatively were excluded. Generalized linear mixed effects models run for PHQ-9 and PROMIS scores. Depression was modeled with a binomial probability distribution with a PHQ-9 score >5 indicating “depressive symptoms.”

Results: At 3 months, PJI patients had 47% lower PHQ-9 scores compared to those with an aseptic revision indicating better psychosocial health. There were no differences in odds of depression between the three groups at any time point. PJI patients had PROMIS depression scores at 3 months that were 7.91 points higher than those who underwent primary arthroplasty, indicating worse depressive symptoms. Patients with a PJI had a higher percentage of 30-day readmissions and longer hospital stays.

Discussion: This is the first study to assess psychosocial outcomes in hip and knee PJI patients using PROMIS depression and PHQ-9 scoring. PROMIS depression scores were significantly higher than in the primary cohort at 3 months, however they did not meet the criteria for depressive symptoms. Interestingly, PJI patients had lower PHQ-9 scores compared to the aseptic cohort at 3 months, however at no point did these scores reflect depressive symptoms (>5).

Conclusion: While there was no difference in the prevalence of depression among groups, patients treated for a PJI have significantly higher PHQ-9 scores at 3 months postoperatively.

Monitor 7

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23-AEP-1208 Maximizing Adherence and Minimizing Time to Antibiotics: A Multi-Disciplinary Institutional Trauma Bay Protocol for Antibiotic Prophylaxis in Open Fracture
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1065 Impact of Covid-19 on the rate and presentation of septic arthritis in the population. Possible impact of reactive arthritis!

Authors: Ram Mohan, Karunakar Veravalli, Parag Panwalkar, Ali Mofidi, Mehdi Tofighi

Background And Rationale: Covid-19 resulted in torrent of arthralgias in the units around the world. It was postulated that Covid-19 and resultant impact in immunity results in septic or inflammatory arthritis.

Study Question: The aim of this study was to see if there was a real increase in septic arthritis and weather if there is a relationship to immunity or Covid-19 infection.

Methods: Patients diagnosed with septic arthritis over the 15th months of lockdown were studied and were compared with the same period prior to Covid-19 infection. The patient characteristics, the rate of septic arthritis, the presence of recent Covid-19 infection, delay in diagnosis and the difference in the microbiology between the two groups was studied. Haematological markers of infection were compared between culture positive and culture negative cohort.

Results: We found 36 septic arthritis cases during Covid-19 period as opposed to 46 during the pre-Covid-19 period. The patients had the same age and sex distribution and the arthritis affected the same joints as well as same rate of diabetes. However, they tended to be more immunosuppressed and had higher frailty ($p>0.05$). There was a higher rate of patients who were treated with washout over 24 hours from diagnosis (P0.05, Neutrophil count $p=0.024$). There was a significant increase in time to theatre in the Covid-19 period when compared to the non Covid-19 period ($P<001$).

Discussion: Time to surgery was delayed by Covid-19 infection. The culture negative group have significantly reduced markers of infection. There was no increase in the rate of septic arthritis however there was an increase in culture negative arthritis denoting a possible outbreak of reactive arthritis in the Covid-19 period. Association of altered immunity and comorbidities in this group is also thought provoking.

Conclusion: During covid-19 there was an increase in culture negative arthritis specifically in patients with patients with altered immunity and comorbidities.

1092 Pharyngoesophageal Perforations after Anterior Cervical Surgery; Literature Review and Illustrative Case Treatment Algorithm

Authors: Brox Felix, Darrel Brodke, Nicholas Spina, William Spiker, Brandon Lawrence

Background And Rationale: Pharyngoesophageal perforations (PEP) are extremely rare, yet very dangerous, complications that may follow anterior cervical spine surgery (ACSS). Despite the complexity of this condition, there is no current consensus on the best treatment method. As recurrent perforations and stubborn infections are two of the largest risks after a PEP operation, proper care should be taken to avoid them without compromising the structural integrity of the cervical spine.

Study Question: What is the best treatment for PEP, which maximizes structural integrity, while minimizing risks of recurrent perforations and infections?

Methods: We present a literature review of the current PEP treatment techniques and retrospectively discuss 10 cases of PEP at our facility. We analyze how various treatment methods had various levels of success in resolution of the PEP compared to the literature and propose a treatment algorithm.

Results: We found that total removal of the anterior hardware, including any cages, in addition to reinforcement of the wall with a muscle flap resulted in the highest rate of success. One patient had several attempted surgeries without hardware removal but developed recurrent perforations/infections until her hardware was removed completely. All other patients had no problems with spinal stability/alignment despite a posterior-only reconstruction after their operations, and each showed surprising levels of bony re-incorporation of the anterior defects after repair and flap coverage allowing for improved vascular inflow.

Discussion: These case illustrations highlight the importance of obtaining a hardware-free anterior cervical field for healing of the esophageal wall and reducing the risk of complex revision cases, especially in the setting of flap coverage. While the patient cohort was small, we believe many things can still be learned from the outcomes of these patients after this rare complication.

Conclusion: In the treatment of PEP after ACSS operations, we advocate for complete removal of all anterior hardware, reconstructing the structural integrity of the spine with posterior fixation, and allowing for vascular ingrowth of the perforation by the placement of muscle flaps. In our experience, this technique achieves the most optimal outcome of achieving spinal stability while allowing the esophagus to heal, drastically decreasing the risk of reoperation due to flap failure or infection.

1093 Does Preoperative Antibiotic Influence Postoperative Infection Outcomes in Closed Fractures Treated with Internal Fixation?

Authors: Mary Hennekes, Elizabeth Cho, Robert Burkhart, Nicholas Romeo

Background And Rationale: Postoperative infection occurs in approximately 1-4% of closed fractures. Cefazolin is recommended as first-line antibiotic prophylaxis for all orthopedic procedures. Many patients with recorded penicillin allergy receive alternative antibiotics due to an often unfounded fear of cross-reactivity between penicillin and cephalosporins. In lower extremity arthroplasty research, both clindamycin and vancomycin are inferior to cefazolin in the prevention of prosthetic joint infections. A study of a similar nature has not yet been undertaken for fractures managed with internal fixation.

Study Question: This study investigated the relationship between preoperative antibiotic prophylaxis choice prior to operative fixation of closed lower extremity fractures and the rate of return to the operating room (OR) for SSI.

Methods: A retrospective chart review was completed of adult patients who underwent surgery for closed lower extremity fractures at a single, urban, Level 1 trauma center between January 2017 to December 2019. Demographic information, surgery specific data, and subsequent return to the OR was recorded and analyzed as appropriate.

Results: A total of 1053 patients with 1251 individual fractures met inclusion criteria. 85.8% received cefazolin, 12.2% clindamycin, 0.8% vancomycin, and 0.2% other antibiotics. The rate of return to the OR for infection was 7.2%. When comparing postoperative infection rate when patients received cefazolin (75/1082, 6.9%) to clindamycin (13/144, 9.0%), there was no significant difference ($p = 0.251$). Table 1 describes the number of SSIs and the number of fractures requiring a return to the OR for infection categorized by type of antibiotic received preoperatively. Choice of antibiotic was not significantly associated with a return to the OR ($p = 0.012$). Only having undergone a staged procedure was associated with a return to the OR for infection (OR = 3.8, $p < 0.001$).

Discussion: In patients undergoing operative management of closed lower extremity fractures, the choice of antibiotic does not appear to alter infection rates. Consistent with prior studies, patients that require staged management of their injuries did have higher infection rates.

Conclusion: Where there is concern for antibiotic allergy, the utilization of antibiotic other than cefazolin will likely not increase rate of return to the OR for infection in closed lower extremity fractures.

Attachments:

Table 1. SSI and Return to OR by Antibiotic Administered

Variable	Cefazolin (n = 1082)	Clindamycin (n = 144)	Vancomycin (n = 9)	Other (n = 2)
SSI occurrence				
No infection	1009 (81.6)	131 (10.6)	7 (0.6)	1 (0.1)
Superficial	30 (2.4)	6 (0.5)	1 (0.1)	0 (0.0)
Deep	45 (3.6)	7 (0.6)	1 (0.1)	1 (0.1)
Return to OR for infection				
Yes	56 (4.5)	8 (0.6)	1 (0.1)	1 (0.1)
No	1026 (82.9)	136 (11.0)	8 (0.6)	1 (0.1)

1103 Local Antibiotic Delivery for Orthopedic Infection Treatment: A Retrospective Analysis

Authors: Mellissa Delcont, Jonathan Layne, Bennie Lindeque, Christopher Kleck

Background And Rationale: Local antibiotic delivery via antibiotic-loaded bone cement is used in orthopedic infection management. Increased antibiotic resistant bacterial strains and novel antibiotic delivery vehicles have stimulated further development of treatment strategies. However, little has been reported regarding these strategies in spine surgery. This retrospective review identifies the range of antibiotics used and reported complications specific to spine cases. This review also provides initial antibiotic bead formulation and dosing recommendations.

Study Question: Can local antibiotics with calcium sulfate beads be safely used in spine surgery?

Methods: A literature review determined the antibiotic spectrum and cement combinations being used in spine infection treatment. Retrospective analysis specific to patients with calcium sulfate antibiotic beads was performed, and treatment protocols described.

Results: No complications were identified with the use of a variety of antibiotics. This included the use of beads in patients with a dural tear or exposed dura. To date, many of our center's calcium sulfate formulations have not been reported in the literature, and their use assists in infection. Currently we are performing further calcium sulfate antibiotic bead outcomes analysis on these formulations.

Discussion: Previous studies show antibiotics which elute at high local concentrations and are bactericidal at lower concentrations have a higher successful infection eradication probability. This study provides a list of beads that have been utilized, and their protocols, including our institution's results. The use of biodegradable calcium sulfate beads provides local antibiotic elution and may further improve spine infection treatment efficacy.

Conclusion: This study highlights the potential of biodegradable calcium sulfate beads to improve spine infection treatment efficacy by providing local antibiotic elution.

Attachments:

Table 2. Formulations which are not recommended.

Cement	PMMA
Ampicillin	Does not elute
Amoxicillin/clavulanate	Does not elute
Cefepime	Does not elute
Oritavancin	Does not elute after 24 hrs
Rifabutin	Does not elute
Rifaximin	Does not elute
Rifapentine	Does not elute
Tigecycline	Does not elute after 24 hrs
Zosyn (piperacillin/tazobactam)	Case report of use resulted in drug fever verified in pt with IV re-challenge positive

1124 Oral Antibiotic Maintenance Therapy May Not Improve Outcomes after Tibia Fracture-Related Infection

Authors: John Twomey-Kozak, Christian Pean, Jessica Seidelman, Malcolm DeBaun, The MMUSKIT Study Group

Background And Rationale: Tibia fracture-related infections (FRIs) are significant complications, typically treated with surgical debridement and antibiotic induction therapy. Currently, practices vary regarding the use of oral antibiotic maintenance therapy following induction therapy or discontinuing antibiotics after the induction period with considerations for the patient's clinical progress informing treatment. The supplementary advantage of antibiotic maintenance therapy is yet to be determined.

Study Question: Does maintenance antibiotic therapy (defined as a continued oral antibiotic regimen after a defined induction therapy period) vs. induction therapy alone without maintenance antibiotics improve clinical outcomes after tibia FRI?

Methods: 174 patients with tibial FRIs from four Level 1 trauma centers were included. Minimum follow-up was 6 months or until radiographic/clinical union. All patients received systemic induction antibiotic therapy. This was followed by maintenance oral antibiotic therapy (maintenance group) (n=82) or discontinuation of antibiotics after induction (induction group) (n=92). The primary outcome was treatment failure, defined as persistent nonunion at the end of the study period. Secondary outcomes were time to debridement from definitive fixation, rate of unexpected debridement, amputations, and endpoint mortality. Post-hoc analysis to detect a clinically significant 25% reduction in published tibia nonunion rates determined our power to be 0.68. Fisher'™s exact test compared outcomes between groups. Î± and Î² level were 0.05 and 0.2 respectively.

Results: Baseline characteristics were similar between groups. No significant differences were observed in persistent nonunion rates (20.73% vs. 29.35%, p=0.192) or secondary outcomes (unexpected debridement surgeries, p=0.744; time to debridement from definitive fixation, p=0.669; amputation rate, p=0.658; mortality rate, p=0.772) between the induction therapy alone and maintenance treatment groups. Average time from original infection surgery to last ID/Ortho follow-up was 571 days.

Discussion: This study found no significant difference in rates of persistent nonunion or secondary outcomes in patients with tibia FRIs between treatment groups.

Conclusion: These findings suggest that maintenance antibiotics after induction therapy may not be beneficial. Further prospective study would provide more guidance on the role of antibiotic maintenance therapy for tibial FRI.

Attachments:

1158 Native joint septic arthritis associated with human bites: a case series

Authors: Jack McHugh, Ryan Khodadadi, Pansachee Damronglerd, Said El Zein, Lainey Bukowiec, Brandon Yuan, Omar Abu Saleh, Gina Suh, Aaron Tande

Background And Rationale: Native joint septic arthritis (NJSA) associated with human bites is a poorly described clinical entity; the literature in this area is largely confined to case reports and expert opinion. The study aims to identify and describe the characteristics, management and outcomes of all cases of septic arthritis associated with human bites over a 10-year period at a tri-site academic institution.

Study Question: To characterize the demographics, microbiology and clinical characteristics of NJSA associated with human bites.

Methods: This was a retrospective study of all adult patients diagnosed with NJSA following a human bite who underwent surgical intervention at three Mayo Clinic facilities from January 2012 to December 2021. The diagnosis was confirmed based on clinical presentation and aspiration or operative cultures.

Results: Seven cases of NJSA were identified (Table 1). All cases occurred in men and were secondary to clenched fist injuries. The mean age was 35, and the mean Charlson co-morbidity index (CCI) was 0.1. Six cases involved a metacarpophalangeal (MCP) joint; one case involved a proximal interphalangeal (PIP) joint . Five cases (71.4%) were associated with overlying soft tissue infection. C-reactive protein (CRP) was elevated in four cases; erythrocyte sedimentation rate (ESR) was elevated in two cases; white blood cell count (WBC) was elevated in four cases. Four cases (57.1%) were associated with polymicrobial oral flora, and two cases were monomicrobial, with methicillin-sensitive and methicillin resistant Staphylococcus aureus (MSSA, MRSA) observed. Open arthrotomy with irrigation and debridement was completed in all cases, and a mean of 3 procedures (range: 1-6) was required to obtain source control. The mean duration of antimicrobial treatment was 36 days (range: 27-58). Oral antimicrobials were used for treatment after surgery in two cases (28.5%), with clinical cure observed in each case.

Discussion: Human bite wounds may result in infection with oral or superficial skin flora. Infections with oral flora are more likely to be polymicrobial. Multiple irrigation and debridement procedures may be required to obtain source control. Oral antimicrobial therapy was shown to be effective in two of our cases.

Conclusion: NJSA associated with human bite wounds requires a multi-disciplinary approach with collaboration between orthopedic and infectious diseases providers.

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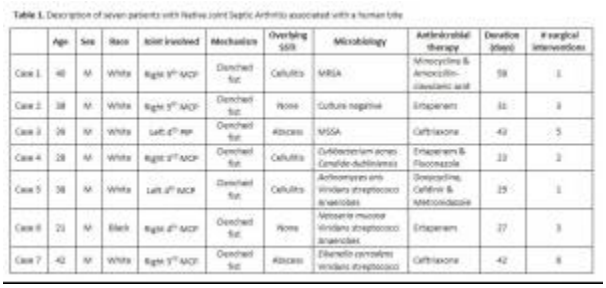


	Age	Sex	Race	Joint involved	Mechanism	Overlying SSTI	Microbiology	Antimicrobial therapy	Duration (days)	# surgical interventions
Case 1	40	M	White	Right 5th MCP	Clenched fist	Cellulitis	MRSA	Minocycline & Amoxicillin-clavulanic acid	58	1
Case 2	38	M	White	Right 5th MCP	Clenched fist	None	Culture negative	Ertapenem	31	3
Case 3	26	M	White	Left d5 PIP	Clenched fist	Abscess	MSSA	Ceftriaxone	42	5
Case 4	28	M	White	Right 2nd MCP	Clenched fist	Cellulitis	Cutibacterium acnes, Corynebacterium tuberculostearicum	Ertapenem & Fluconazole	33	2
Case 5	36	M	White	Left d5 MCP	Clenched fist	Cellulitis	Actinomyces oris, Viridans streptococci & veillonella	Doxycycline, Cefdinir & Metronidazole	29	1
Case 6	21	M	Black	Right d5 MCP	Clenched fist	None	Neisseria mucosa, Viridans streptococci & anaerobes	Ertapenem	27	3
Case 7	42	M	White	Right 5th MCP	Clenched fist	Abscess	Eikenella corrodens, Viridans streptococci	Ceftriaxone	42	4

1160 A 10-Year Experience of Elbow Native Joint Arthritis: A Single Center Retrospective Study

Authors: Pansachee Damronglerd

Background And Rationale: Elbow native joint septic arthritis (NJSA) is rare condition, accounting for 3-9% of the cases of pyogenic arthritis and is associated with higher mortality as well as a higher rate of loss of joint function. The objective of this study was to examine the characteristics, management, and outcomes of elbow NJSA at our institution.

Study Question: To characterize the demographics, microbiology, clinical characteristics, management and outcomes of elbow NJSA

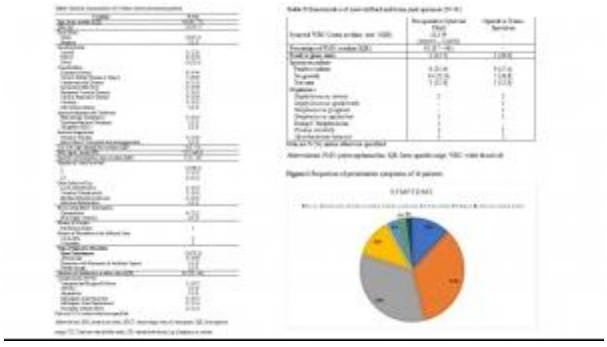
Methods: We conducted a retrospective study of all adults who were diagnosed with elbow NJSA who underwent surgical intervention at Mayo Clinic facilities from January 2012 to December 2021. The diagnosis was confirmed based on clinical presentation, synovial fluid analysis, and aspiration or operative cultures.

Results: A total of 557 patients developed NJSA during the study period, of whom 19 (3.4%) were diagnosed with elbow NJSA with the accompanying baseline characteristics (Table 1). 3 patients (15.8%) had synchronous infections, and 6 (40%) had concomitant bacteremia as shown in Figure 1. 16 (84.2%) of cases had joint aspirations. The median of white blood cell count was 43,139 /mm3 interquartile range (IQR) 16,055 - 72,670 /mm3. Crystals were identified in 3 aspirates (15.8%). The positive rate of Gram stain of synovial fluid and operative tissue cultures was 12.5 and 20% respectively. Almost all patients underwent elbow surgery except one patient who had multiple joint involvement and underwent debridement of other infected joints. Open arthrotomy (72.2%) was the most commonly performed surgical procedure. Synovectomy was performed in 4 (22.2%) patients. The most common pathogen isolated was Staphylococcus aureus in 5 (27.8%) of cases. The median duration of antimicrobial therapy was 30 days (IQR 22 - 44 days). Non-tuberculosis mycobacterium (NTM) was isolated in 2 cases with extend courses of antimicrobial (274 and 374 days) being prescribed. The most common complications were compromised range of motion and subsequent joint resection (Table 1).

Discussion: The prevalence of our study was similar in previous studies. 75% of patients underwent open arthrotomy & treated by ABX about a month.

Conclusion: Elbow NJSA is a very rare condition with high rate of subsequent complications. Bacteremia was common. The low sensitivity of gram stain & higher positivity rate for crystals pose significant diagnostic challenge & highlights the importance of blood and synovial cultures.

Attachments:



1164 Establishment of a Multidisciplinary Care Team (MDT) for treatment of debilitated patients with decubitus ulcers and osteomyelitis

Authors: Rajiv Chandawarkar, Anne Sullivan

Background And Rationale: The WHO has identified Multidisciplinary Care Team (MDT) as the key to organize and coordinate healthcare services. This model has been shown to be successful in complex clinical problems such as cancer or mental health where an integrated care model with practitioners from different clinical services has become a game-changer.

Study Question: To care for debilitated patients suffering from chronic non-healing decubitus ulcers and osteomyelitis we established an MDT. Its goal was simply to deliver higher quality, coordinated patient-centered care via improved collaborative interaction.

Methods: First we established the organizational structure that comprised wound care, orthopedics, plastic surgery, dermatology, general/colorectal surgery, infectious disease, urology, and vascular surgery. Inpatient case managers, social workers and physicians/nurses at the extended care facility were included as were residents and students from various disciplines to provide a broader training opportunity. Next we clearly defined the functional roles and modes of communication between the team members. Last we 'communicated up' and secured support from the health system.

Results: Prompt evaluation and management, co-localized specialty clinics, information sharing, near-real-time communication resulted in prompt decision making, strategic planning of the treatment steps. Coordination of multiple services provided better management of this complex problem with a direct input from the patient and their caregivers. This MDT allowed providers plan patient care more strategically both in the short- and long-term. The care was patient-centered, more efficient, and more cost-effective, and both patient and provider well being and satisfaction improved. Directly this led to fewer outpatient visits, reduced transport burden, especially for mobility-challenged debilitated patients. They had a quicker resolution in terms of a defined treatment plan, improved communication both within the provider group and between them and the patient/ care-givers.

Discussion: Management of osteomyelitis in these patients mandates the establishment of an MDT. All its members benefit (patients, providers and the healthcare system alike) not only by creating a value-added care model and also gaining personally and professionally from its added value.

Conclusion: MDTs improve care delivery for patients with pressure sores.

1206 Native joint septic arthritis associated with cat and dog bites

Authors: Jack McHugh, Ryan B Khodadadi, Pansachee Damronglerd, Said El Zein, Lainey Bukowiec, Brandon Yuan, Gina Suh, Omar Abu Saleh, Aaron Tande

Background And Rationale: Native joint septic arthritis (NJSA) associated with bites from cats or dogs is a poorly described entity; the literature in this area is confined to case reports and expert opinion. This study aims to investigate the characteristics, management, and outcomes of NJSA associated with cat or dog bites.

Study Question: To characterize the demographics, microbiology and clinical characteristics of NJSA associated with cat and dog bites.

Methods: This was a retrospective study of all adult patients diagnosed with NJSA following a cat or a dog bite who underwent surgical intervention at three Mayo Clinic facilities from January 2012 to December 2021. Diagnosis was confirmed based on clinical presentation or operative cultures.

Results: 27 cases of NJSA were identified, 20 involving cat bites and seven involving dog bites. Detailed information related to demographics, co-morbidities, infection characteristics, microbiology and treatment are included in Table 1. Female sex was more commonly associated with cat bites (65.0%), whereas male sex was observed more frequently in dog bites (85.7%). 23 cases (85.0%) involved small joints of the hand. Joint pain and swelling were the most common presenting symptoms. Cellulitis was present in 13 (48%) cases and more common in cases of dog bites (OR 3.75, 95% CI [0.58-24.3]). C-reactive protein (CRP) was elevated in 91% of cases, whereas erythrocyte sedimentation rate (ESR) was elevated in 24% of cases. Of the cases associated with cat bites, 12 cultures grew Pasteurella sp. (60%), and seven (35%) were polymicrobial. Four cases (57.1%) associated with dog bites were culture negative. Ertapenem was the most frequent antimicrobial choice for definitive therapy, and the median treatment duration was 4 weeks in both cohorts. The mean number of surgical procedures associated with a cat bite was 1.75 (SD = 1.06), and 1.14 (SD = 0.37) for a dog bite.

Discussion: Notable findings from this study include the more frequent observation of cellulitis associated with dog bites, and the more frequent presence of polymicrobial infection and need for multiple procedures in cat bites. This may reflect the mechanism of injury, as puncture injuries are associated with cat bites and tearing injuries are associated with dog bites.

Conclusion: Cat bites are frequently associated with Pasteurella sp. and polymicrobial infection and may be more likely than dog bites to require multiple procedures to obtain source control of NJSA.

Attachments:

1208 Maximizing Adherence and Minimizing Time to Antibiotics: A Multi-Disciplinary Institutional Trauma Bay Protocol for Antibiotic Prophylaxis in Open Fracture

Authors: Ian Hong, Erick Heiman, Frank Liporace, Richard Yoon, Jaclyn Jankowski

Background And Rationale: Current standard antibiotic(Abx) prophylaxis for open fractures(Fx) consists of intravenous(IV) administration of a 1st-gen cephalosporin, with the addition of an aminoglycoside for grade2/3 openFx. However, administrating 2 different types of Abx may result in an unnecessary delay. Piperacillin-tazobactam4g(P-T), a single combination Abx, has been shown to be non-inferior to standard therapy. This protocol was designed to streamline time to Abx(T-Abx) prophylaxis during a trauma activation with concurrent openFx.

Study Question: Can the T-Abx for openFx and the compliance be optimized via a multi-disciplinary(Trauma, ED, Orthopaedics, Pharmacy) institutional protocol?

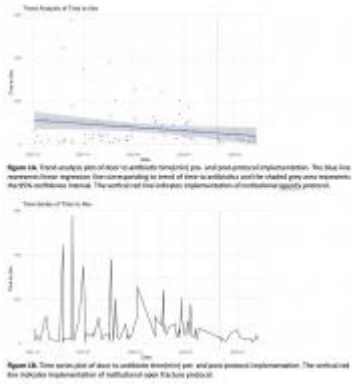
Methods: Institutional protocol was implemented November 1, 2022 at a single academic level II trauma center. Automated dispensing systems were stocked with premix IV bags of P-T, ceftriaxone1g, and cefazolin2g. The Trauma/ED team initiates the protocol for suspected openFx and P-T is administered once, with a goal T-Abx ≤30min. Pediatric patients receive a reduced 75mg/kg dose q6h(max 4.5g) for 48h. Postoperatively, for grade2/3 openFx, P-T IV is continued q8h for 48h. Grade1 openFx were de-escalated to cefazolin2gIV q8h for 48h. The “post” protocol T-Abx was compared to “pre” data from Jan2021–Oct2022.

Results: Seventeen patients(age:42.5±17.7) met protocol criteria compared to 72patients(age:34.3±14.8) pre-protocol. Institutional protocol resulted in significant reduction in T-Abx for openFx(23.7±13.8min VS 87.9±104.6min,$p<0.001$). A post-hoc power analysis revealed that the study was powered at>80% to detect a significant difference.

Discussion: Early administration of IV Abx, ideally within 66min of injury, is recommended to prevent soft tissue infections and complications. The reduction in the mean T-Abx was accompanied by a reduction in the variability of the data, evinced by the lower SD. This suggests that the protocol helped to standardize the Abx administration process and reduce unnecessary delays, leading to more consistent and timely delivery of prophylactic Abx.

Conclusion: A multi-disciplinary institutional protocol for the administration of Abx prophylaxis optimized the T-Abx in cases of suspected openFx. Implementation in other trauma centers may optimize T-Abx for openFx, however, further studies are needed to evaluate the long-term efficacy of this protocol on clinical outcomes.

Attachments:



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Biomech Holdings LLC: Stock or stock Options
DePuy, A Johnson & Johnson Company: IP royalties
Hip Society: Board or committee member
Moximed: Paid consultant
Parvizi Surgical Innovation: Stock or stock Options

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Clinical Spine Surgery: Editorial or governing board

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American Board of Venous and Lymphatic Medicine: Board or committee member
Foundation for Venous and Lymphatic Medicine: Board or committee member

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Medtronic: Paid presenter or speaker
Phlebology: The Journal of Venous Disease: Editorial or governing board

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Biomet: Other financial or material support
Clinical Orthopaedics and Related Research: Editorial or governing board
DePuy, A Johnson & Johnson Company: Other financial or material support
Journal of Arthroplasty: Editorial or governing board
Journal of the American Academy of Orthopaedic Surgeons: Editorial or governing board
MSIS: Board or committee member
SLACK Incorporated: Publishing royalties, financial or material support
Smith & Nephew: Other financial or material support
Stryker: Other financial or material support
Zimmer: Other financial or material support

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Allosource: Paid consultant
Biocomposites: Paid consultant
COR Medical: Paid consultant
Globus Medical: Research support
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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

L

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DJ Orthopaedics: Research support
Foot and Ankle International: Editorial or governing board
Foot and Ankle Orthopaedics: Editorial or governing board
Guided Therapy Systems: Research support

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cerament: Paid presenter or speaker
implantacast: Paid presenter or speaker
Implantcast: Research support
Link: Paid presenter or speaker; Research support
Micocalis: Stock or stock Options
Rapid Molecular Diagnostics: Stock or stock Options

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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

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International Consensus Meeting on Periprosthetic Joint Infection: Editorial or governing board
Parvizi Surgical Innovations: Stock or stock Options
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Zimmer: Research support

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All relevant financial disclosures have been mitigated

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BoneSupport AB: Paid presenter or speaker
Reconstructive Review: Editorial or governing board

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Advanced Healthcare Materials: Editorial or governing board
Agnovos: Stock or stock Options

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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

All relevant financial disclosures have been mitigated

Attivare: Stock or stock Options
Boston Scientific: Paid consultant
Cartesian Therapeutics: Paid consultant
IVIVA: Stock or stock Options
Johnson & Johnson: Paid consultant
Journal of Biomedical Materials Research: Editorial or governing board
Lightning Bio: Stock or stock Options
Lyell: Stock or stock Options
Medicenna: Paid consultant
Norvartis: IP royalties
Novartis: Research support; Unpaid consultant
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Samyang: Paid consultant

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Microgen DX: Other financial or material support
MicroGenDx: Research support
OREF: Research support
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Concentric Analgesics: Research support
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UpToDate: Publishing royalties, financial or material support
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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

All relevant financial disclosures have been mitigated

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Arthroplasty Today: Editorial or governing board
DePuy, A Johnson & Johnson Company: Research support
Journal of Arthroplasty: Editorial or governing board
Operative Techniques in Orthopaedics: Editorial or governing board
Osteal Therapeutics: Research support

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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

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3M: Research support
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Aesculap: Research support
Alphaeon: Stock or stock Options
AO Spine: Research support
Becton Dickenson: IP royalties; Paid consultant
Biomet: Research support
Cardinal Health: Paid consultant
Cempra: Research support
CeramTec: Research support
Ceribell: Stock or stock Options
Coracoid: Stock or stock Options
Corentec: IP royalties; Paid consultant
Datatrace: Publishing royalties, financial or material support
DePuy: Research support
Elsevier: Publishing royalties, financial or material support
Elute: Stock or stock Options
Ethicon: Paid consultant
Hip Innovation Technology: Stock or stock Options
Illuminus: Stock or stock Options
Integra: Research support
Intellijoint: Stock or stock Options
Jaypee Publishers: Publishing royalties, financial or material support
KCI / 3M (Acelity): Paid consultant
Lima: Research support
MicroGenDx: Paid consultant
Molecular Surface Technologies: Stock or stock Options
Myoscience: Research support
Nanooxygenic: Stock or stock Options
National Institutes of Health (NIAMS & NICHD): Research support
NDRI: Research support
Novartis: Research support
OREF: Research support
Orthospace: Research support
Osteal: Stock or stock Options
Parvizi Surgical Innovations and Subsidiaries: Stock or stock Options
Peptilogic: Stock or stock Options
Peptilogics: Paid consultant
Pfizer: Research support
PRN-Veterinary: Stock or stock Options
Rotation Medical: Research support
Simplify Medical: Research support
SLACK Incorporated: Publishing royalties, financial or material support
Smith & Nephew: Research support
Sonata: Stock or stock Options
Stelkast: Research support
Stryker: Research support

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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

All relevant financial disclosures have been mitigated

Synthes: Research support
Tenor: Paid consultant
TissueGene: Research support
Tornier: Research support
Wolters Kluwer Health - Lippincott Williams & Wilkins: Publishing royalties, financial or material support
Zimmer Biomet: Paid consultant; Research support

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Peptilogics: Research support
Smith & Nephew: IP royalties; Research support
TJO (Total Joint Orthopedics): IP royalties; Paid consultant; Paid presenter or speaker
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ISCT: Board or committee member
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Journal of Knee Surgery: Editorial or governing board
Orthopaedic Research Society: Board or committee member
Osteal Therapeutics: Research support
Peptilogics: Research support
RegenLab: Research support
Signature Orthopaedics: Research support
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HSS Journal: Editorial or governing board
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Reconstructive Review: Editorial or governing board
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Pattern Health: IP royalties
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Elsevier: Editorial or governing board
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Monogram Orthopaedics: Stock or stock Options

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Pfizer: Paid consultant; Paid presenter or speaker
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All relevant financial disclosures have been mitigated

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All relevant financial disclosures have been mitigated

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Bicomposites: Research support
Biomet: Research support
COTA: Research support
DePuy, A Johnson & Johnson Company: Paid consultant
Foundation for Physician Advancement: Board or committee member
Foundation of Orthopaedic Trauma: Board or committee member
LIfeNet Health: Paid consultant; Research suppot
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Organogenesis: Research support
ORintelligence: Stock or stock Options
OrthoGrid: Paid consultant
Orthopaedic Trauma Association: Board or committee member
ORTHOXEL: Paid consultant
Pacira: Research support
SI Bone: Research support
SI-Bone: Paid consultant
Springer: Publishing royalties, financial or material support
Stryker: IP royalties; Paid consultant
Synthes: Paid consultant; Research support
Use-Lab: Paid consultant
WNT Scientific: Stock or stock Options

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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

All relevant financial disclosures have been mitigated

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** content of the accredited activity is limited to basic science research, such as preclinical research and drug discovery, or the methodologies of research, and they do not make care recommendations.

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